A SYNOPSIS OF PHYSIOLOGY

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ILLUSTRATED WITH DIAGRAMS SOME OF WHICH ARE COLOURED

BRISTOL: JOHN WRIGHT & SONS LTD.
LONDON: SIMPKIN, MARSHALL, HAMILTON, KENT & CO. LTD.
TORONTO: THE MACMILLAN CO. OF CANADA LTD.

1927

PRINTED IN ENGLAND BY
JOHN WRIGHT AND SONS LTD., BRISTOL.

PREFACE

THIS volume adds another number to the popular series of synopses of SURGERY, of MEDICINE, and of MIDWIFERY AND GYNÆCOLOGY, issued by the same publishers.

The object of the book is to give a fairly full summary of modern physiology, particularly human physiology, in a small compass. It will be necessary for the beginner to consult also an ordinary text-book of physiology or attend a good course of lectures, and to use practical text-books on histology and on chemical and experimental physiology, if for no other reason than to consult their diagrams. But he should be able with the aid of this synopsis to extend his knowledge, or revise it, with a minimum expenditure of time and trouble. We have aimed to give enough information to enable the student to pass the more advanced examinations, including the First Fellowship; the less ambitious candidate may omit the sections printed in small type.

Practitioners who wish to keep abreast of modern physiology will find here a means of making a quick survey. We have taken particular pains to make this a text-book of human and clinical physiology. Unfortunately, in these days of specialism, it has often happened that facts of human physiology which have been part of the everyday knowledge of the clinician have taken years to get into the ordinary text-books of physiology, and some facts worked out on animals appear not to hold good in man.

We are not without hope that this synopsis may also be of use on the desk of our brethren who lecture to classes in physiology, as an *aide-mémoire*.

A. R. S.

CLIFTON, BRISTOL,
October, 1927.

SYNOPSIS OF PHYSIOLOGY

CHAPTER I.

CHEMISTRY.

Proteins.—These are long-linked chains of amino-acids, containing carbon (53 per cent), hydrogen (7 per cent), oxygen (22 per cent), nitrogen (16 per cent), and usually a little sulphur; phosphorus less frequently. They are colloid bodies, though a few can be crystallized (e.g., egg albumen), and will not pass through an animal membrane unless hydrolysed. Many of them can be coagulated by heat. They are usually precipitated by saturation with neutral salts.

AMINO-ACIDS ENTERING INTO PROTEINS.—

MONO-AMINO-ACIDS. — E.g., glycin (amino-acetic acid); alanin (amino-propionic acid); leucin (amino-caproic acid); cystin (dithio-amino-propionic acid—i.e., contains the sulphur of the protein molecule).

DI-AMINO-ACIDS.—Act as bases. Ornithin (di-amino-valeric acid); lysin (di-amino-caproic acid); arginin (guanidine-amino-valeric acid). Are called hexone bases.

DI-CARBOXYLIC ACIDS (i.e., two COOH groups).—Aspartic acid (amino-succinic acid); glutamic acid (amino-glutaric acid).

AROMATIC AMINO-ACIDS. — Tyrosin (hydroxy-phenyl amino-propionic acid); tryptophan (indol-amino-propionic acid); phenyl-alanin.

Leucin (spheres with radiate structure) and tyrosin (sheaves) may be found crystalline in the urine in acute yellow atrophy of the liver. Cystin may be found as flat hexagons in the urine in patients with cystinuria—a rare congenital defect, in which the necessary ferments for handling cystin are absent.

Proteins, *continued.*

TESTS FOR PROTEIN.—

HEAT COAGULATION.

PRECIPITATION BY ALCOHOL, SALICYL-SULPHONIC ACID, OR ESBACH'S REAGENT.

HELLER'S TEST.—Pour on to strong HNO_3: white ring at junction.

XANTHOPROTEIC TEST.—Add strong HNO_3; white precipitate, turned yellow on heating. Add ammonia: turns orange. Due to aromatic amines.

MILLON'S TEST.—Add Millon's reagent (nitrates of mercury): white precipitate, turned red on boiling. Due to tyrosin.

PIOTROWSKI'S TEST.—Add KOH and trace of $CuSO_4$: violet colour.

HOPKINS-ADAMKIEWICZ TEST.—Add a little glyoxylic acid, and pour strong H_2SO_4 down side of tube: purple colour. Due to tryptophan.

[MOLISCH'S TEST.—Add a little alcoholic solution of α-naphthol, then strong H_2SO_4: violet colour, turned yellow by NaOH. Due to sugar in the protein molecule.

NINHYDRIN TEST.—Boil with ninhydrin: blue colour on cooling. Given by proteins and amino-acids.]

VARIETIES OF PROTEIN.—

[PROTAMINES.—Elementary proteins; found in fish-roe. Consist mainly of di-amino-acids; no sulphur, usually no tyrosin. Yield protones like peptones. Do not show heat coagulation.

HISTONES.—Tissue proteins. Contain more amino-acids; are coagulated by heat; precipitated from acid solution by ammonia. E.g., globin of hæmoglobin.]

SCLEROPROTEINS.—E.g., gelatin, collagen (in fibrous tissue or cartilage), elastin (of elastic tissue), keratin (of skin, hair, horn—rich in cystin). Gelatin is obtained by boiling collagen or the ossein of bone. It does not contain any aromatic amino-acids, and will not give the Millon or glyoxylic tests. Will support life for a time, if given with aromatic amino-acids and vitamins, not without.

CONJUGATED PROTEINS (i.e., united with other substances).—Examples are :—

Glucoproteins, conjugated with glucose, as mucin.

Chromoproteins, coloured, as oxyhæmoglobin.

Nucleoproteins, in which the protein is united with *nuclein*, which contains *nucleic acid* and a protein.

Nucleic acid yields :—

Sugars (hexoses or pentose) + Purin (guanin, adenin) + Pyrimidine bases (cytosin, uracil, thymine) + H_3PO_4

Nucleoprotein is contained in cell nuclei. Obtained by mincing with NaCl and pouring into water ; the nucleoprotein rises to the top as a sticky mass, soluble in alkali. Precipitated by acid.

PHOSPHOPROTEINS.—Probably esters of phosphoric acid with protein. E.g., vitellin (of eggs) ; caseinogen, 0·8 per cent of phosphorus (in milk) ; casein (in cheese). Unlike nucleoproteins, they do not contain purins, and are easily decomposed by NaOH.

NATIVE PROTEINS.—Animal proteins include *albumins* and *globulins* (rich in glycin, insoluble in water). These contain sulphur, and most of the amino-acids found in proteins. Coagulated by heat. Albumin is precipitated by full saturation with Am_2SO_4 ; globulin by half-saturation, or by saturation with $MgSo_4$.

[Vegetable proteins include :—
Phyto-albumins and Phyto-globulins.—In cereals. Contain C, H, O, N, S. Coagulated by heat.
Gliadins.—Also in cereals. Soluble in alcohol. Make dough sticky. Zein of maize contains no lysin or tryptophan.
Glutelins.—Insoluble in alcohol. Gluten of wheat contains glutelin and gliadin.]

DERIVED PROTEINS.—E.g., proteoses, peptones. *See* pp. 72, 73.

Carbohydrates.—These are ketones or aldehydes, containing carbon, and oxygen-hydrogen in the ratio of 1 : 2. The monosaccharides have the formula $C_6H_{12}O_6$ (glucose, lævulose, galactose) ; the disaccharides $C_{12}H_{22}O_{11}$ (saccharose, maltose, lactose) ; the polysaccharides $(C_6H_{10}O_5)_n$ (starch, glycogen, dextrin, cellulose). Pentoses contain 5 carbon atoms.

TESTS.—

REDUCING TESTS.—Many of them reduce copper sulphate, thus :—

Trommer's Test.—Strong KOH, a few drops of $CuSO_4$; add sugar ; heat : red or yellow precipitate of cuprous oxide or hydrate.

Fehling's Test.—NaOH, a few drops of $CuSO_4$, Rochelle salt (to keep black copper oxide from

Carbohydrates—Tests for, *continued.*

coming down); boil; if clear, add sugar: precipitate as above.

[*Nylander's Test.*—To sugar solution add bismuth subnitrate and Rochelle salt and NaOH; boil: black precipitate of bismuth.]

The *reducing sugars* include glucose, lævulose, maltose, lactose, galactose, but not the starches or saccharose.

FERMENTATION TESTS.—Some sugars are acted on by yeast, yielding alcohol and CO_2. Shown by frothing after keeping warm for some hours. Such are glucose, saccharose, lævulose, and usually maltose. Some yeasts ferment lactose, not all.

POLARIMETRY TESTS.—Most sugars and starches rotate polarized light rays to the right. Lævulose rotates them to the left. When saccharose is converted into glucose and lævulose, the mixture rotates the ray to the left, because lævulose is more active than glucose.

PHENYL-HYDRAZINE TESTS.—To sugar solution add phenyl-hydrazine hydrochloride and sodium acetate; heat on water-bath; cool: yellow crystals called osazones come down, either at once (glucose), or very slowly (lactose). Identify by microscope, or melting point (put in capillary tube, strap to thermometer, heat in strong H_2SO_4).

Glucosazone.—Yellow sheaves; M.P. 205° C.

Maltosazone.—Stellate clusters of broad-bladed crystals; M.P. 206° C.

Lactosazone.—Tufts of slender crystals; M.P. 200° C.

THE MONOSACCHARIDES.—

GLUCOSE (dextrose, grape sugar).—In fruit, honey, blood, urine of diabetics. Very soluble in water and alcohol. Quantity estimated by Fehling method: run solution into boiling Fehling till blue colour goes. Or, better, run into boiling Benedict's solution (anhydrous Na_2CO_3, $CuSO_4$, sodium citrate, and potassium thiocyanate and ferrocyanide): a white precipitate forms, and the disappearance of the blue colour is easier to read.

LÆVULOSE (fructose).—Obtained by 'inverting' saccharose.

GALACTOSE.—Obtained by splitting up lactose. Enters into certain galactosides (cerebrins) found in brain.

THE DISACCHARIDES.—

SACCHAROSE (cane sugar, sucrose).—In cane and beet sugar. 'Inverted' by yeast, ferments, or boiling with acids; yields glucose and lævulose. Does not reduce copper salts.

MALTOSE.—Prepared by action of malt or ferments on starch. Reduces Fehling's; has two-thirds the reducing power of glucose; estimated quantitatively thus. On hydrolysis, yields two molecules of glucose.

LACTOSE.—In milk. Yields glucose and galactose. Has seven-tenths the reducing power of glucose. Souring of milk is due to its conversion into lactic acid by bacteria.

THE POLYSACCHARIDES.—On boiling with acids yield glucose. Give colour with iodine (starch gives blue; glycogen and dextrin red-brown), discharged by heat, returning on cooling.

STARCH.—In many vegetable cells, e.g., rice, potato, bread. Ptyalin and amylopsin turn it into maltose. Soluble in hot water, giving opalescent colloidal solution.

GLYCOGEN.—In liver and muscle and placenta. Precipitated by basic lead acetate. Gives opalescent solution in water; precipitated by 55 per cent alcohol. For method of preparation, *see* p. 125.

DEXTRIN.—First stage in action of ferments on starch. Gummy. Clear solution in water; precipitated by 85 per cent alcohol. Not precipitated by basic lead acetate.

CELLULOSE.—In cell-walls of vegetable cells; it forms stringy fibres. Insoluble. Converted into glucose by long boiling with acids. Broken up by certain bacteria.

Fats and Lipoids.—

FATS.—Consist of fatty acids and glycerin. Greasy substances, insoluble in water or cold alcohol, soluble in ether, chloroform, hot alcohol. Capable of *saponification*—i.e., conversion into glycerin and soaps (alkali salts of fatty acids, soluble in water)—by boiling with strong alkalis. Capable also of *emulsification*—i.e., resolution into tiny drops held in milky suspension; requires an alkali, and shaking; aided by bile, and mucin.

The principal fats are *olein*, *palmitin*, *stearin*.

Fats and Lipoids, *continued.*

OLEIN.—M.P. 5° C. Oleic acid is $C_{17}H_{33}COOH$. Is unsaturated. Gives black colour (OsO_2) with osmic acid. Absorbs iodine.

PALMITIN.—M.P. 45° C. Palmitic acid is $C_{15}H_{31}COOH$. Saturated.

STEARIN.—M.P. about 60° C. Stearic acid is $C_{17}H_{35}COOH$. Saturated.

Body fats, or milk fats, contain mixtures of the above. They are analysed by the melting point, the saponification value (i.e., amount of alkali needed to saponify), and iodine value (which estimates the olein).

Histologically, fats are stained by osmic acid, Sudan III, or Scharlach R ; acid fats by Nile blue.

LIPOCHROMES (luteins).—Fatty pigments—e.g., in corpus luteum.

LIPOIDS.—Fatty substances. There are three main groups :—

CHOLESTERIN.—$C_{27}H_{45}OH$. An alcohol of the terpene series. Found in nervous tissue, blood, red blood-corpuscles, gall-stones. Probably forms the semi-permeable membrane of red corpuscles ; is shed out by inflamed mucous surfaces. For tests, etc., *see* p. 81.

CEREBRINS.—Are galactosides in nervous tissue.

PHOSPHATIDES OR PHOSPHOLIPINS.—The principal one is *lecithin*, which is a compound of cholin, fatty acid (oleic, stearic), glycerin, and H_3PO_4. It is a waxy substance, soluble in alcohol and ether, found in nervous tissue, red corpuscles, and bile. Turns black with osmic acid. Cholin is a nitrogenous base, found in cerebro-spinal fluid if degeneration of nervous tissue has occurred. Gives crystals with platinum chloride. Causes fall of blood-pressure if injected.

[Other phosphatides are *kephalin* and *sphingomyelin*. The first is insoluble in alcohol ; the latter contains no glycerin.]

CHAPTER II.

BLOOD, LYMPH, AND CEREBROSPINAL FLUID.

THE BLOOD.

Reaction of Blood.—

REACTION OF ANY FLUID.—Depends on the relative proportions of hydrogen (H) and hydroxyl (OH) ions. When these are equal, fluid is neutral.

EXPRESSION OF REACTION.—Expressed in terms of H-ion concentration. In a neutral solution, product of H and OH ions is a constant—namely, 10^{-14}: hence the H-ion concentration is 10^{-7}, or 0·0000001 grm. per litre. This is expressed as pH, obtained by taking the logarithm of the reciprocal of the number expressing the H-ion concentration. Thus for a neutral solution the pH is 7. Figures less than 7 express acid reactions, over 7 alkaline ones. 'Strong' acids completely dissociate, and so give a low figure—e.g., $\frac{1}{1000}$ normal HNO_3 has pH = 3.

DETERMINATION OF THE H-ION CONCENTRATION IN THE BLOOD.—

1. ELECTROLYTIC METHOD.—Measurement of difference in electrical potential between an electrode surrounded by blood and one in solution of known H-ion concentration.
2. COLORIMETRIC METHOD.—Indicators such as neutral red and phenolphthalein are used, which give different colours with different concentrations of H-ions. Examination must be made at body temperature and in an atmosphere containing same amount of CO_2 as the tissues. Dialysed plasma is tested against mixtures of phosphate of known pH.

The pH of blood is 7·39, *i.e., slightly alkaline.* The reaction of blood is dependent on the relative amounts of CO_2 and sodium bicarbonate.

CONSTANCY OF REACTION OF BLOOD.—Although, as a result of metabolism, acids are constantly added to the

Reaction of Blood, *continued.*

blood, the reaction remains remarkably uniform, any considerable change being incompatible with life.

MEANS BY WHICH REACTION OF BLOOD IS KEPT CONSTANT.—

1. Buffer Salts.—A buffer is a substance which, when present in a solution, tends to prevent its reaction changing on addition of acid or alkali. Substances are present which unite with strong acids, liberating weak ones. During muscular exercise, lactic acid is liberated, but the sodium of the sodium bicarbonate in the blood combines with it, liberating carbonic acid. Carbonic acid produced during activity of tissues combines with alkali of protein compounds, and weaker acid, protein, is set free. The chief buffer salt in the plasma is sodium bicarbonate, but sodium phosphate and potassium salts of proteins also act in this way. Amount of sodium bicarbonate available is termed the alkali reserve of the blood.

   Hamburger Reaction or '*Chlorine Shift*'.—When CO_2 is added to blood, it reacts with NaCl of plasma thus :—

   $$H_2CO_3 + NaCl = NaHCO_3 + HCl.$$

   The HCl passes into interior of red blood-corpuscle, acidifies hæmoglobin, and forms KH_2PO_4 from K_2HPO_4. Thus more $NaHCO_3$ is left free in the plasma.

2. Activity of the Lungs and Kidneys.—

   a. Lungs.—Increase of CO_2 in the blood stimulates respiratory centre, so that more CO_2 is given off by lungs.

   b. Kidneys.—Excess of acids in food, and fixed acids such as lactic formed in the body, are excreted as ammonia compounds ; also acid sodium phosphate may be excreted in preference to Na_2HPO_4.

ACIDOSIS.—This is a condition in which amount of fixed acids passing into blood is increased. Reaction of blood is still actually alkaline, but alkali reserve is diminished.

[Tests for Diminution in Alkali Reserve.—

1. Decreased capacity of plasma to absorb CO_2. Normally 100 c.c. of plasma absorb 65 c.c. of CO_2.

2. Amount of sodium bicarbonate necessary to make urine alkaline is increased.]

Specific Gravity.—In adult male, varies from 1041 to 1067, that of corpuscles being slightly higher than that of plasma. Varies with age and sex, is diminished after eating, increased by exercise, and shows a diurnal variation, rising during the night.

DETERMINATION OF THE SPECIFIC GRAVITY.—Chloroform (specific gravity 1526) and benzol (889) are mixed in varying proportions, until one is found in which a drop of blood floats. Specific gravity of this fluid is then that of the blood—measured by a hydrometer.

[**Osmotic Pressure.**—Osmotic pressure of plasma and corpuscles is the same. Found by determining freezing point, which is 0·56° C. below that of distilled water, which corresponds to that of a 0·9 per cent solution of NaCl.]

Red Blood-corpuscles.—In man and mammals, red blood-corpuscles are biconcave, yellowish-red, non-nucleated discs (nucleated before fully formed), about 7·7 μ in diameter, oval in camel, circular in man and other mammals. In other vertebrates they are nucleated.

In human beings, there are normally about 5,000,000 per c.mm. in the male, 4,500,000 in the female, 6,000,000 in the new-born child.

METHOD OF COUNTING NUMBER OF RED BLOOD-CORPUSCLES.—By *hæmocytometer*, consisting of capillary pipette having a mark at 1 and 101, and glass slide with a cell having depth of $\frac{1}{10}$ mm. and area of 1 sq. mm. divided into 400 squares.

METHOD.—Blood is sucked up to mark 1 and diluting fluid to mark 101. Diluting fluid is isotonic sodium sulphate or Toisson's fluid, which prevents coagulation. Cell is filled with mixture, and corpuscles are counted under microscope. Number in 1 c.mm. can then be calculated.

CHEMICAL COMPOSITION OF RED CORPUSCLES.—

WATER.—63·3 per cent.

SOLIDS.—36·7 per cent.

a. Hæmoglobin.—90 to 95 per cent of total solid material.

b. Lipoids (lecithin and cholesterin).

c. Nucleoprotein and Cell-globulin.

d. Inorganic Salts.—Especially potassium phosphate.

Red Blood-corpuscles, *continued.*

STRUCTURE OF CORPUSCLES.—Two views :—

1. Stroma, consisting largely of lecithin and cholesterin, forming a meshwork or spongy mass in which hæmoglobin is deposited.
2. Vesicles, consisting of an envelope in which lecithin and cholesterin are found, and containing hæmoglobin, not in solution, but apparently in colloid or amorphous form and possibly loosely attached to nucleoprotein.

HÆMOLYSIS.—Means setting free of hæmoglobin from corpuscles, so that it becomes dissolved in the plasma—i.e., laked blood.

CAUSES OF HÆMOLYSIS.—

1. *Physical.*—Lowering of osmotic pressure of plasma, as by diluting with water. Water passes into corpuscles owing to their higher osmotic pressure, until they rupture and hæmoglobin is discharged.
2. *Chemical.*—By ether, chloroform, bile salts, and soaps, which probably act by uniting with lipoid element in stroma, and so altering constitution of stroma that hæmoglobin is set free.
3. *Hæmolysins.*—(*a*) Snake venom (viperine snakes) ; (*b*) Serum from some other animals—e.g., rabbit's blood-corpuscles added to the serum of a dog are rapidly destroyed ; this power is destroyed by heating the serum to 55° C.

   Artificial Hæmolysins.—Serum of a guinea-pig has little effect on rabbit's corpuscles, but if rabbit's blood is injected into guinea-pig, blood of this animal develops hæmolytic action on rabbit's red corpuscles.

HÆMOGLOBIN.—Hæmoglobin exists both as a colloid and as a red crystalline solid, soluble in ether, slightly soluble in water.

COMPOSITION OF HÆMOGLOBIN.—Is a chromo-protein, consisting of : (1) *Globin*, about 90 per cent, a histone. (2) *Hæmatin*, about 4 per cent, an iron-containing substance. If decomposition occurs in absence of oxygen, hæmochromogen is formed instead of hæmatin. Power to combine with oxygen is due to iron in the hæmatin, one molecule of oxygen combining with each atom of iron.

FORMULA OF HÆMOGLOBIN.—$C_{758}H_{1203}N_{195}S_3FeO_{218}$. The amount of iron in hæmoglobin is about 0·34 per cent. Molecular weight is 16,669.

CRYSTALS OF HÆMOGLOBIN (really oxyhæmoglobin).—In man and most mammals crystals are rhombic prisms, in guinea-pig tetrahedra, in squirrel hexagonal plates.

Method of Isolating Hœmoglobin Crystals.—

1. Defibrinated blood from a rat is shaken with ether in a test-tube. The ether causes hæmolysis, and hæmoglobin crystallizes out from ether extract.
2. If a drop of defibrinated rat's blood and a drop of water are mixed, and a cover-slip is applied, crystals of hæmoglobin gradually separate out.

ESTIMATION OF AMOUNT OF HÆMOGLOBIN.—Standard is taken as 100 in adults, 70 in babies (except just after birth).

Hœmoglobinometer is used. Consists of two tubes, one containing solution of carboxyhæmoglobin diluted to standard tint. A little distilled water and 20 c.mm. of blood are placed in the second tube, and coal gas bubbled through to convert hæmoglobin into carboxyhæmoglobin. Solution is diluted until its colour is the same as the standard. Level of fluid gives percentage of normal hæmoglobin.

Tallqvist scale is a rough clinical method. A drop of blood on blotting-paper is compared with a paper colour scale. The tints range from 10 to 100 per cent.

DERIVATIVES OF HÆMOGLOBIN.—

1. *Oxyhœmoglobin.*—Scarlet solution, yellowish when very dilute. 100 grm. of hæmoglobin combine with 18·5 grm. of oxygen (probably one molecule of hæmoglobin unites with one of oxygen). *Reduced hœmoglobin*, i.e., oxyhæmoglobin minus its oxygen, is formed by exposure of oxyhæmoglobin to a vacuum or by treating it with reducing fluid, e.g., ammonium sulphide or Stoke's fluid.
2. *Carboxyhœmoglobin* (= carbon monoxide and hæmoglobin).—Much more stable than oxyhæmoglobin, affinity of hæmoglobin for CO being so

Red Blood-corpuscles—Hæmoglobin, *continued.*

much greater than that for oxygen that a small quantity of carbon monoxide in the air is injurious. When exposed to a vacuum carbon monoxide is given off, but it is unaffected by ammonium sulphide. Fatal effects of breathing coal gas or 'after-damp' in mines are due to CO. Carboxyhæmoglobin gives a cherry-red colour even in dilute solutions. (Nitric oxide forms an even more stable compound.)

3. *Methæmoglobin.* — Brownish - red solution, which crystallizes in needles, produced by treating blood with potassium ferricyanide or potassium permanganate, or exposing to the air for some time. Probably contains same amount of oxygen as oxyhæmoglobin, but combined in a different way. Unaffected by exposure to a vacuum, but reduced by ammonium sulphide.
   In some cases of poisoning, especially by potassium chlorate, by acetanilide, etc., methæmoglobin is produced in the body and excreted in the urine.
4. *Hæmatin.*—Formed by action of an acid or alkali on hæmoglobin. It is an amorphous dark-brown substance, soluble in acids or alkalis.
5. *Hæmin.*—Formed by action of hydrochloric acid on hæmatin, and consists of small dark-brown rhombic crystals. These crystals are used as a means of identification of old blood-stains.
   Method of obtaining hæmin from dried blood. —A little dried blood is powdered with a few crystals of sodium chloride and placed on a slide. A few drops of glacial acetic acid are run underneath the cover-slip, and gently heated, but not boiled.
6. *Hæmochromogen* (= reduced hæmatin).—Formed by action of ammonium sulphide on hæmatin.
7. *Hæmatoporphyrin.*—An iron-free substance formed by the action of strong acids or alkalis on hæmoglobin or hæmatin.
8. *Hæmatoidin.*—Occurs in old blood-clots. It is iron-free, identical with bilirubin.
9. *Histohæmatins.*—Under this term is included the colouring matter of the body which can take up

oxygen—e.g., myohæmatin, the red colouring matter of muscles.

10. *Biliary and Urinary Pigments.*

BLOOD SPECTRA.—

1. *Oxyhæmoglobin.*—Two absorption bands between D and E lines, also Soret's band in the violet.
2. *Reduced Hæmoglobin.*—One broad band in the green between D and E lines.
3. *Carboxyhæmoglobin.*—Similar to oxyhæmoglobin, but slightly nearer blue end of spectrum.
4. *Methæmoglobin.*—Characteristic band in orange between C and D lines. In alkaline solutions it also has two bands similar to oxyhæmoglobin.
5. *Hæmatin.*—(*a*) *Acid hæmatin :* Single band in red between C and D lines. (*b*) *Alkali hæmatin :* Rather faint band just to red side of D line.
6. *Hæmochromogen.*—Dark band midway between D and E lines, and less defined band in green practically over E line.
7. *Hæmin.*—No absorption bands.
8. *Hæmatoporphyrin.*—(*a*) *Acid hæmatoporphyrin :* Two bands, one on either side of D line. (*b*) *Alkali hæmatoporphyrin :* (i) Narrow band between C and D lines ; (ii) Two narrow bands between D and E lines ; (iii) Darker, broader band between E and F lines.

ORIGIN OF RED BLOOD-CORPUSCLES.—

IN ADULT.—Formation occurs in red bone-marrow. Colourless nucleated cells known as *erythroblasts* show presence of hæmoglobin as multiplication occurs, cells being now known as *normoblasts.* (With some writers, erythroblast = normoblast.) Later, nucleus of normoblast disappears, leaving a fully formed red corpuscle.

After severe hæmorrhage, and in blood-destroying diseases, corpuscles pass into circulation before they are fully formed, and normoblasts are found in the blood.

IN EMBRYO.—From primitive mesenchyme cells of vascular area are formed *hæmocytoblasts* (like large lymphocytes). These invade the marrow of bones, and also constitute lymphoid tissues. They are the parents of marrow cells, and of red and white corpuscles.

DESTRUCTION OF RED CORPUSCLES.—Length of life of a red blood-corpuscle is unknown, but, since a transfused

Red Blood-corpuscles, *continued.*

corpuscle may live for a month or more, it is probably longer than used to be supposed.

MODE OF DESTRUCTION.—Two main views :—

1. *Phagocytosis* in the spleen, liver, or lymph glands by cells of reticulo-endothelial system such as the Kupffer cells in liver and pulp cells in spleen. These may be found to contain red corpuscles or fragments of them. Iron can be demonstrated in the liver, the amount being increased in blood-destroying diseases, e.g., pernicious anæmia.

   Method of Staining Liver for Iron.—Treated with potassium ferrocyanide and hydrochloric acid (to liberate iron from organic combination). Prussian-blue colour results.

2. *Fragmentation* of corpuscles to a fine powder. Fragments are found in blood and spleen. but cause of process is unknown.

Leucocytes, or White Blood-corpuscles.—

VARIETIES OF LEUCOCYTES.—

1. POLYMORPHONUCLEARS. — 10 μ in diameter. Form about 70 per cent of total leucocytes. Nucleus is lobulated ; protoplasm contains fine granules staining with faintly acid or neutral dyes. Show active amœboid movement and phagocytosis, i.e., power of ingesting foreign particles and bacteria. Increased in pneumonia and septic infections. (*Fig.* 1, A.)

2. EOSINOPHIL LEUCOCYTES.—About 10 μ in diameter. About 1 to 5 per cent of total leucocytes. Nucleus lobulated or kidney-shaped ; protoplasm contains large granules staining with acid dyes, e.g., eosin. Only show slight amœboid movement, and are not phagocytic. Increased in cases of worm infections and in asthma. (*Fig.* 1, B.)

3. MAST CELLS, OR BASOPHIL LEUCOCYTES.—10 μ in diameter. Scanty. Nucleus lobular ; protoplasm contains large granules staining with basic dyes, e.g., methylene blue. (*Fig.* 1, C.)

4. LYMPHOCYTES.—About 20 per cent ; 40 per cent in infants. Small, 7·5 μ in diameter. Large spherical nucleus, and small amount of clear cytoplasm.

LEUCOID CELLS

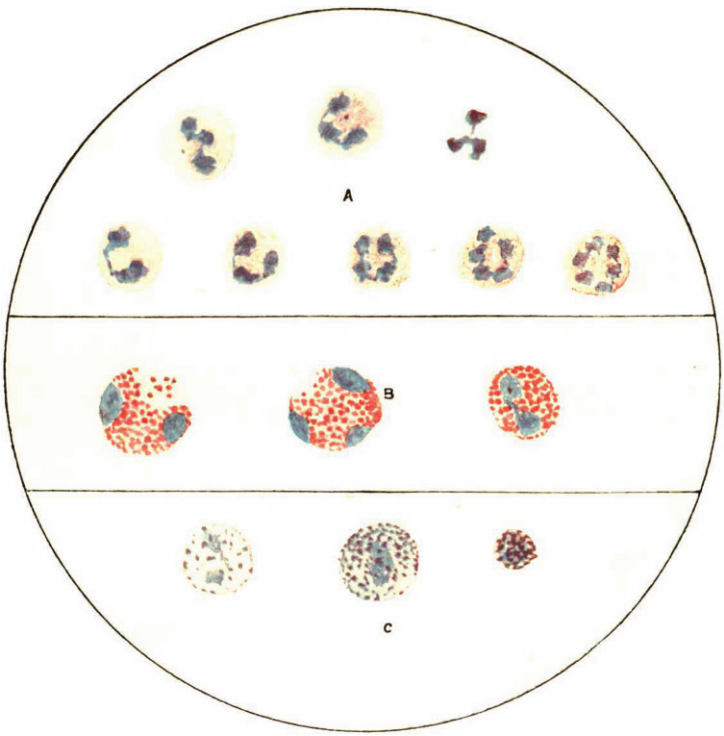

Fig. 1.—A, Polymorphonuclear leucocytes. B, Eosinophils. C, Mast cells.

Figs. 1 *and* 2 *by permission from Cecil Price-Jones's* '*Blood Pictures*'. *Bristol : John Wright & Sons Ltd.*

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LYMPHOID CELLS

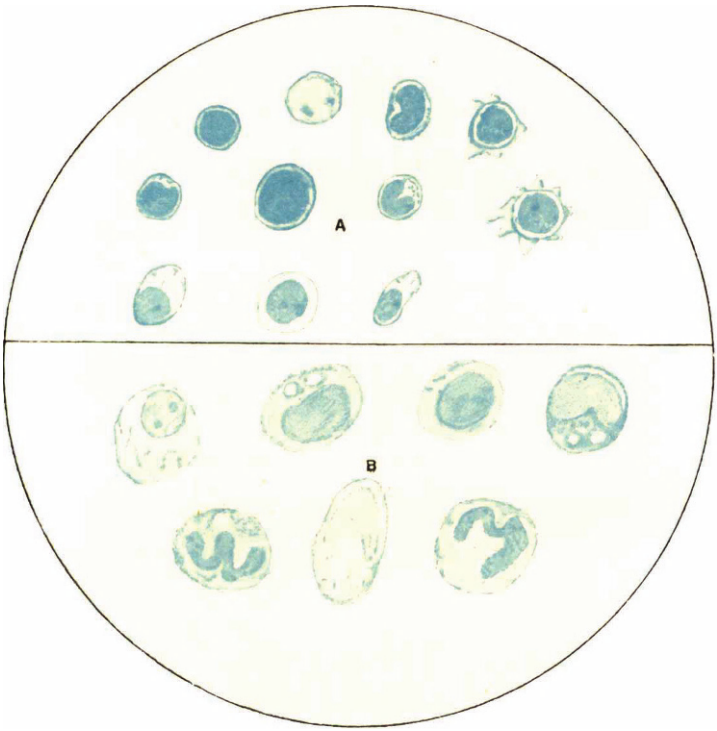


Fig. 2.—A, Lymphocytes. B, Large mononuclear cells.

Not actively amœboid. Increased in typhoid and other fevers and during digestion. (*Fig.* 2, A.)

5. LARGE LYMPHOCYTES.—1 to 2 per cent. About 10 μ in diameter. (*Fig.* 2, A.)
6. MONONUCLEARS (macrocytes, hyalines).—About 1 to 2 per cent. Single nucleus and abundant cytoplasm. Amœboid and actively phagocytic. Derived from cells of reticulo-endothelial system. Increased in malaria, etc. 10 μ in diameter. (*Fig.* 2, B.)
7. TRANSITIONALS.—10 μ in diameter. 1 to 2 per cent. Horseshoe-shaped nucleus.

ENUMERATION OF THE LEUCOCYTES.—Performed in the same way as enumeration of red corpuscles, diluting blood ten times with solution of 1 per cent acetic acid with a little methyl green, which stains nuclei of leucocytes and dissolves the red corpuscles.

Normal number of leucocytes is 7000 to 10,000 per c.mm. At birth there are 17,000, but the number drops to normal by the end of the third year.

VARIATIONS IN NUMBER OF LEUCOCYTES.—

1. May increase as much as 20 per cent during *digestion*, mostly lymphocytes.
2. Slight leucocytosis (i.e., increase in number of leucocytes) occurs normally during exercise, cold baths, and in pregnancy.
3. In many infective conditions, considerable leucocytosis occurs.
4. Leucopenia occurs in starvation, and in some diseases.

FUNCTIONS OF THE LEUCOCYTES.—There are similar wandering cells in the tissues which share in these functions.

1. Protect the body against micro-organisms by ingesting and destroying bacteria directly, or by forming substances which destroy bacteria (bacteriolysins). Polymorphonuclears are especially concerned in this process.
2. Aid in removal of damaged tissues, possibly in actual regeneration by promoting cell proliferation. Carrel suggests that leucocytes may synthetize (out of the blood) growth-promoting substances described as *trephones*, which connective tissue and epithelial cells need and cannot produce themselves.
3. Take part in coagulation of blood by forming some thrombogen and thrombokinase.

White Blood-corpuscles—Functions, *continued.*

4. Help to maintain the normal protein content of plasma.
5. Aid in absorption of fat from columnar cells of the intestine, and conveyance of it to central lacteal of villus. They may also carry other material, e.g., iron particles from liver, probably to bone-marrow, and possibly glycogen from liver to tissues. All doubtful.

ORIGIN OF WHITE BLOOD-CORPUSCLES.—

1. POLYMORPHS and EOSINOPHILS are formed in bone-marrow from large clear cells with single nucleus, *myelocytes.*
2. LYMPHOCYTES are formed in lymph glands and scattered lymphoid tissue. In fœtus, erythrocytes, leucocytes, and lymphocytes are all derived from small round cells in bone-marrow.
3. MONONUCLEARS are formed from cells of reticulo-endothelial system (*see* SPLEEN).

DESTRUCTION OF WHITE BLOOD-CORPUSCLES.—Probably chiefly in spleen. Spleen is rich in purin bodies, some of which may be derived from nucleoprotein of white blood-corpuscles.

Blood-platelets. — About 300,000 per c.mm. Colourless, rather irregular-shaped bodies, considerably smaller than a red blood-corpuscle, found only in freshly shed blood. In shed blood, appear to take part in process of coagulation, but function is uncertain. There is still some doubt as to whether blood-platelets can be seen in circulating blood, or whether they are merely precipitates from plasma during cooling of blood. Said to be derived from fragmentation of megakaryocytes.

Plasma.—The fluid part of the blood *before* coagulation—i.e., blood minus corpuscles.

SERUM is the fluid part of the blood *after* coagulation—i.e., blood minus corpuscles and fibrin.

DEFIBRINATED BLOOD results from removal of fibrin, by whipping blood with a glass rod—i.e., serum plus corpuscles.

COMPOSITION OF PLASMA.—

WATER.—About 91 per cent.

SOLIDS.—About 9 per cent.

a. Proteins.—6 to 8 per cent. Fibrinogen, serum albumin, and serum globulin.

b. Fats and Lipoids.—Visible fat may be found in blood after a meal rich in fats, but it soon disappears.

c. Glucose.—0·1 to 0·18 per cent. Perhaps blood glucose is an isomer of ordinary glucose. In lactating women, lactose is occasionally present.

d. Non-protein Nitrogenous Bodies.—Urea, about 0·02 to 0·04 per cent. Traces of uric acid, creatinine, and amino-acids.

e. Inorganic Salts.—Most abundant are sodium chloride and sodium bicarbonate. Sulphates and phosphates of sodium, and chlorides, bicarbonates, sulphates, and phosphates of potassium, calcium, magnesium, and iron, also occur. Molecular concentration of plasma is isotonic with a 0·9 per cent solution of sodium chloride.

f. Gases in Solution.—Oxygen, carbon dioxide, and nitrogen.

g. Protective Substances.—Many substances (called 'antigens') when introduced into the circulation lead to formation of bodies which tend to destroy or precipitate the substance introduced.

PROTEINS OF PLASMA.—

a. Serum Albumin.—About 4 per cent. Precipitated by complete saturation with ammonium sulphate. Three varieties, which coagulate at different temperatures, viz., 73°, 77°, and 84° C.

b. Serum Globulin and Paraglobulin.—About 3·8 per cent. Coagulate at 75° C. May be divided into: (1) *Euglobulin*, precipitated by one-third saturation with $(NH_4)_2SO_4$. (2) *Pseudoglobulin*, precipitated by half saturation with $(NH_4)_2SO_4$. (3) *Fibrinogen*, about 0·4 per cent; insoluble in distilled water, but soluble in normal saline (0·9 per cent); coagulates at 56° C.; is precipitated by half-saturation with NaCl, or by passing CO_2 through it.

Coagulation of Blood.—Blood within a few minutes of leaving blood-vessels sets into a jelly-like material, which gradually shrinks and becomes firmer, serum being squeezed out. In the living body, or if blood-clot is kept at 40° C., there is partial resolution of the fibrin, presumably owing to presence of fibrinolysin.

Coagulation of Blood, *continued.*

COMPOSITION OF BLOOD-CLOT.—(*a*) *Reticulum* of delicate threads of fibrin, an insoluble protein. Shrinking of clot is due to contraction of these threads of fibrin. (*b*) Red and white blood-corpuscles, and blood-platelets.

CAUSE OF COAGULATION.—

1. ESSENTIAL CHANGE IS CONVERSION OF FIBRINOGEN INTO FIBRIN.

   Evidence.—

   a. If fibrinogen is precipitated or coagulated as above, blood will not clot.

   b. Fresh blood may be drawn into an equal volume of half-saturated sodium sulphate; corpuscles settle and plasma remains on top. On dilution, this plasma clots, but if fibrinogen is precipitated by addition of an equal volume of saturated solution of sodium chloride, plasma no longer clots.

   Fibrinogen is probably formed in the liver, not in the bone-marrow. It is unaltered in the disease known as aplastic anæmia, but reduced in liver disease such as phosphorus or chloroform poisoning.

2. CONVERSION OF FIBRINOGEN INTO FIBRIN IS DUE TO ACTION OF SUBSTANCE KNOWN AS THROMBIN, NOT PRESENT IN ITS ACTIVE FORM IN BLOOD-VESSELS, BUT FORMED WHEN BLOOD IS SHED.

   Evidence.—

   a. If solution of pure fibrinogen is obtained from blood by precipitation, clotting does not occur, but on addition of blood serum it does.

   b. Serum proteins are precipitated by excess of alcohol; the precipitate is dried, ground up, and extracted with water. This solution contains thrombin, and causes coagulation when added to solution of pure fibrinogen. Thrombin is also obtained by steeping clot in alcohol, then extracting with water.

   c. Blood drawn directly into alcohol does not contain any thrombin.

NATURE AND MODE OF ACTION OF THROMBIN AND FIBRINOGEN.—

NATURE OF THROMBIN.—Unknown.

MODE OF ACTION.—Most generally accepted theory is that a precursor of thrombin, prothrombin or thrombogen, is present in circulating blood, and that, for its conversion into thrombin, calcium salts and a thromboplastic substance called thrombokinase (derived from damaged tissue cells, leucocytes, or blood-platelets) are necessary.

Evidence that Calcium is Essential.—

a. If sodium oxalate, citrate, or fluoride is added to freshly shed blood, clotting will not occur. Addition of calcium chloride leads to clotting.

b. If thrombin is added to oxalated plasma, clotting occurs, although no calcium is present, so that apparently calcium is necessary for formation of thrombin, but not for interaction of thrombin and fibrinogen.

Evidence that Thrombokinase is Essential and Formed from Tissues or Blood-platelets.—

a. If pigeon's blood, which contains no platelets, is drawn directly into a clean test-tube without contact with tissues, clotting is greatly delayed. Addition of tissue extract accelerates it.

b. If mammalian blood is drawn straight into a clean tube, it clots rapidly, though time is slightly lengthened. In the mammal, thrombokinase is probably formed from leucocytes and blood-platelets, which disintegrate very rapidly when blood is shed.

c. If oxalated blood plasma from a mammal is allowed to stand on ice for several days, a precipitate of blood-platelets forms. The plasma no longer clots on addition of lime salts, but if some of the precipitated platelets are added also, clotting occurs.

d. Living test-tube experiment. Tie off a length of the jugular vein of the horse. Blood does not clot.

THEORIES AS TO NATURE OF PROCESS OF CONVERSION OF THROMBOGEN INTO THROMBIN.—It is generally accepted that thrombogen is activated by

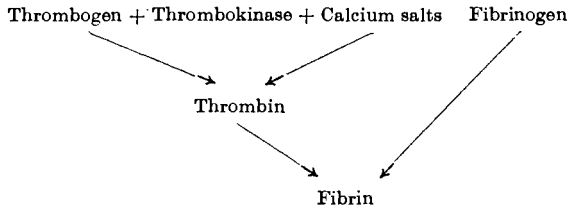
Coagulation of Blood, *continued.*

some substance in tissue extract, but nature of this substance is uncertain.

MORAWITZ'S THEORY.—Thrombogen is activated by combined action of calcium and tissue extract, the calcium being present in circulating blood, the thrombokinase supplied by the breaking down of platelets and extravascular tissues. According to Howell, the essential constituent of tissue extract is cephalin, a lipoid.

[HOWELL'S THEORY.—Assumes that prothrombin can be converted into thrombin by action of calcium alone, this being prevented in the circulation by an inhibitory substance which affects the prothrombin. This substance is neutralized by the cephalin set free from tissues.]

SUMMARY OF COAGULATION OF BLOOD.—



REASONS WHY INTRAVASCULAR CLOTTING DOES NOT OCCUR.—Since thrombokinase can be formed from blood-platelets, all elements necessary to produce coagulation are present in the circulation. This is prevented by antithrombin.

[ANTITHROMBIN is said to be the result of interaction of: (*a*) *Heparin*, derived from liver; (*b*) *Proantithrombin*. Both are in the blood, and heparin activates proantithrombin when necessary.
Evidence for Presence of Antithrombin.—If fibrinogen is removed from a specimen of oxalated blood, filtrate has an antithrombic action on a mixture of thrombin and fibrinogen.]

The endothelial lining of vessels protects against clotting. The circulation of the blood also helps to prevent clotting, since obstruction of blood-flow at one point, as by ligature of an artery, results in clotting.

[MEASUREMENT OF COAGULATION TIME.—Use capillary tube. Break off a short length every minute, till jelly-like thread of clot is seen. Use a control. Normal: about 5 minutes.
MORE ACCURATE METHOD.—1 to 2 c.c. of blood are taken from a vein and emptied into a vessel of known size. Coagulation time is noted.

INTRAVASCULAR CLOTTING.—Occurs under certain abnormal circumstances.

CAUSES.—

1. Damage to endothelial lining of blood-vessel.
2. Introduction of foreign material—e.g., air in veins, if not absorbed, may lead to clotting. Injection of tissue extracts may lead to clotting, but result is variable. Body probably protects itself by forming antithrombin.
3. Vascular stasis—e.g., in varicose veins.]

MEANS OF ACCELERATING COAGULATION.—

1. Increasing area of foreign surface with which blood is in contact. Breaking down of leucocytes and blood-platelets is hastened by contact with rough foreign surfaces.
2. Heat.
3. Use of thrombin solutions or tissue extracts.

MEANS OF RETARDING COAGULATION.—

1. PREVENTION OF CONTACT WITH A FOREIGN SURFACE. —e.g., blood drawn into vessels lined with paraffin.
2. COOLING.—This only succeeds when blood normally clots slowly.
3. REMOVAL OF ONE OF THE SUBSTANCES CONCERNED IN PRODUCTION OF FIBRIN.
   a. *Oxalate solution*, by precipitating calcium.
   b. *Sodium fluoride or citrate*, which combine with calcium, sodium fluoride also combining with thrombogen.
   c. *Solution of magnesium sulphate* 27 per cent, probably precipitating thrombogen. If thrombin solution is added, or if blood is sufficiently diluted, clotting occurs again.
4. INJECTION OF CERTAIN SUBSTANCES.—E.g., peptone or leech extract (Hirudin). Probably prevent action of thrombin on fibrinogen. Peptone probably acts by stimulating production of antithrombin in liver; it does not retard clotting of shed blood.

HÆMOPHILIA.—A disease in which the coagulation time is markedly prolonged, so that death may result from a simple operation—e.g., extraction of a tooth.

[Cause of this delayed coagulation is uncertain. Delay is in conversion of prothrombin to thrombin, not fibrinogen to fibrin (Addis). Probably defect is in prothrombin. Addition of normal plasma or a few washed corpuscles restores coagulation power.

Sahli considers defect is in thrombokinase, since addition of washed leucocytes leads to clotting; but these leucocytes may bring in prothrombin as well as thrombokinase.]

Functions of the Blood.—

1. To convey oxygen, nutritive substances such as glucose and amino-acids, and internal secretions to the tissues.
2. To receive waste products from the tissues, such as carbon dioxide, uric acid, etc., and convey them to lungs and kidneys, where they are excreted.
3. To protect the body against micro-organisms and toxins.

FUNCTIONS OF PLASMA PROTEINS.—

1. To maintain proper viscosity and so keep up the blood-pressure.
2. To keep the blood volume fairly constant. They do not pass through the capillary walls, and thus they exert an osmotic pressure, though small, which prevents exudation of plasma into the tissues.

Total Quantity of Blood.—In the dog, the blood forms 7·7 per cent of the body-weight, in the cat 5 per cent, in birds 10 per cent, in man (by carbon monoxide method) about 5 per cent (Haldane and Smith).

DETERMINATION OF TOTAL QUANTITY OF BLOOD.—

In Killed Animal.—Animal is bled, and quantity of blood weighed. Blood-vessels are then washed out with water, and tissues extracted with water, and amount of hæmoglobin in washings and tissue extract calculated.

In Living Animal.—A small quantity of blood is withdrawn, and percentage volume of oxygen combined with blood determined. Animal then breathes air containing known volume of carbon monoxide, another specimen of blood is taken, and percentage volume of oxygen determined. Diminution in volume of oxygen is equal to volume of carbon monoxide absorbed, since carbon monoxide displaces an equal volume of oxygen. Hence total quantity of blood is calculated.

Vital Red Method, used in Man.—A few c.c. of blood are withdrawn, citrated, and centrifuged. 3 mgrm. of a coloured dye known as vital red are injected, and after 3 to 6 minutes another sample of blood is withdrawn, citrated, and centrifuged. The original plasma is mixed with three parts of saline, and vital red added until colour is the same as that of second sample of

plasma. Ratio of volume of plasma to volume of total blood is found by centrifugalizing blood in a graduated tube.

Mode of Recovery from a Big Hæmorrhage.—

1. Blood is rapidly diluted by taking up water from the tissues.
2. Arteries and peripheral veins contract so that blood-pressure is maintained.

REGENERATION OF BLOOD-CORPUSCLES.—Occurs by activity and, if needful, overgrowth of red marrow.

[RESTORATION OF SERUM PROTEINS.—

1. After a large hæmorrhage, red blood-corpuscles were suspended in Locke's fluid, and returned to the circulation. It took some weeks for restoration of protein to normal.
2. Starvation led to retarded recovery, while plenty of meat hastened it.

THE PROTEINS MAY BE FORMED BY LIVER.—*Evidence:* (*a*) In a dog with an Eck's fistula, recovery is slow and poor; (*b*) In phosphorus poisoning, destruction of liver and diminution in serum proteins both occur.]

Blood Transfusion.—Abel found that the effects of a big hæmorrhage in animals are overcome as well by injection of red blood-corpuscles, washed and suspended in Locke's fluid, as by whole blood. If corpuscles are kept in citrate-dextrose solution, they may be preserved for weeks in an ice chest. Effective in man.

BLOOD GROUPS.—Blood of different individuals is not always compatible, since plasma of one person may affect corpuscles of another in one of two ways: (1) Hæmolysis; (2) Agglutination. There are four blood groups:—

Donor's group	*Frequency in white races*	*Suitable if patient belongs to*
I	5 per cent	I
II	40 „ „	I or II
III	10 „ „	I or III
IV	45 „ „	I, II, III, or IV.

It is the effect of patient's plasma on donor's corpuscles which matters, not the reverse. It is best, of course, to use a donor of the *same* group.

DETERMINATION OF BLOOD GROUP.—A drop of donor's blood can be tested against preserved stock sera belonging to Groups II and III. Or donor's blood can be tested against patient's serum, it being noted whether any agglutination occurs in 5 minutes.

Blood Transfusion—Blood Groups, *continued.*

Group I is agglutinated by II, III, and IV
„ II „ „ „ III and IV
„ III „ „ „ II and IV
„ IV „ „ „ no other

[**Sedimentation of Corpuscles.**—Rate at which corpuscles sink in standing blood varies; quicker in cat than man. Increased during pregnancy and in pneumonia. May favour tendency to intravascular clotting. Depends, not on the corpuscles, but on some substance present in plasma.]

Antibodies.—Consist of: (1) *Amboceptor*, which is specific, and not destroyed by heat; (2) *Complement*, not specific, and destroyed by heat.

ANTITOXIN destroys invading toxins.

BACTERIOLYSIN or ALEXIN destroys invading bacteria.

HÆMOLYSIN lakes foreign red blood-corpuscles.

AGGLUTININ clumps foreign red blood-corpuscles or bacteria.

PRECIPITIN precipitates foreign proteins.

OPSONIN prepares bacteria, so that they are readily taken up by leucocytes.

All are greatly increased if the foreign substance is injected, in a non-fatal dose.

Tests for Blood.—

1. GUAIACUM TEST.—On shaking with tincture of guaiacum and adding ozonic ether, a blue ring forms at the junction of the two fluids.
2. ADLER'S TEST.—On addition of a few drops of benzidin in glacial acetic acid, and hydrogen peroxide, a blue colour forms.
3. Blood corpuscles can be seen under the microscope.
4. Hæmin crystals (*see* p. 12).
5. Blood spectra (*see* p. 13).

TEST FOR HUMAN BLOOD.—On injection of human blood into a rabbit, the serum of the rabbit develops a specific precipitin for human blood—i.e., a precipitate forms on adding it to human blood, but not to the blood of any other animal (except apes).

THE LYMPH.

The lymph is the fluid contained in the lymph-vessels and thoracic duct, and includes the fluid which bathes the tissues, though some authors exclude the latter. The blood is not in

direct contact with the tissues in most regions, and probably the lymphatic system is also a closed one.

Function of Lymph.—

1. Lymph forms a medium for interchange between blood and cells, oxygen and nutrient material passing from blood via tissue fluids to cells, and tissue fluid receiving waste products from the cells, some of which diffuse directly back into blood capillaries, others into lymph-vessels.
2. Lymph-vessels act as a drainage system, keeping the water content at a constant level. Tissue fluid can interchange its water and dissolved substances in three directions—viz., with capillaries, cells, or lymph-vessels. Especially it drains off toxic matter and particulate foreign bodies.

Composition of Lymph from Thoracic Duct.—Yellowish, alkaline fluid, usually clear, milky just after a meal. It clots on standing. Specific gravity, 1015. Consists of :—

1. Water, 94 per cent.
2. *Proteins*, 4 to 5 per cent (amount being 6 to 8 per cent in lymph from liver, 2 to 3 per cent in lymph from limbs). The proteins are the same as those of plasma.
3. *Fat*, in fine emulsion, amount being increased after a meal.
4. Extractives—e.g., urea.
5. Inorganic salts in same proportion as in plasma.
6. Carbon dioxide in solution.
7. Some lymphocytes, but apparently no blood-platelets.

Mode of Formation of Lymph.—Two theories : (1) Filtration and diffusion, and osmosis—generally accepted ; (2) Secretion.

EVIDENCE IN FAVOUR OF FIRST THEORY.—

1. Pressure in blood capillaries is greater than in tissues, so that fluids may be forced from capillaries into tissues.
2. Conditions that alter blood-pressure in capillaries affect flow of lymph. Capillary pressure is altered more by changes in venous than arterial pressure.
3. Inorganic salts are in same concentration in lymph and plasma, whereas proteins are in smaller concentration in lymph.

OBJECTIONS.—

1. Heidenhain found that occlusion of inferior vena cava

Mode of Formation of Lymph, *continued.*

not only caused increased flow of lymph, but also increased concentration of proteins.

EXPLANATION.—Lymph from liver is more concentrated than from rest of body, and in obstruction of inferior vena cava there is a marked increase of capillary pressure in liver, so that most of increased amount of lymph comes from this organ (Starling).

2. Heidenhain found that injection of certain substances such as peptone or egg-albumen led to increased flow of lymph in greater concentration than usual, while arterial pressure did not increase and in some cases even fell. He supposed they acted by stimulating epithelial cells to secrete.

EXPLANATION.—The substances increased the permeability of the capillaries, there being a temporary rise in portal blood-pressure (Starling). Supported by Popoff, who found that injection of peptone increased flow of lymph from abdominal organs, but not from head and neck. He also observed a rise in portal blood-pressure, dilatation of intestinal vessels, and extravasations in intestine.

3. Injection of crystalline substances such as NaCl or glucose leads to increased flow of dilute lymph without a rise in arterial blood-pressure, so apparently increased flow is not due to increased filtration (Heidenhain).

EXPLANATION.—Starling has shown that intracapillary pressure may be increased, and considers rise of osmotic pressure following injection of these salts leads to hydræmic plethora, followed by increased outflow into lymph-vessels.

4. Asher has shown that stimulation of chorda tympani causes vasodilatation and increased saliva, and increases lymph flow from salivary gland; after atropine there is vasodilatation, but no increase of saliva or lymph. Lymph may therefore be looked upon as a secretion of the active cells, and does not merely depend on increased vascularity.

EXPLANATION.—Koranyi and Starling consider this result is due to breaking down of larger molecules

into more numerous smaller ones, thus increasing osmotic pressure.

Circulation of Lymph.—From periphery to thoracic duct and right lymphatic duct.

CAUSES OF FLOW IN THIS DIRECTION.—

1. DIFFERENCE IN PRESSURE.—The pressure where the thoracic duct opens into the great veins is very low and may be negative ; in the tissues it is considerably higher.
2. MUSCULAR MOVEMENTS. — These compress lymph-vessels, which are valved, and force lymph from periphery. Peristalsis has same effect on lacteals in intestine. Fixing a limb in plaster causes œdema.
3. EFFECT OF RESPIRATION.—During inspiration, intra-thoracic pressure, and consequently pressure on the veins, is diminished, and lymph is sucked into them from thoracic duct. At the same time intra-abdominal pressure is increased, so that lymph is squeezed out into thoracic duct.
4. LYMPH HEARTS.—Occur in frogs, not in mammals.

THE CEREBROSPINAL FLUID.

The cerebrospinal fluid is the fluid in the subarachnoid space surrounding the cord and brain, more at the base of the latter than the vertex. Communicates with ventricles of brain, and extends along cranial and spinal nerves in tissue spaces in their sheaths.

Composition.—(Practically that of Locke's fluid.) A thin, watery fluid, resembling lymph. Alkaline. Specific gravity, 1007. Inorganic salts as in blood plasma. Glucose. Urea. Only a trace of protein (chiefly globulin), much increased in inflammation of meninges. A few leucocytes, also increased in inflammation of meninges. Much CO_2.

Mode of Formation and Course.—Formed from choroid plexus in ventricles, probably by active secretion. Passes by foramen of Majendie in roof of 4th ventricle into sub-arachnoid space, and is absorbed into venous sinuses, probably by Pacchionian bodies, i.e., pear-shaped protrusions of the arachnoid into a sinus.

Blocking of foramen of Majendie causes hydrocephalus (increased fluid in ventricles).

The Cerebrospinal Fluid, *continued.*

Pressure.—Stated to be the same as cerebral venous pressure.

LUMBAR PUNCTURE.—Needle is inserted between 3rd and 4th lumbar vertebræ. At normal pressure, fluid drips out steadily, a drop at a time.

Amount.—About 60 c.c. If fluid escapes—e.g., in fractured base of skull—it can be rapidly replaced, and 200 c.c. may drain off in a day.

Variations in Flow and Pressure.—

INCREASED by: (1) Excess of CO_2 or lack of oxygen in the blood; (2) Anæsthetics; (3) Injection of extracts of choroid plexus or brain tissue; (4) Injection of pituitary extract.

DIMINISHED by: Injection of thyroid extract.]

CHAPTER III.

THE HEART.

Structure.—Shows three layers :—

1. ENDOCARDIUM. — Consists of pavement endothelium resting on a fibrous membrane ; in some mammals Purkinje fibres are also present.
2. CARDIAC MUSCLE.—Consists of oblong cells, faintly striated both longitudinally and transversely, often branching, and probably forming a syncytium, with nuclei at intervals. The muscle is arranged in rings round the ventricles and auricles. There is no connection between the musculature of the auricles and of the ventricles except a band of specialized muscle, the auriculo-ventricular bundle (of His, Kent, or Tawara ; Kent describes a second smaller bundle to the right).
3. PERICARDIUM.—Like endocardium. Fat often present.

Conduction.—The cardiac beat is initiated at the *sinu-auricular node*, a tiny nodule of specialized tissue, a cross between nerve and muscle, very vascular, at the junction of the superior vena cava and right auricular appendix. From this the stimulus passes into the auricular muscle, causing its contraction. It is taken up again by the larger auriculo-ventricular node, in the inter-auricular septum below and to the right of the coronary sinus. From this a bundle of pale muscle (Purkinje fibres, striated at edge only, and beaded), passes down beneath the right side of the septum, then as the A-V bundle passes to the right ventricle, breaks into right and left branches which run beneath the septal endocardium to the apex of the ventricles, and finally is distributed to the ventricular and papillary muscles.

Cooling the sinu-auricular node slows heart-rate ; warming quickens it. No other part of heart responds like this.

Stimulation of excised heart at sinu-auricular node gives a contraction showing normal electrocardiogram ; stimulation elsewhere gives an abnormal reaction.

Injury or disease of the A-V bundle causes heart-block—

Conduction of Cardiac Stimulus, *continued.*

i.e., ventricle does not respond to auricular beats, but beats at a slower rhythm of its own (Stokes-Adams syndrome). Cf. Stannius' experiment in frog's heart: (*a*) Ligature between sinus and auricle—sinus goes on beating, auricle and ventricle stop; (*b*) Ligature between auricle and ventricle—ventricle now resumes with a rhythm of its own.

[Rate of conduction of wave in heart-muscle is 1 metre per second, in A-V bundle 5 metres, but there is delay at the A-V node.
Normally the impulse starts at sinu-auricular node, but it *can* start at the A-V node, or in the Purkinje fibres in the ventricle.]

Events of Cardiac Cycle.—

1. AURICULAR SYSTOLE.—Auricles contract, venæ cavæ distend from back-pressure, blood passes through open tricuspid and mitral valves into ventricles. Time, $\frac{1}{10}$ second.
2. VENTRICULAR SYSTOLE.—Ventricles contract. Apex-beat felt. First heart-sound heard. Auriculo-ventricular valves close, aortic and pulmonary valves open. Blood passes into aorta and pulmonary artery. Time, $\frac{3}{10}$ second.
3. DIASTOLE.—Ventricles cease contracting. Aortic and pulmonary valves close with a snap, causing second heart-sound. Blood is sucked into auricles and ventricles by the negative pressure. Time, $\frac{4}{10}$ second.

Apex-beat.—In 5th left intercostal space, $\frac{1}{2}$ to 1 in. internal to nipple line. Due to: (*a*) Ventricle hardening itself against chest wall; (*b*) Curve of the aorta being opened out by the inflow of blood, causing apex of heart to 'kick'.

May be recorded by cardiograph—a tambour + rubber tube + another tambour with recording lever.

The heart gets smaller from base to apex and from side to side during contraction, but not from back to front.

Heart-sounds.—(Mnemonic: *lub-dup.*) Can be electrically recorded.

CAUSES.—

FIRST SOUND due to: (1) Contraction of ventricle; (2) Tension of chordæ tendineæ. Is audible in an excised beating donkey's heart, when valves cannot be working. Replaced by a murmur when valve is diseased.

SECOND SOUND due to slap of closing aortic and pulmonary

valves. Replaced by a murmur if they are diseased, or held back by a needle.

[A third heart-sound, mid-diastolic, is described (? due to flapping of auriculo-ventricular valves against sides of ventricles).]

Methods of Study of Human Heart:—

Palpation; percussion; auscultation.

Screening with X rays. Changes in size can be estimated thus.

The polygraph. Records, by means of tambours connected by rubber tubes with writing points, the apex-beat (often omitted), the radial pulse, the jugular pulse, and the time simultaneously.

The electrocardiograph.

The output (nitrous-oxide method). (*See* p. 35.)

In the animal heart other methods are available; the frog or tortoise heart will go on beating outside the body, and so will the mammalian heart if perfused with warm Ringer's fluid containing glucose and oxygen. The glucose is gradually used up.

(Ringer's fluid contains NaCl 0·7 per cent, KCl 0·03 per cent, CaCl 0·025 per cent (Howell). Locke's fluid contains also 0·1 per cent glucose.)

Pulse-tracings (*Fig.* 3.)—

RADIAL TRACING.—Taken by Dudgeon's sphygmograph or the polygraph. Shows:—

Percussion stroke—due to ventricular systole.

Dicrotic notch and wave—due to closure of the aortic valves, and rebound of pressure from them when closed.

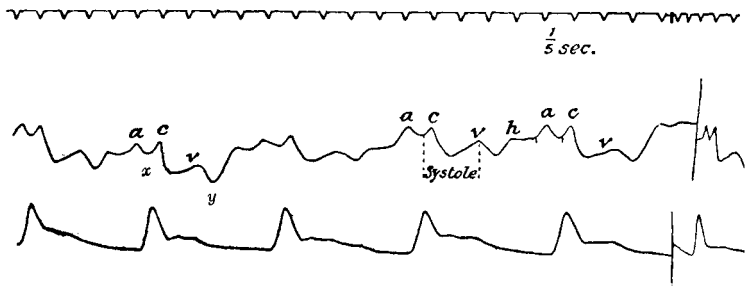


Fig. 3.—Pulse-tracings (human). Top line = time marker. Second line = venous pulse tracing. Third line = radial pulse tracing.

Pulse-tracings, *continued.*

Pre- and post-dicrotic waves—due to instrumental error.

Anacrotic wave, on upstroke—rare and pathological.

The dicrotic wave can often be felt in a very soft pulse, and is shown in a *hæmautogram*—a spouting artery is swung round and the blood-jets write on paper.

JUGULAR TRACING.—Taken on jugular vein in man by tambour. Shows three waves, named *a*, *c*, *v*.

a is due to filling up of vein during auricular systole.

c is due to floating up of cusps of tricuspid valve when ventricle starts contracting (once said to be due to carotid).

v is due to filling of auricle towards the end of ventricular systole.

The *a*–*c* interval, normally $\frac{1}{5}$ second, measures the conductivity of the A-V bundle.

Electrocardiography.—The electrocardiogram (*Fig.* 4) is obtained by means of a string galvanometer, by photography. It shows 3 upstrokes separated by 2 downstrokes, called P, Q, R, S, T.

P is due to auricular systole.

R (a large stroke) is due to ventricular systole.

T is due to return of the wave to the base of the ventricle and the bulbus arteriosus.

Q, R, S, T are all ventricular.

P–R measures the conductivity of the A-V bundle ; normally it is about 0·15 second.

There are several 'leads' in use, the most used being right arm and left leg.

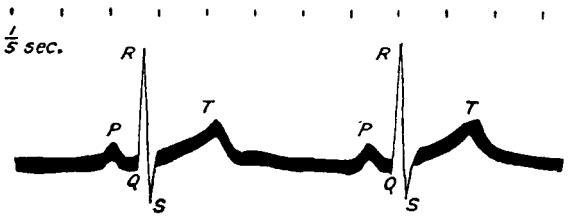


Fig. 4.—Electrocardiogram from human heart.

Properties of Cardiac Muscle.—Heart muscle has the general properties of muscle, with the following special features :—

1. *Rhythmicality*, probably due to inorganic salts in the blood acting on the sinu-auricular node. Calcium promotes contraction, and potassium relaxation.
2. Remarkable resistance to fatigue.
3. Long refractory period (seen in the heart stopped by the first Stannius ligature—no response to a second stimulus too soon after a first).
4. 'Staircase' contractility (also seen in Stannius heart—the 2nd contraction is bigger than the 1st, 3rd bigger than 2nd, and so on for 4 or 5 beats).
5. Long latent period.
6. Cannot be tetanized.
7. 'All or nothing' response—i.e., a weak stimulus either causes a full contraction, or none at all ; whereas with striped muscle contraction increases with strength of stimulus. (This is more apparent than real ; very tiny striped muscles show 'all or nothing', because all the fibres receive the stimulus.)
8. Tone probably absent. Over-distention prevented by the pericardium, and by the following laws of the heart.

Laws of the Heart.—

a. MAREY'S LAW.—Rise of blood-pressure in aorta slows rate of heart-beat (this does not hold in muscular exercise).

b. STARLING'S LAW.—Power of contraction varies with the stretch of the fibres during diastole.

c. BAINBRIDGE'S LAW.—Rate of heart-beat varies with stretch of fibres of right auricle—distention increases pulse-rate reflexly.

These laws may be studied by the *heart-lung preparation* : it is possible to maintain an artificial circulation through the heart and lungs isolated from the body.

Nerves of the Heart.—

THE VAGUS weakens and slows the beat. Section causes heart to beat more quickly. Action is principally, if not entirely, on auricle. May stop heart altogether, but it soon starts again. Governed by the *cardio-inhibitory centre* in region of vagus nucleus in medulla ; heart may be reflexly slowed or weakened through this centre, e.g., by tapping intestines in frog, or by sudden painful impulses in man ; also in psychical fainting. The vagus supplies the heart through the superior, middle, and inferior cardiac nerves on

Nerves of the Heart, *continued.*

each side. Right vagus principally affects rate; left vagus, conduction.

THE SYMPATHETIC strengthens and accelerates the beat; stimulation has this effect, and section causes slowing. It supplies the heart through three nerves on each side, from each of the three cervical ganglia. Eventually it is derived from the white rami communicantes of the 2nd, 3rd, and 4th thoracic nerves.

[Thus the heart-rate and strength of beat are controlled by a balance of these nervous messages. The vagus inhibition acts perhaps by liberating potassium (Howell), or a neurine-like body (Locwi), in the auricle wall; it is accompanied by an electro-positive variation, and has been described as 'anabolic'.]

GANGLIA OF FROG'S HEART.—Remak's, at junction of sinus venosus and auricle. Bezold's, in interauricular septum. Bidder's, in auriculo-ventricular groove.

DEPRESSOR NERVE.—Seen in rabbit, horse, etc.; in carnivora and man is bound up in vagus. Purely afferent; stimulation of central end depresses the vasomotor centre, causing fall of blood-pressure by splanchnic vasodilatation. This allows relief to an overworked heart. (Stimulation of central end of vagus usually causes rise of blood-pressure.)

SENSORY PATH.—Painful sensations can be derived from the heart, probably travelling by the sympathetic.*

ACTION OF DRUGS.—Muscarine, physostigmine, pilocarpine all stimulate vagus nerve-endings, therefore slow or stop the heart. Atropine paralyses vagus nerve-endings, therefore quickens auricle, but does not act on isolated ventricle; it overcomes action of muscarine, etc. Nicotine first slows, then quickens; digitalis slows and strengthens.

Myogenic v. Neurogenic Theories of Heart's Action (i.e., muscle-driven or nerve-driven).—That nerves influence the heart-beat does not prove that they initiate it; the excised heart beats, but that might be due to nerve ganglia inside it.

PRO NEUROGENIC THEORY.—If nerve ganglia are dissected away from heart of *Limulus*, the king-crab, heart

* Recent work by Daniélopolu, of Bucarest, suggests that in man the *accelerator fibres* reach the heart by the rami communicantes of the 2nd, 3rd, and 4th dorsal nerves, the 1st thoracic and inferior cervical ganglia, and the inferior cardiac nerves. The *cardiac sensory fibres* run in the vagus branches to the heart, and the superior, middle, and inferior cardiac sympathetic nerves. All these must be cut to relieve angina pectoris. Daniélopolu advises leaving the inferior ganglion to preserve the accelerators.

stops (but *Limulus* heart-muscle does not conform to properties of cardiac muscle in other respects). There is a point in the interventricular septum a stab of which throws the heart into fibrillary twitchings; but no special nerve structures can be demonstrated there.

PRO MYOGENIC THEORY.—The chick's heart beats before nerves form. Strips of muscle free from nerve-cells can be got to beat, or a heart cut zig-zag to sever all nerves. The atropinized heart beats. Section of A-V bundle stops conduction of impulse, although nerves remain. Undoubtedly, therefore, isolated muscle can beat.

The controversy becomes rather pointless now that we know that the sinu-auricular node is composed of tissue intermediate between nerve and muscle, and containing nerves.

[**Output of Heart.**—

Measured, in animals, by a *cardiometer*—e.g., a glass ball fitted over the ventricles, with a rubber ring to grip the auriculo-ventricular groove, and a tube leading off to a recording drum. The filling and emptying times are much the same; the maximum output per minute is obtained in a fast heart when there is no pause at diastole. Ventricles do not expel every drop of blood.

Output can also be measured directly in the heart-lung preparation.

In man, Krogh's *nitrous-oxide method* is used. Patient inhales air with a known volume of N_2O; the amount retained by the body is estimated. Now solubility of N_2O in blood is known. Hence calculate volume of blood passing through the lungs in the time of the experiment. Divide by number of heart-beats in that time. This gives output per beat. Usually is about 60 c.c. for right ventricle; left must be the same.

More recent is the *ethyl-iodide method*. Calculation similar to N_2O method. In women, average heart output at rest is 100 c.c. (Cullis).

Work of Heart.—Is equal to (i) work done in ejecting a given volume of blood against a known pressure, plus (ii) giving it a definite velocity; i.e.—

$$W = QR + \frac{mv^2}{2g}$$

= 60 grm. × 110 mm. Hg + 60 grm. × $(0{\cdot}5)^2$ metres per sec. ÷ 2 × 981.

Works out at about 100 gram-metres per beat for the human heart at rest.]

Endocardiac Pressure.—Obviously the pressure inside the left ventricle develops just before that in the carotid, and is a trifle higher. The main difference between arterial and intraventricular pressure is that, during diastole, in the artery pressure falls to, say, 80 mm. of Hg, but in the ventricle a negative pressure (suction) is developed, from which the artery is protected by the aortic valves. This is due to the general negative pressure in the thorax determined by the elastic pull of the lungs, and to suction from

Endocardiac Pressure, *continued.*

relaxation of the ventricular wall. (This negative pressure has recently been denied.)

Measured by passing a sound into ventricle through carotid, and recording pressure-changes by a rubber diaphragm with a mirror to reflect light, or using a maximum and minimum valve. (A column of mercury would not react quickly enough.)

Coronary Circulation.—The coronary arteries fill at the beginning of ventricular systole, but the squeeze of the contracting muscle stops the circulation in the arterioles till diastole begins; thus there is a double rise in pressure, the first due to the systole, the second to the shut arterioles and veins. Adrenalin, and the sympathetic, have little or no effect on the coronary circulation. Tying the larger branches of these arteries may stop the heart. Angina pectoris, and sudden death, are often due to partial blocking of these arteries.

When cardiac muscle is starved of blood, or diseased, the proper contractions are apt to be replaced by a state of fibrillary twitching, of course with no driving power.

Pulse-rate. — Normally 70 for men, 75 for women, 120 in infants. Increased by exercise or excitement, or during thyroid intoxication, or fever, or some disturbed cardiac rhythms.

In elephant, 25; dog, 110; mouse, 700.

CHAPTER IV.

THE CIRCULATION.

Structure of Vessels.—

ARTERIES.—Show three coats :—

1. INTIMA.—Pavement endothelium, resting on stout elastic lamina. Purpose of endothelium is to minimize friction, and prevent clotting : if damaged, clotting occurs.
2. MEDIA.—Circular unstriped muscle, mixed with elastic tissue. Purpose of elastic tissue is to convert the pulsations into a steady flow ; of muscle to regulate calibre at need—governed by vasomotor nerves.
3. ADVENTITIA.—Fibrous tissue, to give strength.

In the *aorta*, there are numerous layers of stout elastic laminæ. Large arteries show vasa vasorum in the walls. Arterioles have no elastic tissue.

VEINS.—Show the same layers, but much thinner, and no elastic tissue (except in large veins).

CAPILLARIES.—Show only the pavement endothelium, with a film of connective tissue supporting, and stellate (Rouget) cells, which are contractile, embracing the capillary (*Fig.* 5). It is on account of the elastic tissue in the arteries that the pulse disappears in the capillaries and veins and becomes a steady flow ; but in conditions of vasodilatation, or aortic

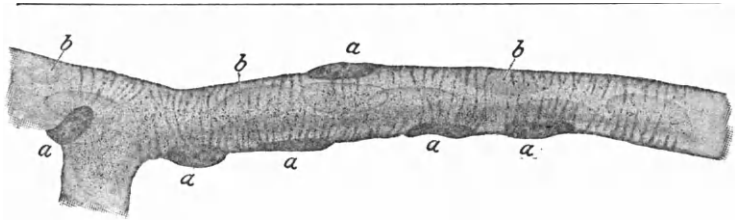


Fig. 5.—Rouget cells on blood capillaries (Winiwarter). a, Rouget cells ; b, Endothelial cell-nuclei.

(*From Krogh Ebbecke's 'Anatomie und Physiologie der Capillaren', Julius Springer, Berlin.*

Structure of Vessels, *continued.*

regurgitation, pulsation may be seen in the capillaries and veins.

[Rhythmical contraction is normally seen in veins of bat's wing.]

Blood-pressure.—In man, about 110 mm. of Hg in arteries (diastolic, about 70); 22 in capillaries; 10 in veins of arm; 5 to −8 in big veins of neck. After middle life pressure rises.

Pressure in veins of legs in man standing is much higher than in arms.

[In dogs, arterial pressure is about 120 mm.; venous pressure in peripheral veins, 4 mm.; venous pressure close to heart, during inspiration, −3 mm.—i.e., a suction is exerted by the thorax.]

METHODS OF DETERMINING BLOOD-PRESSURE IN MAN.—By means of Riva-Rocci *sphygmomanometer*, consisting of rubber bag covered with canvas tied round arm, connected with pressure pump and mercury gauge.

a. Pump up pressure till pulse at wrist just goes and comes back. This gives *systolic pressure* in artery.

b. Pump up pressure till artery is occluded; listen with stethoscope at elbow. Pressure at which sharp sound returns is systolic pressure; then a murmur is heard; then a knocking sound; when this fails, the reading gives *diastolic pressure.*

c. *Pulse pressure* is the difference between systolic and diastolic pressures, and is of great value in showing the power of the heart.

[*Venous Pressure.*—With patient recumbent, elevate limb till distended veins collapse. Height above heart level gives venous pressure in millimetres of blood. Or glass bulb connected with water manometer may be pressed on vein till this collapses (Hooker).

Capillary Pressure.—Oil skin, and watch with microscope under strong light; apply pressure till capillaries are emptied. Methods based on blanching of skin are unreliable, colour of skin depending on other vessels besides capillaries.]

METHODS OF DETERMINING BLOOD-PRESSURE IN ANIMALS.—By means of the *kymograph*, consisting of a T-shaped cannula introduced into an artery (one limb for cleaning out clot), with a tube leading off to mercury manometer; connected by a side-tube with a pressure-bottle; the whole is filled with $MgSO_4$ solution to stop clotting, or hirudin may be injected into the animal. For more accurate work, a Hürthle membrane manometer is used instead of the sluggish mercury column. To read maximal and

minimal pressures, valves may be introduced. The record obtained shows three curves: small curves due to cardiac systoles, larger due to respiratory movements, and very wide ones due to rhythmical vasomotor impulses (Traube-Hering curves).

[In animals inspiration increases blood-pressure, expiration reduces it; but this may be due to artificial respiration, and is not usually seen in man, in fact may be reversed. In animals the rise is due to better filling of heart during inspiration, and opening up of lung capillaries. In man it depends on extent to which pulse-rate is quickened during inspiration by sympathy of cardiac centre with respiratory centre.]

FACTORS REGULATING BLOOD-PRESSURE.—Rate and power of heart; elastic resistance of arterial walls; vaso-constriction of arteries; capillary resistance (capillaries may be open or shut); adrenalin in the circulation.

BLOOD-PRESSURE MAY BE REDUCED BY: Bleeding or fainting; stimulation of vagus (peripheral end); cutting spinal cord high up (cuts off vasoconstrictor impulses descending from centre); stimulation by depressor drugs that depress heart, or by vasodilators (as nitrites); surgical shock, etc.

BLOOD-PRESSURE MAY BE RAISED BY: Intravenous injections; stimulation of sympathetic; exercise; stimulation of medulla; stimulation of splanchnic nerves; injection of adrenalin or pituitary, or drugs such as ergot or digitalis, etc.

Hanging up a hutch rabbit by its ears may make it faint from accumulation of blood in belly; with wild rabbit, vasomotor control and abdominal muscles are too good for this.

Surgical shock is variously attributed to poisoning with toxic products liberated from damaged tissues, loss of muscular tone and of vasomotor control, and accumulation of stagnant blood in peripheral capillaries.

Blood Velocity.—In arteries, about 300 mm. per sec. during systole, 150 per sec. during diastole. In capillaries, 1 mm. per sec. In veins, 60 to 120 mm. per sec.

The slowing in the smaller arteries and capillaries is due to the increase of the total sectional area, which in all capillaries put together is 800 times that of the aorta, becoming reduced again in the larger veins.

METHODS OF DETERMINATION.—In capillaries, by direct microscopic observation. In arteries and veins, by stromuhr,

Blood Velocity, *continued.*

dromograph, etc. The *stromuhr* consists of a pair of bulbs, one containing oil and the other blood, which can be connected with an artery and the bulbs rotated as they fill; requires calibration to get readings. The *dromograph* depends on a needle in a tube tied into the artery; point of needle is deflected by the flow, and deflection shown on a scale.

The time of circulation from one point to another is measured by injecting strong saline; when it arrives at the measured distance, electrical resistance suddenly falls, and time can be recorded. May be measured from aorta to femoral, or round the pulmonary or other circulation. Roughly, complete circulation by quickest route takes 27 heart-beats.

[*Rate of flow in a single organ* can be got by suddenly blocking vein and measuring swelling in plethysmograph (underestimates somewhat).]

[*The velocity of the pulse-wave* is, of course, quite a different thing; it is about 7 metres per second in man.]

Vasomotor System.—

VASOMOTOR CENTRE.—Situated in medulla in floor of 4th ventricle; bilateral; constantly sending out pressor impulses down the cord. High section of cord reduces blood-pressure to about 20 mm. of Hg. Section through upper pons does not alter blood-pressure much. Subsidiary centres exist in spinal cord, for some recovery of blood-pressure takes place in time, after transection.

Stimulation of any sensory nerve causes reflex rise of blood-pressure.

VASOCONSTRICTOR NERVES.—Emerge from cord by white rami communicantes from 1st or 2nd thoracic to 3rd or 4th lumbar nerves. Are derived from lateral horn of spinal cord. May form synapse in corresponding sympathetic ganglion, or run upwards or downwards in sympathetic chain, and synapse in another ganglion. From ganglion starts a post-ganglionic (non-medullated) fibre, which runs in grey ramus communicans to join somatic nerves; in head region, grey fibres form plexus on big arteries; in abdomen, the splanchnics are vasoconstrictor, with cell-stations in ganglia of solar plexus. Twigs finally end in muscle of arterial wall. Most arteries carry a plexus of fine nerve-fibres in the adventitia, partly vasomotor, partly sensory.

PROOFS OF EXISTENCE OF VASOCONSTRICTOR NERVES.—

1. Stimulate cervical sympathetic: rabbit's ear blanches. Cut it: ear flushes.
2. Stimulate splanchnics: intestines and other viscera blanch; spleen or kidney shrinks in an oncometer.
3. Stimulate any somatic nerve, e.g., sciatic: limb shrinks in a plethysmograph (water-filled glass cylinder with rubber dam to fit over arm, connected with water manometer, to register changes in bulk).

(For methods of tracing position of synapses, *see* Chap. XIX.)

These experiments show that the vasoconstrictors are in constant tone. Arteries can, however, recover tone after nerve section.

VASODILATOR NERVES.—Are medullated; come off from central nervous system in all cranial and spinal nerves, by posterior nerve-roots. They show the same nerve-cell and T-shaped junction that fibres of the main sensory neuron do.

PROOFS OF EXISTENCE OF VASODILATOR NERVES.—

1. Stimulate chorda tympani: flushing of submaxillary gland.
2. Stimulate nervi erigentes (1st to 4th sacral): erection of penis.
3. Stimulate sciatic with *slowly interrupted* shocks: limb swells in a plethysmograph. Or cut sciatic, wait a day or two for vasoconstrictors to die, then stimulate: limb swells.
4. Stimulate posterior nerve-roots: vasodilatation occurs.

When any skin area is injured, a reflex vasodilatation occurs. After application of a tourniquet, vasodilatation occurs when it is removed. It is suggested that the axon of a sensory nerve divides, one twig going to the skin and another to the vessels, allowing axon reflexes. Thus irritation of skin may cause vasodilatation in three ways: directly on vessels, by true reflex via spinal cord, or by axon reflex.

Capillary Circulation.—May be seen in web of frog's foot, dog's omentum, frog's tongue, human skin after oiling and with high illumination.

Capillary Circulation, *continued.*

Total capillary area varies exceedingly; may be 800 times that of aorta.

Capillaries may be seen to open out during activity of the part, e.g., frog's tongue when scratched; invisible vessels may spring into sight. After injection of Indian ink, many more capillaries are visible in active muscle than in inactive.

[In brain, all capillaries are always open. May be studied in man by stroking the skin, which leaves a red or white line (tache); lasts a few minutes. This is due to capillary dilatation or contraction, and the latter may resist a blood-pressure up to 100 mm. of Hg. In irritable skins a little lymph may exude along the line and form a wheal (dermatographia). Thus the colour of the skin is due to capillaries; the temperature of the skin to arterioles.

Histamine contracts arteries but dilates capillaries; adrenalin probably contracts them. Either adrenalin or pituitary appears to control capillary tone. Capillaries are supplied by both vasoconstrictor and dilator nerves.]

FUNCTION OF CAPILLARIES.—

1. To contract and dilate. Due either to the Rouget cells embracing them, or to contraction of capillary endothelium.
2. To yield oxygen, amino-acids, sugar, salts, etc., dissolved in water, to the tissues. Some protein also may get through, especially in liver. Dilated capillaries will let starch solution through; after histamine, and apparently in surgical shock, and in some dropsical conditions where capillary wall is starved or poisoned, proteins get through any capillaries, especially if pressure is raised, e.g., in feet, by gravity.
3. To absorb CO_2 and products of tissue katabolism. If methylene blue is injected into pleura, it appears in urine in 5 minutes—proving absorption by blood-stream.

Venous Circulation.—Venous pressure, velocity, and pulse have already been considered.

Venous flow is due to: (1) *Vis a tergo* from heart. (2) Muscular contraction squeezing veins: as they are valved, blood can only advance. Descent of diaphragm acts similarly. (3) Suction from negative pressure in thorax during inspiration.

Some veins have a vasomotor supply, well marked in the portal vein. After hæmorrhage, superficial arm veins are tightly contracted.

Pulmonary Circulation.—Pulmonary artery is said not to be contracted by adrenalin, and probably has no efficient vasomotor nerves. Circulation therefore is largely influenced by systemic circulation—e.g., pulmonary hæmorrhage may be stopped by a systemic vasodilator, such as amyl nitrite. Pulmonary blood-pressure is low, because capillaries are large.

Intracranial Circulation.—Being enclosed in bone, the quantity of blood inside the skull cannot vary, except for trifling changes due to escape of cerebrospinal fluid along nerve-root sheaths, and pulsating fontanelle in infants. If encroached upon by a foreign body, depressed bone, or blood-clot, there must be so much the less blood circulating.

Vasomotor nerves in brain are either feeble or absent; the vasoconstrictor action of adrenalin and acetyl-choline is also feeble or absent.

During activity, or when space is encroached upon as above, brain can only get more blood by increasing *rate of flow* of blood through it; this is effected by generalized vasoconstriction. High blood-pressure after cerebral hæmorrhage may therefore be a protection to the brain, not a disaster.

[There is always a venous pulse in the brain, except under high pressure conditions. Shown by tracings from torcular Herophili.

Intracranial pressure is measured by manometer in a trephine hole. Normally equals venous pressure. Introduction of a very little fluid (or laminaria, which expands when wet) suffices to raise intracranial pressure. If watched through another trephine hole through glass window, it will be seen that, as pressure rises, the brain is first congested, with irritation symptoms, then it suddenly becomes white, with paralytic symptoms.]

Hæmorrhage.—A big loss of blood causes transient fall of blood-pressure, with faintness, soon corrected by generalized vasoconstriction of arteries and veins. Circulating blood is diluted by fluid from the tissues, so specific gravity and hæmoglobin-count fall. Breathing is quick and deep to bring sufficient oxygen to brain. Pulse fast, for same reason. Coagulability of blood rises. During recovery, young reticulated red corpuscles and normoblasts may appear in blood. It takes a few hours to recover blood volume, but weeks to restore hæmoglobin and proteins. Loss of 3 or 4 pints in man is fatal, unless spread over days; often less may suffice to kill. Loss of 1 pint (e.g., for blood-transfusion) does no harm.

CHAPTER V.

THE RESPIRATORY SYSTEM.

Histology.—

TRACHEA shows columnar ciliated epithelium, basement membrane, mucous glands, and horseshoe hoops of cartilage, completed by unstriped muscle.

BRONCHI are similar. They break up into smaller bronchi and bronchioles, lined by non-ciliated cubical epithelium. Outside this is a layer of circular unstriped muscle, function of which is probably to regulate tension of air in infundibulum—i.e., space into which a bronchiole opens.

ALVEOLI are dilatations of wall of infundibulum. Lined by flattened cells. Between adjacent alveoli are numerous capillaries. Surface area of lungs is 90 square metres.

Respiratory Movements.—

NORMAL INSPIRATION.—

1. *Contraction of diaphragm.* Muscular dome moves down more than central tendon.
2. *Elevation of 2nd to 5th pairs of ribs* by external intercostals, interchondrals, and levatores costarum, and at same time outward rotation of them.
3. Lifting forward of sternum by ribs.

Men usually show abdominal, women costal type of respiration; latter said to be due to clothing of civilized women.

FORCED INSPIRATION.—Scaleni, trapezius, sternomastoid, and pectoralis major come into play. Accessory respiratory movements also occur—e.g., opening of external nares and dilatation of glottis.

EXPIRATION.—

1. *Recoil of elastic tissue in lungs.*
2. *Depression of ribs* by costal part of internal intercostal muscles.

FORCED EXPIRATION.—Abdominal muscles come into play.

METHODS OF RECORDING RESPIRATORY MOVEMENTS.—

IN MAN.—Marey's pneumograph.

IN ANIMALS.—

1. *Recording changes of circumference of chest or abdomen.*
2. *Recording changes of pressure in air-passages*, by tube in nose connected with tambour and lever, or connecting nose or trachea with a bottle of air.
3. *Recording changes of pressure in thoracic cavity*, by: (*a*) Cannula inserted into pleural cavity; (*b*) Catheter passed down œsophagus to its intrathoracic portion, so that changes in pressure in mediastinum synchronous with respiration affect œsophagus.
4. *Recording movements of diaphragm*, by lever thrust between liver and diaphragm, or by hooks attached to muscular slips of diaphragm.

Volume of Respired Air.—Measured by a gas metre, the *spirometer.*

TIDAL AIR.—Air breathed in normal inspiration. 500 c.c.

SUPPLEMENTAL AIR.—Air which can be forcibly expelled. About 1500 c.c.

COMPLEMENTAL AIR.—Air which can be inspired after normal inspiration. 1500 c.c.

VITAL CAPACITY.—Amount of air breathed out on deepest possible expiration after taking deepest possible inspiration. About 3500 c.c. in man, smaller in women.

RESIDUAL AIR.—Air left in lungs after most forcible expiration. About 1000 c.c. Estimated by inhaling known volume of hydrogen, and analysing expired air.

MINIMAL AIR.—When thorax is opened, lungs collapse, almost all air being driven out; but as smaller bronchi collapse before alveoli are completely empty, a small amount of air—minimal air—is left.

DEAD SPACE.—The capacity of the bronchial tree. This is about 140 c.c., so that in normal inspiration 360 c.c. of air penetrate to the alveoli.

[**Intrapulmonary Pressure.**—Measured by a water manometer connected to one nostril. Is -1 mm. of water at end of normal inspiration, $+3$ mm. at end of normal expiration. During forced breathing, marked change of pressure may occur.]

Intrathoracic Pressure.—Normally negative, i.e., less than atmospheric; due to elastic recoil of lungs. If chest wall is opened, lung collapses.

MEASUREMENT OF INTRATHORACIC PRESSURE.—

1. *Donder's method.* Manometer attached to trachea, and chest wall opened. In this way, elastic recoil of lungs, and consequently negative pressure, is determined.
2. By thrusting a trocar through chest wall into pleural or mediastinal cavity, the other end being connected with a manometer. Pressure varies from −4·5 mm. of mercury at end of expiration to −7·5 mm. at end of inspiration. At end of deep inspiration, may fall to −30 mm. of mercury. At end of deep expiration, if glottis is still open, pressure is still slightly negative, but if glottis is closed during forced expiration, pressure may become positive. In newborn infant, lungs completely fill chest cavity, and negative pressure is only gradually produced; there is no measurable negative pressure on 4th day.

PNEUMOTHORAX.—Signifies air in the pleural cavity. If opening into pleural cavity is kept patent, lung will collapse completely, and eventually become solid, residual air being absorbed by the blood. Single pneumothorax, if left open, causes shock by displacement of heart and mediastinum. Double pneumothorax is fatal.

Composition of Inspired and Expired Air.—

	Inspired	*Expired*
Oxygen	21 per cent	16 per cent
Carbon dioxide	0·04 „ „	4 „ „
Nitrogen	79 „ „	79 „ „
Water	varies	saturated

Traces of hydrogen and methane are found in expired air. Temperature is raised to that of the body.

VENTILATION.—When CO_2 rises to 4 per cent, symptoms such as cyanosis and dyspnœa occur. CO_2 is apparently the only noxious substance in expired air.

For satisfactory ventilation, 3000 cubic feet of fresh air per hour per person are required. To avoid draughts, 1000 cubic feet of space per person is necessary. Effects of insufficient ventilation are due more to absence of movement in air than to chemical changes. Moving air has stimulating, still air depressing, effect (Leonard Hill).

Temperature and degree of moisture are important, optimum being a temperature of about 65° F. and a relative humidity of about 50 per cent.

RESPIRATORY QUOTIENT (R.Q.).—

$$\text{R.Q.} = \frac{\text{volume of carbon dioxide discharged}}{\text{volume of oxygen retained.}}$$

On ordinary mixed diet—

$$\text{R.Q.} = \frac{4 \text{ per cent}}{21 \text{ per cent} - 16 \text{ per cent}} = \frac{4}{5} = 0{\cdot}8.$$

On diet of carbohydrate only, R.Q. should be 1, because carbohydrates contain enough oxygen to oxidize all the hydrogen. On fats, which are poor in oxygen, R.Q. is only 0·7, on protein about 0·8.

VARIATIONS IN RESPIRATORY QUOTIENT.—Increased in convalescence from wasting diseases, and just before hibernation in animals, when carbohydrate is being stored as fat. Decreased during hibernation, fat probably being converted into glucose. During starvation, high at first while store of glycogen is being used up, low afterwards when energy is derived from fat and tissue proteins.

Determination of Composition of Alveolar Air.—(For R.Q. during exercise and sleep.) Mouthpiece and long glass tube; attached to proximal end is a sampling tube which has been rendered vacuous. At end of normal inspiration, subject expires deeply through mouthpiece, and sample of last portion of air (i.e., alveolar air) is collected. Another sample is taken after a normal expiration. Samples are analysed, and the mean of two results taken.

COMPOSITION OF ALVEOLAR AIR.—Nitrogen, 80·5 per cent; carbon dioxide, 5·5 per cent; oxygen, 14 per cent.

ZUNTZ AND LOEWY'S METHOD OF CALCULATION.—Normal expiration contains 500 c.c., but 140 c.c. of this is from 'dead space', and its composition is practically that of the atmosphere. Expired air contains 4·38 per cent of carbon dioxide. Alveolar air constitutes only $\frac{360}{500} = \frac{18}{25}$ of total air. Hence carbon dioxide in alveolar air is $4{\cdot}38 \div \frac{18}{25} = 6$ per cent.

Gases of the Blood: Estimation of Amount.—

1. IN BULK.—Gases of blood are evolved on exposure to a vacuum. Vacuum is obtained by a mercury gas pump. Kept at body temperature during experiment. All the oxygen and nitrogen and part of the CO_2 are given off under these conditions. CO_2 is absorbed in NaOH or KOH, and oxygen in alkaline solution of pyrogallic acid. Residual gas is nitrogen.
2. BARCROFT'S APPARATUS.—Only a small amount of blood is needed. In each bottle is placed 1 c.c. of blood covered with ammonia. Solution of potassium ferricyanide is added to liberate the oxygen. Difference in level between the two limbs of manometer is amount of oxygen evolved. During experiment temperature is kept constant. Tartaric acid is then added to liberate CO_2. (Oxygen must be estimated before CO_2, because addition of acid to blood leads to evolution of some oxygen.)

PERCENTAGE OF VARIOUS GASES IN BLOOD.—

AVERAGE FIGURES FOR DOG.—

	Oxygen	*Carbon dioxide*	*Nitrogen*
Arterial blood	20	38	1·7
Venous blood	12	45	1 7

HUMAN BLOOD.—Figures vary considerably, especially for venous blood. Hill and Nabarro have found venous blood from limbs contains about 6 per cent oxygen and 46 per cent CO_2, while that of brain contains 14 per cent oxygen and 42 per cent CO_2.

Gaseous Exchange in the Lungs.—Air in alveoli is separated from the blood by the walls of the pulmonary capillaries and by the alveolar epithelium. Exchange of gases probably takes place by process of simple diffusion, depending on partial pressure (*see below*) of the gases. Oxygen in alveolar air is at partial pressure of 100 mm., while that in venous blood is only 37 mm., consequently oxygen passes from alveoli to blood, converting it into arterial blood. CO_2 passes from venous blood to alveoli. Pressure of CO_2 in venous blood is about 45 mm., that in alveolar air about 40 mm.; although this is only a small difference in tension, CO_2 is very easily diffusible.

Partial pressure of a gas in a mixture of gases is the proportion of the total pressure exerted by this gas on walls of containing vessel and surface of fluid: e.g., pure oxygen exerts a pressure of 760 mm., while oxygen in air (about 20 per

cent) exerts a pressure of about $\frac{1}{5}$ atmosphere, i.e., 152 mm. The amount of gas dissolved in water varies directly with the pressure of the gas, provided temperature is constant.

Tension of a gas in a fluid is the tendency of the molecules to leave the fluid. It is determined by exposing the fluid to atmospheres with varying partial pressures of the gas until one is found in which the fluid neither takes up nor gives off the gas—i.e., fluid and gas are in equilibrium. The tension is then equal to the partial pressure of the gas in the atmosphere used.

DETERMINATION OF TENSION OF GASES IN THE BLOOD.—Pflüger's *aerotonometer* was formerly used. Blood was exposed to atmospheres containing different quantities of nitrogen, oxygen, and CO_2, until one was found in which no change occurred after being in contact with blood.

A modern aerotonometer is Krogh's, the tubes feeding which are tied into an artery or vein. Contains a bubble of gas mixture, exposed to a large volume of blood. Bubble can be drawn into capillary tube for analysis.

Theory of Pulmonary Secretion.—Bohr, by his aerotonometer, and Haldane, by a carbon monoxide method, found that the tension of oxygen may be even higher in arterial blood than in alveolar air, especially on mountain-tops (Pike's Peak). This would involve secretion of oxygen from alveolus to blood by pulmonary epithelium. Such secretion certainly occurs in swim-bladder of fish; prick it—fish sinks till it secretes fresh gas, rich in oxygen; cut vagi—no new gas is secreted. However, theory of pulmonary secretion is not generally accepted. The experimental methods used to prove it are thought unreliable.]

Exchange of Gases in the Tissues.—Oxygen passes from plasma to tissues, oxyhæmoglobin being almost completely saturated—i.e., nearly 100 mm. of mercury—while oxygen tension in the tissues is almost zero. CO_2 passes from tissues, where its tension is about 50 to 70 mm., to plasma, where tension is about 35 mm. (arterial). Dissociation of oxyhæmoglobin is probably helped by this increased tension of CO_2.

TISSUE RESPIRATION.—Tissues have a great affinity for oxygen. In animal killed shortly after intravenous injection of methylene blue, blood is found to be blue, but muscles are a normal colour. On exposure to air, tissues become blue, showing that muscles had removed oxygen from the methylene blue.

Tissue respiration may be studied by means of the *micro-respirometer* (*Fig.* 6)—like a double Barcroft apparatus. In

Exchange of Gases in the Tissues, *continued.*

one flask put the living tissue floating in Ringer's fluid, in atmosphere of oxygen, with a trace of NaOH in flask to absorb CO_2. Measure absorption of oxygen by rise of meniscus in manometer. Repeat without NaOH, hence calculating R.Q. of tissue. Minced tissue respires, but not if cell-nuclei are destroyed by grinding with sand. Oxygen can be stored in cells till required.

[NATURE OF OXIDATIONS.—Guaiacum turns blue when oxidized; this needs (i) a ferment, and (ii) a source of oxygen, e.g., a peroxide. Potato contains both, and turns guaiacum blue; horse-radish will not do so until H_2O_2 is added: i.e., both contain a *peroxidase* ferment. Hæmoglobin can act like a peroxidase in presence of H_2O_2, and so may other tissues; but it is not possible to demonstrate peroxides in them. *Glutathione* (cystein and glutamic acid) is present in most tissues—not in blood. It exists in two forms, oxidized and reduced; in life nearly all is reduced. When it is converted into oxidized form, hydrogen is liberated, which in presence of oxygen forms H_2O_2; this, with peroxidases, is available for tissue oxidations.]

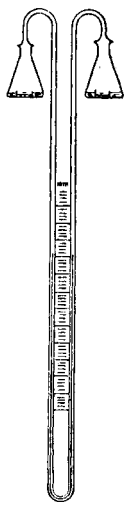


Fig. 6.—The microrespirometer. (*From C. L. Evans' 'Recent Advances in Physiology'.*)

Basal Metabolism.—This means the metabolism when the body is at rest and starving—i.e., the minimum necessary for respiration, circulation, and other essential processes. It is expressed in terms of heat produced. It is proportional to the *surface area* of the individual, not to the weight. Thus corrected, the basal metabolism is fairly constant for normal individuals—namely, 40 calories per hour per square metre of body surface in men, slightly less in women, and about 50 calories in children. For a man of average weight, this means 1700 calories a day.

Basal metabolism is increased in Graves' disease and fevers, reduced in myxœdema and starvation.

ESTIMATION.—Collect expired air in Douglas bag. Analyse for oxygen and CO_2. Result is converted into calories by calculating-tables.

Condition of the Gases in the Blood.—

NITROGEN.—Apparently in simple solution. *Evidence:*

(1) Amount present in blood corresponds with this view;

(2) Varies directly with pressure of nitrogen.

OXYGEN.—100 c.c. of blood contain 20 c.c. of oxygen, 19·7 being combined with the hæmoglobin of the red blood-corpuscles. The remaining 0·3 per cent is dissolved in the plasma according to the ordinary laws of diffusion.

DISSOCIATION CURVE OF HÆMOGLOBIN.—When pressure of oxygen in surrounding air falls below 100 mm., hæmoglobin gives off its oxygen, dissociation becoming much more rapid below 70 mm. Hæmoglobin is nearly completely saturated at pressure of oxygen in atmosphere.

Determined in aerotonometer. Blood is exposed to various partial pressures of oxygen, and then the oxygen in blood is estimated by Barcroft's method.

Dissociation is facilitated by: (1) Presence of CO_2 or other acids; (2) Rise of temperature. Dissociation curve in man is usually determined in an atmosphere containing same amount of CO_2 as alveolar air.

CARBON DIOXIDE.—Only small proportion in simple solution. Mostly combined with sodium as sodium bicarbonate in plasma, remainder possibly being combined with proteins of plasma and hæmoglobin of corpuscles.

POSSIBLE MEANS OF TRANSPORT OF CARBON DIOXIDE.—

1. *Combined with alkaline part of protein of plasma and corpuscles.*—Hæmoglobin has acid properties and combines with alkalis. When CO_2 enters the blood, the theory is that it combines with this alkali, the hæmoglobin being liberated. In the lungs, the compound breaks down, possibly because oxyhæmoglobin has stronger acid properties than reduced hæmoglobin, and the alkali recombines with hæmoglobin, CO_2 being liberated.
2. *Theory based on Hamburger's reaction.*—When blood is exposed to CO_2, some of the chlorine combined with sodium in the plasma diffuses into the corpuscles. This reaction is reversed when pressure of CO_2 is reduced. In the tissues, therefore, chlorine passes to corpuscles and CO_2 combines with sodium, while, in the lungs, chlorine passes back into plasma to form sodium chloride, and CO_2 is liberated.

Regulation of Respiratory Movements.—

1. NERVOUS MECHANISM.—

RESPIRATORY CENTRE.—Situated in floor of 4th ventricle (calamus scriptorius) on either side of mid-line. Destruction of this region, or section of cord between it and origin of phrenic nerves, causes death from cessation of respiration. Respiratory centre sends out rhythmic impulses; in adult about 18 a minute. It is really an inspiratory centre, expiration normally being passive. Active expiration does occur—e.g., in coughing or during parturition—so presumably there is an expiratory centre, probably in medulla.

AFFERENT IMPULSES.—

Along Vagus.—Vagus apparently contains two types of afferent fibres: (1) Inhibiting respiration, stimulated by expansion of lung alveoli; (2) Inspiratory, increasing respiration, stimulated by collapse of alveoli.

Section of both vagi results in respiration becoming much slower and deeper. (This is merely due to narrowing of glottis from double abductor paralysis of cords; not present after tracheotomy—Schafer.) If only one vagus is cut, there may be some slowing and slight deepening of respiration.

Evidence for two types of afferent fibres in vagus:—

a. Electrical stimulation of central end of cut vagus: with weak stimulation, respiration is inhibited; with stronger current, it is increased and diaphragm may remain in inspiratory position.

b. Einthoven's experiment: Vagus nerve is cut, and connected with a string galvanometer. Deflection of thread occurs with inspiration, indicating passage of current, and another electrical variation during expiration.

c. Head's experiment: A slip of anterior part of diaphragm of rabbit is isolated, and fixed to a lever. If lungs are artificially distended, diaphragm becomes relaxed; if lungs are collapsed by sucking air out, diaphragm contracts.

Other Afferent Impulses to Respiratory Centre.—

i. Stimulation of cutaneous nerves—e.g., by a dash of cold water or a painful stimulus. If a child does not breathe at birth, a smart slap with a wet towel often starts respiration.

ii. Stimulation of splanchnic nerves frequently causes temporary arrest of respiration—e.g., a blow on upper abdomen.

iii. Impulses from the larynx, pharynx, and nose due to irritation of the mucous membrane. E.g., crumb in larynx stimulates superior laryngeal nerve, causing inhibition of inspiration, followed by spasmodic forcible expirations, i.e., coughing. Stimulation of glossopharyngeal nerve also leads to inhibition of respiration, e.g., during swallowing. Stimulation of nasal mucous membrane may cause inhibition of respiration ; if the stimulus is a harmful gas, this is a protective mechanism. Sneezing is frequently caused by stimulation of the nasal mucous membrane.

[iv. *Stimulation of walls of external auditory meatus*, as by a plug of wax, frequently results in coughing, owing to irritation of auricular branch of vagus.

v. *Impulses from brain.* There is a certain amount of voluntary control of respiration. Effect on respiration of emotions—e.g., fear, anger, or excitement—is well marked.]

EFFERENT IMPULSES FROM CENTRE.—

a. In 3rd, 4th, and 5th cervical anterior nerve-roots by phrenic nerves to diaphragm. If spinal cord is injured below 5th cervical segment, respiration can still continue.

b. By anterior nerve-roots in dorsal region to intercostal and abdominal muscles.

c. By vagi to muscles abducting vocal cords and widening glottis during inspiration, and to bronchi. Stimulation of vagus causes constriction of bronchioles and diminished air-entry. On section of vagus, bronchioles dilate. Injection of atropine leads to greater air-entry into lungs, while injection of muscarine causes spasm of bronchioles. Irritation of nose causes reflex broncho-constriction. Adrenalin dilates.

Regulation of Respiratory Movements, *continued.*

2. CHEMICAL REGULATION OF RESPIRATION.—Respiratory centre is stimulated by increased CO_2 in blood, and to lesser extent by diminished oxygen. During quiet breathing, CO_2 in alveolar air (and therefore in blood) is very constant, but oxygen may vary. Effect of reduced oxygen is probably due to incomplete oxidation of acids formed in the body and consequently increased H-ion concentration in the blood. Slight rise of CO_2 in alveolar air (with consequent increase of CO_2 in blood) results in increased volume of respired air; e.g., 0·2 per cent rise will double inspired air.

If a number of deep breaths are taken in rapid succession, CO_2 falls markedly, and respiration ceases for a time—i.e., apnœa. Apnœa occurs when tension of CO_2 in blood falls to 19 to 24 mm. (Zuntz).

If breath is held, respiration occurs inevitably in about 30 seconds, CO_2 tension having risen to 6 to 7 per cent. If breathing in and out of a bag, KOH to absorb the CO_2 greatly delays asphyxia, in spite of diminution of oxygen.

CAUSE OF STIMULATION OF RESPIRATORY CENTRE, OTHER THAN BY CARBON DIOXIDE.—

a. During muscular exercise, there is increased formation of lactic acid. If there is insufficient oxygen to oxidize it, it enters blood unchanged, and stimulates respiratory centre.

b. In condition of acidosis, where there is increase of fixed acids of the blood, centre is stimulated, and CO_2 in alveolar air is diminished.

Thus respiratory centre serves to keep H-ion concentration of blood constant, which is of importance, since change in reaction of blood rapidly causes death.

Effects of Increased Oxygen Pressure.—Warm-blooded animals die when oxygen pressure reaches 3 atmospheres—i.e., 15 atmospheres of air.

[**Cause of Respiration at Birth.**—Three views:—

1. *Increased amount of CO_2 in blood, due to interruption of placental circulation.* Evidence: Respiration has been shown to occur in utero, on interruption of placental circulation.
2. *Stimulation of skin.* Evidence: On stimulation of skin in utero with placental circulation intact, respiration has occurred.
3. *Combination of the two factors.* Probably correct, interruption of placental circulation being chief factor.]

Asphyxia.—Signifies the phenomena occurring when there is a lack of oxygen in the blood, probably partly due to increased CO_2. Three stages seen :—

1. STAGE OF INCREASING DYSPNŒA.—Lasts ½ to 1 minute. (*a*) Increased rate and depth of respiration, leading to difficulty in breathing (dyspnœa) ; (*b*) Exaggerated movements of inspiratory muscles, soon replaced by exaggerated expiratory ones ; (*c*) Rise of blood-pressure, consequently heart beats quicker and more forcibly ; (*d*) Animal becomes blue and consciousness is lost ; (*e*) Pupils are equally contracted.
2. STAGE OF EXPIRATORY CONVULSIONS.—Lasts about 1 minute. (*a*) Marked expiratory efforts ; (*b*) Convulsive movements of limbs accompanying expiratory efforts ; (*c*) Blood-pressure gradually falls owing to failure of heart from lack of oxygen.
3. STAGE OF EXHAUSTION.—Lasts about 3 minutes. Animal lies still except for occasional deep inspiration. Blood-pressure falls, but on a tracing shows several curves, Traube-Hering curves, due to vasoconstrictor impulses. Pupils dilated.

POST MORTEM.—Great veins and right heart distended with dark fluid blood ; lungs distended, often small hæmorrhages. Left heart and arteries empty (except pulmonary artery).

Apnœa.—Temporary arrest of respiration. There are three types :—

1. APNŒA VERA.—Produced by rapid and deep respiration, so that all CO_2 is removed from alveolar air. Condition can be cut short by blast of CO_2 into the lungs. If CO_2 in inspired air is increased to 4·5 per cent, apnœa cannot be produced.
2. VAGAL APNŒA.—Results from rapid inflation of lungs with air, and is said to be due to stimulation of endings of vagus nerve. There is also a chemical factor, since it cannot be produced by inflation with CO_2. Apnœa is much more difficult to produce after section of vagi.
3. APNŒA SPURIA.—Due to stimulation of sensory surface. When duck plunges into water, respiration stops, and remains arrested while it is under water.

CHEYNE-STOKES RESPIRATION.—Consists of groups of about 10 to 30 respirations, separated by apnœic periods of about 30 seconds. After each pause, respiratory movements are at first small, increase to maximum, and then diminish to next pause. Seen in cases of intracranial

Apnœa—Cheyne-Stokes Respiration, *continued.*

pressure, or when respiratory centre is oxygen-starved, or in sleeping children.

[Eyster has divided cases of Cheyne-Stokes respiration into two types: (1) Dyspnœic phase accompanied by fall in blood-pressure and pulse-rate; (2) Dyspnœic phase accompanied by rise in blood-pressure and pulse-rate. The latter contains cases with evidence of increased intracranial tension.]

EXPLANATION OF CHEYNE-STOKES RESPIRATION.—The apnœa is due to washing out of CO_2 in lungs. During apnœic phase, oxygen in blood decreases, rendering respiratory centre more sensitive, and at the same time CO_2 in blood is increasing. Respiration recommences, until CO_2 again diminishes, and also oxygen inspired lowers excitability of centre, and respiration again ceases. The apnœic phase is relieved by giving oxygen or CO_2.

Effects of Changes in Barometric Pressure.—

1. INCREASED PRESSURE.—Pressure greater than 5 atmospheres is dangerous.

CAISSON DISEASE.—Occurs on too sudden return to normal pressure. Due to blocking and rupture of capillaries by sudden evolution of gases dissolved at high pressure.

Symptoms.—(*a*) Paralysis; (*b*) Pain in muscles, joints, and abdomen; (*c*) Collapse.

2. DIMINISHED PRESSURE.—

MOUNTAIN SICKNESS may occur on ascending from sea level to height of about 10,000 ft. Symptoms appear when oxygen pressure falls below 13 to 15 per cent, varying with individuals. Probably due to lack of oxygen, though diminution of CO_2 has been suggested as the cause (Mosso).

Symptoms.—(*a*) Urgent dyspnœa; (*b*) Muscular prostration; (*c*) Nausea and vomiting. These symptoms are more marked after muscular exertion. At greater heights, there is inability to move or speak; then loss of consciousness, and death. May be imitated in laboratory by reducing oxygen breathed, or in carbon monoxide poisoning.

ADAPTATIONS IN BODY WHEN LIVING AT HIGH ALTITUDES.—(*a*) Increased rate and depth of respiration, even at rest; (*b*) Increased heart-rate, and slightly increased systolic blood-pressure; (*c*) Gradual increase in number of red blood-corpuscles. Also occurs in diving birds.

CHAPTER VI.

VOICE.

Structure of Vocal Cords.—Thick bands of yellow elastic tissue covered with stratified epithelium. In man they are about 15 mm. long, in woman about 11 mm.

Ventricles of larynx act as resonating chambers, aided by nasopharynx, mouth, and accessory sinuses of nose.

Laryngoscope.—Mirror used to examine larynx; gently presses up the soft palate. False vocal cords appear pink, true vocal cords white. Normally opening of glottis is wide and triangular. On deep inspiration cords move farther apart, and may move slightly on normal respiration.

Voice Production.—When note is produced, vocal cords are brought together and vibrate. They are adducted by the lateral crico-arytenoid muscles, abducted by the posterior crico-arytenoids.

LOUDNESS.—Depends on force of expiration.

PITCH.—Depends on :—

1. LENGTH OF CORDS.—In children these are short, and pitch is high, but at puberty larynx increases in size, especially in the male, and the boy's voice 'breaks', i.e., becomes lower.
2. TENSION OF CORDS.—Increased by crico-thyroid muscle, which separates points of attachment of vocal cords. Decreased by thyro-arytenoid muscles, which approximate points of attachment.

QUALITY.—Depends on resonating chambers.

Nerve-supply of Larynx.—Cricothyroid by external laryngeal nerve. Intrinsic muscles by recurrent laryngeal nerve.

PARALYSIS OF RECURRENT LARYNGEAL NERVE.—Although all intrinsic muscles are paralysed, abductors are affected first, and cord assumes a more median position.

Speech.—

CONSONANTS.—Produced by various settings of the mouth, lips, etc.—e.g., explosives such as *p* (closed lips burst open)

Speech—Consonants, *continued.*

and *t* (with tongue at root of teeth); *b* and *d* are similar with voice sound added; *m* sound escapes through nose with lips closed; *n* sound escapes through nose with tongue to teeth; *h* is merely an expiration; *f* is an expiration with upper teeth to lower lip; etc.

VOWELS.—A vocal-cord sound, with mouth and throat set in a particular position to act as a resonator. Shown by bringing F tuning fork to mouth shaped for *oo*—the *oo* sound is produced by resonance.

WHISPERING.—This is possible with larynx excised.

FALSETTO.—Vocal cords vibrate in short segments.

CHAPTER VII.

MOVEMENTS OF THE ALIMENTARY CANAL.

MASTICATION.

Mechanism.—

a. TEARING MOVEMENTS by incisor teeth, which involve elevation, protrusion, and retraction of lower jaw.

b. GRINDING MOVEMENTS between molar teeth, due to elevation, protrusion, retraction and side-to-side movements of lower jaw.

All the movements in (*a*) and (*b*) are innervated by the inferior maxillary branch of the 5th nerve.

c. Movements of tongue and muscles of cheek serve to keep food properly placed for action of teeth and for swallowing.

Function.—To reduce food to minute subdivision so that there is a large area for action of gastric juice.

DEGLUTITION, OR SWALLOWING.

Observed by X rays while swallowing barium meal.

Stages.—Three in number :—

Stage 1 : PASSAGE OF FOOD FROM MOUTH TO PHARYNX.—Voluntary. Food is collected in a bolus on dorsum of tongue. Tongue is pressed up against palate, from before backwards, and bolus of food driven past anterior pillars of fauces.

Stage 2 : PASSAGE FROM PHARYNX TO ŒSOPHAGUS. —Involuntary. Due either to : (*a*) Action of constrictor muscles ; or (*b*) Series of sharp short contractions of mylohyoid muscles. Latter is probably correct view. Tongue being drawn farther back helps in process.

MODE OF PREVENTING FOOD ENTERING NOSE OR LARYNX.—

Posterior Nares.—Protected by elevation of soft palate by levator palati muscle, supplied by 10th

Deglutition—Stage 2, *continued.*

nerve. If this nerve is paralysed—e.g., after diphtheria—food regurgitates into nose.

Superior Aperture of Larynx.—(*a*) Larynx is raised under back of retracted tongue; (*b*) Superior aperture of larynx is closed by aryteno-epiglottidean muscular ring; (*c*) Arytenoid cartilages are internally rotated, approximated, and drawn forwards, so that glottis becomes a T-shaped slit.

Stage 3: PASSAGE DOWN ŒSOPHAGUS.—Involuntary.

LIQUID FOOD.—May pass straight down to lower end of œsophagus, owing to original contraction of mylohyoid and pharyngeal constrictors, and may pass immediately into stomach, or be forced slowly in by peristalsis.

SOLID FOOD.—Carried down by peristaltic waves of the œsophagus, consisting of: (*a*) Wave of relaxation; followed by (*b*) Wave of contraction. A wave of peristalsis takes about 6 seconds in passage down œsophagus. Food may be held up at the cardiac orifice until a peristaltic wave reaches orifice; then cardiac sphincter is inhibited, food passes through, and orifice closes again. A second peristaltic wave usually occurs to sweep on any remains.

Nervous Control of Deglutition.—The 2nd and 3rd stages are essentially reflex.

SENSORY.—Sensory area is in neighbourhood of tonsils and fauces.

AFFERENT NERVES.—Chiefly glossopharyngeal and superior maxillary. Stimulation of central end of the glossopharyngeal nerve will reflexly inhibit respiration at any phase, to allow food to be swallowed.

CENTRE.—Possibly in medulla, but its existence is uncertain.

EFFERENT NERVES.—Chiefly vagus; to some extent the 5th. The motor impulse is transmitted from cell to cell in the vagus nucleus, so that one segment after another of œsophagus will contract.

EVIDENCE.—

1. If vagus is cut, swallowing is paralysed, but cardiac sphincter is contracted. On stimulation of peripheral end of vagus, œsophagus contracts and cardiac sphincter is inhibited.
2. If œsophagus is cut, but vagi are intact, bolus of food falls out of cut end, but peristalsis jumps the gap.

3. In condition of cardiospasm, vagal fibres are supposed to be paralysed; œsophagus is paralysed and greatly dilated, and sphincter contracted.

Thus mechanism of swallowing is neurogenic, and quite unlike that of the small intestines.

In animals, a few days after section of vagi, power of swallowing returns, so apparently muscle acquires control apart from nerve.

During vomiting, peristalsis in œsophagus is reversed.

THE STOMACH.

Structure of Stomach Wall.—

1. MUCOUS MEMBRANE (*see* DIGESTIVE SYSTEM, p. 71).—Beneath it is the muscularis mucosæ.
2. SUBMUCOSA.
3. MUSCLE.—Three layers:—
   i. OUTER LONGITUDINAL LAYER.—Continuous with that of œsophagus and small intestine. Thick at curvatures.
   ii. CIRCULAR OR INTERMEDIATE LAYER.—Thin at fundus, thick at pylorus, especially pyloric ring.
   iii. OBLIQUE OR INTERNAL LAYER.—Very incomplete.

Nerve-supply.—

1. VAGI.—Increase contractions of all or part of musculature of stomach.
2. SPLANCHNICS.—In wall of stomach are two plexuses consisting of finely medullated nerve-fibres and some nerve-cells: (i) Auerbach's, between longitudinal and circular coats; (ii) Meissner's, in submucosa. The splanchnics are mainly inhibitory, but cause constriction of pylorus.

Methods of Studying Stomach.—

1. X-ray observation after barium meals.
2. Washing out stomach contents at varying periods after meals.
3. Watching gastric movements with abdomen opened (greatly hampered by anæsthetic).
4. Passing tambours or balloons into stomach through fistulous opening or œsophagus, and measuring pressure changes.

Movements of Stomach.—When food enters the stomach, the organ relaxes sufficiently to contain the food swallowed without tension. In health, we are not conscious of this

Movements of the Stomach, *continued.*

act, but when tone is disturbed there are complaints of flatulence, and a feeling of fullness.

MOVEMENTS OF STOMACH AND DUODENUM AS OBSERVED UNDER X RAYS AFTER BARIUM MEAL.—Meal flows into stomach along longitudinal rugæ, and more or less completely fills it, except that fundus is occupied by an air-bubble. The stomach shows two types of movement: systole-diastole, and peristalsis. During gastric systole waves of peristalsis are deep; during diastole they are shallow. Meanwhile, fundus is exerting a steady pressure on gastric contents. From two to four waves of peristalsis may usually be seen at a time, starting about middle of body of stomach and advancing on a straight front towards pylorus. Naturally they travel faster on the greater curvature than on the lesser. Each fourth wave, or thereabouts, during a gastric systole, opens the pylorus, and a gush of contents passes through and fills first part of duodenum (the duodenal cap). When it is well filled it contracts and contents pass through rest of duodenum at a rush, assuming a feathery appearance as they do so. The meal then traverses jejunum at a good pace, in feathery form.

Emotion, fever, or hard substances in the stomach make for delay in emptying; in first two by feeble peristalsis, in last by pyloric spasm in face of vigorous and painful peristalsis.

TYPES OF NORMAL STOMACH.—Two types are described with all grades between:—

1. TONIC TYPE.—Empties in 1 to 2½ hours after an ordinary meal. Associated with high gastric acidity.
2. ATONIC TYPE.—Takes 3 to 4 hours after a meal to empty. Associated with low gastric acidity.

ACID CONTROL OF PYLORUS.—In animals, emptying of stomach is controlled by pyloric sphincter. For relaxation of pyloric sphincter: (1) Duodenal contents must be alkaline; (2) Food in pyloric part of stomach must be well mixed with gastric juice and acid in reaction. If solid food comes in contact with it, closure occurs. When the acid chyme enters the duodenum, pyloric sphincter closes until the acidity has been neutralized by pancreatic and intestinal juices; then sphincter opens if gastric contents are acid.

[The mechanism is apparently different in man, as alkalis introduced into the duodenum through a swallowed duodenal tube do not cause visible opening of the pylorus, as observed under X rays.]

Vomiting.—

CAUSES.—

1. Irritation of mucous membrane of stomach by irritating particles, drugs, etc.
2. Obstruction lower down in alimentary tract.
3. Reflex from almost any abdominal viscus.
4. Psychic and chemical influences acting on vomiting centre.

MECHANISM.—

1. Contraction of abdominal muscles and diaphragm.
   Proof.—In some animals vomiting can be obtained if stomach has been replaced by a bladder.
2. Contraction of stomach by retroperistaltic waves (i.e., reverse way to normal), and relaxation of cardiac orifice. Stomach peristalsis is probably strong enough to force contents up œsophagus.
   Proof.—During an operation, with peritoneal cavity laid open and muscles retracted, vomiting may occur.

REFLEX CHARACTER.—Vomiting is a reflex act, and involves :—

1. AFFERENT IMPULSES.—Most commonly from mucous membrane of stomach by sensory fibres of vagus, but may come from almost any system of the body. (Section of splanchnic nerves will abolish gastric pain, but not vomiting.)
2. VOMITING CENTRE.—Not definitely located, but probably near respiratory and vasomotor centres in medulla.
3. EFFERENT IMPULSES.—Pass by vagus, phrenics, and spinal nerves to abdominal muscles.

CONDITIONS ACCOMPANYING VOMITING.—

1. Retching, i.e., spasmodic contraction of diaphragm.
2. Nausea.
3. Reflex flow of saliva and increased bronchial and tracheal secretions.
4. Sweating, pallor, and feeble pulse.

THE SMALL INTESTINE.

Structure.—

1. MUCOSA.—Shows columnar epithelium, villi, and tubular glands (the crypts of Lieberkühn). Between the glands are collections of lymphoid tissue (Peyer's patches).

The Small Intestine—Structure, *continued.*

2. SUBMUCOSA.—Separated from mucosa by double layer of muscle, the muscularis mucosæ. Contains fibrous tissue, blood-vessels, and lymphatics.
3. MUSCULAR COAT.—Consists of outer longitudinal fibres, inner circular ones.
4. PERITONEUM.

Nerve-supply.—Right vagus and splanchnics through the solar plexus.

In the wall are two plexuses: (1) Auerbach's between circular and longitudinal coats—nerve-strands stout; (2) Meissner's in submucous coat—nerve-strands slender. These can be stained with gold chloride to show the cords, or with Bielchowsky's stain to show the nerve-cells.

Methods of Studying Movements of Small Intestine.—

1. Direct inspection in an anæsthetized animal.
2. Inserting a balloon connected with a recording tambour.
3. Barium meal and X rays.

Movements of Small Intestine.—(1) Peristalsis; (2) Segmentation; (3) Pendulum movement, due to combined effect of peristaltic and segmental movements. Small intestine is in almost continuous movement, but in lower part it is more quiescent.

1. PERISTALSIS.—Consists of succession of waves passing slowly along intestine. Each wave consists of: (*a*) Wave of relaxation; followed by (*b*) Wave of contraction. Excitation of any point of intestine is followed by contraction above and relaxation below point of stimulus.

   Peristalsis can be stimulated by: (*a*) Bolus of food or other material; (*b*) Distention by gas; (*c*) Flicking of the intestine.

   Normal wave of peristalsis is a few inches in length, and travels at rate of 1 inch a minute. When wall of intestine is irritated—e.g., by a purge—wave of peristalsis may pass whole length of intestine.

   The food moves forwards and then a little backwards.

   PERISTALSIS NORMALLY PASSES DOWNWARDS.—Proofs:

   a. Mall's experiment.—He removed a piece of intestine and sutured it in position again with end towards stomach. Death occurred, and post-mortem showed food accumulated at head of reversed piece of intestine.

b. If piece of small intestine is resected, tied at both ends, and left in abdomen, and the continuity of the bowel restored, the animal dies in 48 hours from toxæmia. Shows contents of intestine must be kept moving.

2. SEGMENTATION.—Rhythmical local contractions of circular muscle, dividing intestine for the time being into segments. Constrictions occur in the centres of segments, dividing them into two, but halves soon unite by relaxation of original contraction.

FUNCTIONS OF SEGMENTATION.—(*a*) Aids digestion by causing thorough mixture of food with digestive juices; (*b*) Facilitates absorption. During six rhythmical contractions, there is no progress of the food.

Nervous Control of Small Intestine Movements.—

Stimulation of vagus increases tone of intestinal muscle and increases peristalsis.

Stimulation of splanchnics decreases muscular tone, but contracts pyloric and ileocæcal sphincters and arterioles.

If all nerves are cut, peristalsis continues, but is abolished by painting with nicotine, which paralyses the plexus in the wall.

Contraction of circular muscle is neurogenic; of longitudinal muscle, myogenic.

Action of Drugs on Intestine.—

ATROPINE paralyses circular coat, but does not affect longitudinal.

PHYSOSTIGMINE stimulates nerve-endings of vagus.

PITUITARY increases contraction by direct action on muscle fibres.

COCAINE paralyses sensory nerve-endings.

OPIUM diminishes peristalsis by a central action.

Sphincters of Alimentary Canal.—There are 4 generally recognized: (1) Cardiac; (2) Pyloric; (3) Ileocæcal; (4) Anal.

[Keith describes 3 others, situated at: (1) Duodenojejunal junction; (2) Middle of transverse colon; (3) Pelvirectal junction.]

When food passes through one of these, there is a tendency for peristalsis to open the next. This accounts for tendency for defæcation to occur after a meal. Similarly many conditions low down in alimentary tract result in reflex delay in emptying of stomach, with pain and vomiting.

Sphincters of Alimentary Canal, *continued.*

ILEOCÆCAL SPHINCTER OR VALVE.—Acts almost entirely as a sphincter. Is a distinct thickening of circular muscle of intestine. Is ordinarily shut, but relaxes on receipt of reflex from stomach. It opens 2 to 3 minutes after the taking of food, and remains open about 20 minutes. This has been observed directly in man, in a patient with extroversion of the cæcum.

THE LARGE INTESTINE.

Structure.—

1. MUCOUS MEMBRANE.—Epithelium similar to that of small intestine. No villi. Contains smaller collections of lymphoid tissue, solitary follicles.
2. SUBMUCOSA.
3. MUSCULAR COAT.—Characterized in man by three bands of longitudinal muscle, the tæniæ coli. Otherwise musculature is similar to that of small intestine.

Movements.—

1. Chiefly mass peristalsis, which occurs about 3 to 4 times in the 24 hours, usually after food, and moves contents about 18 inches. May be observed by X rays; has been seen at operations.
2. Occasional movements of antiperistalsis, especially in ascending colon.

Time Taken by Barium Meal in Passing.—Head of column reaches cæcum in 4 to 4½ hours; splenic flexure in 9 to 10 hours; pelvic colon in about 24 to 36 hours. Meal is all out of ileum in 9 hours. Small foreign bodies pass through in 24 hours, or more often in 48 hours.

Nervous Control of Large Intestine.—

1. From lumbar sympathetic, by way of hypogastric plexus. Inhibits peristalsis.
2. Motor supply from 2nd, 3rd, and 4th sacral nerves. They stimulate peristalsis.

Defæcation.—There is disagreement as to whether fæces are or are not always present in the rectum.

MECHANISM.—A reflex more or less under control of the brain. Rectum becomes full of fæces, and normally at same time there is mass peristalsis in colon.

1. Sensory impulse passes up 3rd and 4th sacral nerves.

2. Centre in spinal cord, in region of 3rd, 4th, and 5th sacral segments, is stimulated.
3. Efferent impulses pass down the same nerves, causing contraction of rectum. At same time the sphincters are inhibited by sympathetic nerve. The act is aided by voluntary contraction of diaphragm and abdominal muscles.

CHAPTER VIII.

THE DIGESTIVE SYSTEM.

ENZYMES.

Many chemical changes in the body are due to the activity of these agents.

Characteristics of Enzyme Action.—

1. Specific action—e.g., trypsin hydrolyses proteins but has no effect on fats.
2. Act on unlimited quantity of material, provided products of reaction are frequently removed.
3. Enzyme is not destroyed in process.
4. Have an optimum temperature, and also an optimum H-ion concentration—i.e., some act better in an alkaline, some in an acid medium. Most act in solution.
5. Destroyed by boiling.
6. No enzyme has yet been isolated. They are possibly protein in nature.
7. Rate of reaction is proportional to amount of enzyme present.
8. *Have reversible reactions* in some cases—e.g., maltase converts maltose into glucose, but maltase acting on strong solution of glucose may form maltose.

SALIVARY GLANDS.

The parotid, submaxillary, and sublingual glands.

Structure.—They are compound racemose glands—i.e., they may be compared to a bunch of grapes, stem and branches representing the ducts, and grapes the acini or alveoli. Closely packed spherical alveoli, bound together by connective tissue. Mucous glands show darker-staining cells forming crescents at the periphery of the alveoli.

CELLS OF SEROUS GLANDS.—

a. RESTING.—Show numerous fine granules, especially near lumen.

b. ACTIVE.—Fewer granules, especially at periphery; nucleus nearer centre of cell.

CELLS OF MUCOUS GLANDS.—
Filled with large granules—mucinogen granules. Nucleus peripherally placed.

PAROTID is almost entirely serous.

SUBLINGUAL, chiefly mucous.

SUBMAXILLARY, in man mixed ; in dog mucous.

Nerve-supply.—All three glands have a double nerve-supply. The *submaxillary* and *sublingual* are supplied by the chorda tympani, which leaves the facial nerve and runs down in the lingual ; the *parotid* by glossopharyngeal, by way of the tympanic branch, small superficial petrosal, otic ganglion, and auriculotemporal nerve ; these nerves carry vasodilator and secretory fibres. The sympathetic supplies all three glands, carrying vasoconstrictor fibres, but very little secretion is produced.

Secretion of Saliva.—Probably a nervous reflex : (1) Afferent nerves are those of sight, smell, and taste ; (2) Centre in brain ; (3) Efferent nerves to salivary glands.

PROOFS OF NERVOUS CONTROL.—

1. Results of stimulation of peripheral end of cut chorda tympani : (*a*) Copious, dilute saliva ; (*b*) Vasodilatation of gland ; (*c*) Increased flow of lymph from gland.
2. Stimulation of chorda tympani after giving atropine to paralyse its sensory nerve-endings results in vasodilatation, but no secretion of saliva and no increased lymph-flow.
3. Stimulation of sympathetic results in a few drops of mucous saliva and vasoconstriction.
4. Action of Drugs.—
   Atropine stops secretion by paralysing nerve-endings.
   Pilocarpine increases secretion by stimulation of nerve-endings.

PROOFS THAT SECRETION OF SALIVA IS NOT A PURELY VASOMOTOR PHENOMENON, BUT INVOLVES VITAL ACTIVITY OF SALIVARY GLANDS.—

1. Saliva continues to be secreted even if pressure in duct is higher than blood-pressure.
2. After atropine, vasodilatation takes place, but no secretion.

PARALYTIC SECRETION.—If the chorda tympani is cut, a continuous flow of saliva takes place.

Salivary Glands, *continued.*

Composition of Saliva.—A colourless, turbid or slightly viscid fluid; slightly alkaline; specific gravity 1002 to 1005. Contains :—

Water, about 99 per cent.
Ptyalin, a ferment.
Mucin.
Inorganic salts, chiefly calcium, potassium, and magnesium salts—carbonates, phosphates, sulphates, and chlorides.
Tendency exists to deposit calcium phosphate and carbonate as a calculus in the ducts, or tartar on teeth, but they are usually kept in solution, probably by the large amount of CO_2.
Traces of potassium sulphocyanide (gives red colour with ferric chloride).
May contain a few loose squamous cells from buccal cavity, and granular spherical corpuscles which are probably altered leucocytes, also bacteria and food débris.

Saliva from parotid gland is rich in ptyalin, but contains no mucin. Saliva from submaxillary glands just the reverse.

[*Pawlow's Work on Saliva.*—Type of saliva secreted depends on kind of food taken :—
1. *Dry food* (e.g., biscuits) causes large flow of parotid type of saliva with much ptyalin.
2. *Meat* causes saliva rich in mucin.
3. *Gravel.* Large quantity of watery saliva is formed to assist in spitting out the gravel.
4. Food containing much water needs little saliva.]

Functions of Saliva.—

1. To moisten mouth and tongue and to assist speech.
2. To moisten food so as to form a convenient bolus and lubricate the bolus.
3. To bring about action of ptyalin on starch, gradually converting it into maltose. Stages: (*a*) Starch; (*b*) Soluble starch; (*c*) Erythro-dextrin—reddish colour with iodine; (*d*) Achroö-dextrin—no colour with iodine. End-result is $\frac{4}{5}$ maltose, $\frac{1}{5}$ achroö-dextrin.

Characteristics of Action of Ptyalin.—

1. Requires neutral medium.
2. Optimum temperature 40° C.; destroyed at 65° to 70° C.
3. Action on cooked starch much more rapid than on raw starch.
4. 1 minim of saliva will act on 1 lb. of starch, if sufficient time is allowed.

Action of ptyalin usually continues for about 1 hour in fundus of stomach before it is arrested by acid of gastric juice.

THE STOMACH AND ITS SECRETION.

Structure of Gastric Mucous Membrane.—Contains an immense number of tubular glands, like test-tubes. The deeper part of each gland is lined by cuboidal cells containing granules (less numerous after vigorous secretion). The mouths of the glands are lined by columnar epithelium forming a sort of duct. The glands also show *oxyntic* or *parietal* cells, found in body of stomach, especially middle half; they are larger and darker staining, and are supposed to secrete the HCl, being present only in that part of the stomach which forms HCl. Between the glands is connective tissue and a free supply of blood-vessels.

Control of Gastric Secretion.—Regulated by: (1) Nervous mechanism—a reflex; (2) Chemical mechanism.

1. NERVOUS MECHANISM.—

SECRETORY NERVE.—The vagus. Evidence:—

Pawlow's Experiment.—Œsophagus of dog is cut across and open ends are sewn to the skin, so that no food can enter the stomach. Part of the stomach is isolated so as to preserve its vessels and nerves intact, and made to communicate with the surface of the abdominal wall.

a. On giving food to swallow, there is copious flow of gastric juice, although food given falls out of cut end of œsophagus.

b. Section of both vagi abolishes secretion of juice.

c. If one vagus is cut, and 48 hours later, when cardio-inhibitory fibres have degenerated, peripheral end is stimulated, there is flow of gastric juice, after a latent period of 5 minutes.

STIMULATION OF SECRETION (AFFERENT PATH).—Note that:—

a. Stimulus is mainly *psychical.* Due to sensations of taste, odour, etc.

b. Introduction of undigested foods or mechanical objects into stomach has no effect.

c. Reflexes farther down alimentary canal to some extent influence secretion of gastric juice—

Control of Gastric Secretion, *continued.*

e.g., in chronic appendicitis there may be hyperchlorhydria.

2. CHEMICAL MECHANISM.—If certain extractives or dextrin are applied to the pyloric end of the stomach there is a copious flow of gastric juice. It has been stated that a chemical substance, *gastrin* or *gastro-secretin*, is liberated, absorbed into blood, and stimulates gastric glands to secrete. The phenomenon is undoubted, but the explanation is discredited. Usually flow of gastric juice is started by nervous mechanism, continued by chemical one.

Observations on Flow of Gastric Juice in Man.—If stomach tube is passed before breakfast, and various beverages are given in turn, and gastric flow observed :—

Beef tea gives best flow.
Tea next best flow (Craven Moore).
Water and albumin, small flow.
Egg-albumen and sugar, no flow.
Milk inhibits flow owing to fat content.

Composition of Gastric Juice.—Clear, colourless liquid ; sour smell. Reaction, acid. Contains :—

Total solids, about 1 per cent.
Free HCl, 0·4 per cent as secreted ; diluted by gastric contents to 0·1 to 0·2 per cent, with pH = 1·6.
A very little protein and mucin.
Inorganic salts—chiefly chlorides of potassium, sodium and calcium, and phosphates of magnesium, calcium, and iron.
Ferments—pepsin, rennin, and possibly lipase.
Organic acids—e.g., lactic acid, rarely present ; probably due to disease.

Origin of HCl.—Probably from chlorides, possibly by interaction with acid phosphates ; but exact origin uncertain.

Artificial Gastric Juice.—Obtained by extracting the mucosa with glycerin or water. Contains no HCl, and pepsinogen instead of pepsin. Converted into pepsin by addition of 0·2 per cent HCl.

Functions of Gastric Juice.—

1. ACTION ON PROTEIN METABOLISM.—Conversion of protein into proteoses and peptones, thus :—

Albumin, acted on by gastric juice.
↓
Acid metaprotein.
↓
Primary proteoses, precipitated by magnesium sulphate crystals or half saturation with ammonium sulphate.
↓
Secondary proteoses, more soluble, precipitated by complete saturation with ammonium sulphate.
↓
Peptones, not precipitated by neutral salts.

Proteoses and peptones give biuret reaction (rose-red colour with weak copper sulphate and potassium hydrate). Peptones will pass through a semi-permeable membrane.

2. CLOTTING OF MILK.—Formation of insoluble casein from soluble caseinogenate. Takes place in two stages :—
   a. Rennin + caseinogenate = soluble casein.
   b. Soluble casein + calcium salts = insoluble casein.
   Proof.—If soluble calcium salts are removed by addition of oxalate or citrate solutions, rennin does not cause coagulation. Boil to destroy rennin; add calcium salts; coagulation occurs.

   FUNCTION OF CLOTTING.—To delay milk in stomach until it is thoroughly digested.
   For babies, 2 gr. of sodium citrate may be added to 1 oz. of milk, reducing amount of curdling almost to that of human milk.

3. EFFECT ON FATS.—Practically none. By digestion of surrounding connective tissue, fat is set free from combination with other food-stuffs, liquefied, and prepared for action of pancreatic juice.
   Some observers state that lipase occurs in gastric juice, causing hydrolysis of neutral fat into fatty acid and glycerol.

4. EFFECT ON CARBOHYDRATES.—Probably none.

5. ANTISEPTIC ACTION.—Stomach is comparatively free from germs. Most varieties are killed by the acid juice.

Does the Stomach Digest Itself ?—

1. It may do—e.g., when a healthy person dies suddenly after a meal, or in patients with gastric ulcer.
2. Normally, protection depends on an intact circulation; said to be due to an antipepsin.

Examination of Acidity of Human Stomach during Life.—FRACTIONAL TEST MEAL.—Patient is given cup of weak tea with very little milk, and slice of thinly buttered toast, or whisky. One hour later, a Rehfuss stomach-tube is passed, and contents of stomach are drawn up about every ¼-hour until stomach is empty. Specimens are analysed (*Fig.* 7).

1. PEPSIN and RENNIN.—Very rarely absent.
2. TOTAL ACIDITY.—Estimated by titrating against normal solution of an alkali.
3. FREE HCl.—Tests :—
   a. Günzberg's (vanillin and phloro-glucinol).—Reagent is evaporated and solution to be tested streaked over it. If free HCl is present, rose-red streak is observed on drying.
   b. Töpfer's Reagent (dimethyl-amino-azo-benzene).—Used in quantitative estimation. Free HCl gives bright-red colour.

[4. ABNORMAL ACIDS.—Lactic acid occurs in cancer. Tests :—
a. Uffelmann's Test.—Solution of ferric chloride, carbolic acid, and water. Colour of solution is violet, changing to yellow on addition of trace of lactic acid.

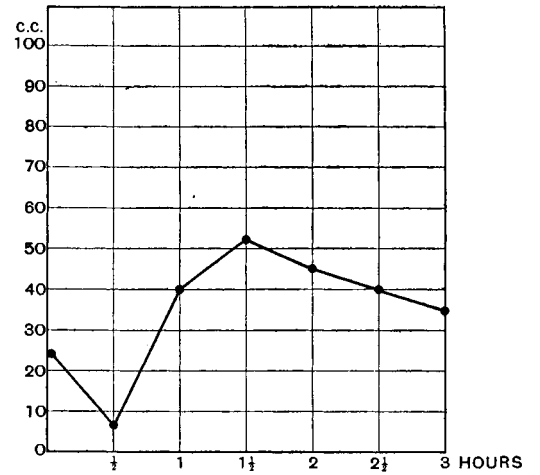


Fig. 7.—Chart of fractional test meal. The figure shows the number of c.c. of HCl in 100 c.c. of gastric juice, at various times after the meal.
30 c.c. = 0·1 per cent HCl.
60 „ = 0·2 „ „

b. Hopkins' Test.—Trace of lactic acid, concentrated sulphuric acid, and few drops of saturated solution of copper sulphate are mixed and kept warm for 4 minutes. Mixture cooled, and drop of 2 per cent alcoholic solution of thiophene added. On warming, pink colour results.]

NORMAL VARIATIONS IN ACIDITY OF GASTRIC JUICE.—With atonic type of stomach, not above 0·1 per cent; with hypertonic type, about 0·2 per cent.

Absent HCl is very suggestive of cancer, but occurs in some normal people (4 per cent), and in some dyspeptics.

[**Determination of Activity of Gastric Juice by Means of Mett's Tubes.**—Fibrin stained with carmine is digested by various gastric juices. Activity is measured by carmine liberated.]

Composition of Chyme Entering Duodenum.—Semi-digested, yellowish substance. Highly acid. Considerable amount of protein is in form of proteoses and peptones. Fat unchanged, except set free from its combination with other substances in adipose tissue. Carbohydrates chiefly as starch, some as maltose.

PANCREATIC DIGESTION.

Structure of Pancreas.—Consists of two parts: (1) Tubulo-racemose part; (2) Islets of Langerhans.

1. TUBULO-RACEMOSE PART.—
   - *a.* MAIN DUCT.—The *duct of Wirsung*, lined by cubical epithelium.
   - *b.* DUCTULES.—Branch and re-branch to end in alveoli.
   - *c.* ALVEOLI.—Elongated; lined by single layer of glandular epithelium. These cells contain numerous granules which disappear during activity. Packed round alveoli is loose connective tissue.
2. ISLETS OF LANGERHANS.—Not connected with any ducts. Cells more rounded, paler staining, and not so granular. Good blood-supply. Apparently not connected with digestion, but with internal secretion of pancreas.

   [In some fish, islets form a separate gland.]

Methods of Examination of Pancreatic Juice.—

1. EXTRACTS of pancreas with glycerin and water prepared and examined. This solution contains no lipase.
2. PAWLOW'S METHOD.—Small area of mucosa containing opening of Wirsung's duct excised, and stitched to skin. Duodenum closed.

   500 to 800 c.c. of juice are secreted a day (so one case, in man).

   Secretion starts a few minutes after a meal, but curve of secretion depends on nature of food taken.

Control of Pancreatic Secretion.—

1. NERVOUS MECHANISM.—Reflex through vagus, stimulation of which causes a flow of juice, very rich in ferments.
2. CHEMICAL MECHANISM.—Due to hormone, *secretin*, in duodenal wall. Secretin is carried by blood-stream to pancreas. Acts even after section of nerves to pancreas.

Proofs.—

a. Injection intravenously of extract of duodenal mucosa of dog treated with 0·4 per cent HCl into dog with pancreatic fistula leads to flow of dilute pancreatic juice.

b. Blood is taken from vein of dog just after a meal and injected into vein of a starving dog with a Pawlow's fistula—flow of juice observed.

It was originally believed that secretin is liberated by HCl of gastric juice. Recently shown to be always present, but needs bile salts to enable it to get into portal vein (Mellanby).

Composition of Pancreatic Juice.—Clear, strongly alkaline liquid. Contains about 4 per cent solids :—

Inorganic salts, especially sodium carbonate.

Enzymes.—Steapsin, trypsinogen, amylase, probably erepsin, possibly rennin.

Trypsinogen is activated by enterokinase of succus entericus in duodenum or upper part of jejunum, trypsin resulting.

Functions of Pancreatic Juice.—

1. ACTION ON PROTEINS (by trypsin).—Proteins are broken down to peptones, erepsin being needed for further breaking down into amino-acids. If action of trypsin is allowed to proceed for 24 hours undisturbed, digestion continues as far as amino-acids.

STAGES OF DIGESTION.—

Albumin.
↓
Alkali metaprotein.
↓
Deutero-proteoses.
↓
Peptones.
↓
Polypeptides and amino-acids.

Common amino-acids obtained are tyrosin, leucin, aspartic acid, and glutamic acid.

VALUE OF THIS ACTION OF PANCREATIC JUICE.—Whatever the nature of the protein given, it is broken down into proteoses and peptones, and can then be built up into the particular variety of protein the body requires.

DIFFERENCE BETWEEN ACTION OF PEPSIN AND TRYPSIN.—

a. Pepsin acts in acid medium, trypsin in alkaline one.

b. Pepsin only carries process of digestion as far as peptone, while trypsin carries it to amino-acids.

c. Trypsin misses primary proteose stage.

d. Trypsin digests keratin, pepsin will not.

2. ACTION ON CARBOHYDRATES (by amylase).—Similar to that of ptyalin, but action of amylopsin is quicker and more complete. Converts starch (cooked or uncooked) into achroö-dextrin and maltose.
3. ACTION ON FATS (by lipase or steapsin).—Splits emulsified fat into glycerin and fatty acid.
4. ACTION ON MILK.—Pancreatic juice may coagulate milk in presence of calcium salts. Explanation is unsettled (? rennin in pancreatic juice, ? trypsin).

SUCCUS ENTERICUS.

Secreted by crypts of Lieberkühn.

Methods of Studying Succus Entericus.—

1. THIRY-VELLA FISTULA.—Small portion of intestine resected with blood-supply intact and one or both ends brought to skin.
2. EXTRACT OF MUCOSA.—Extracts of wall of intestines or juice squeezed from them contain several important enzymes.

Composition and Functions of Succus Entericus.—

Yellowish, alkaline fluid. Contains :—

Inorganic salts, chiefly sodium carbonate.

Enzymes :—

1. Acting on carbohydrates :—

a. *Invertase*, converting sucrose into glucose and fructose.

b. *Lactase*, converting lactose into glucose and galactose.

Succus Entericus—Enzymes, *continued.*

c. Maltase, converting maltose into 2 of glucose. Thus all carbohydrates are eventually reduced to monosaccharides.

2. Acting on proteins :—

Erepsin, which breaks down peptones to amino-acids, completing process begun by pepsin and trypsin. Native proteins are unacted on, except caseinogen.

3. *Enterokinase*, which activates trypsinogen.

4. ? *Diastase*, converting starch into sugars.

THE BILE.

Function of Gall-bladder.—Uncertain. In some animals, e.g., horse, gall-bladder is absent. Theories :—

1. RESERVOIR FOR BILE.

OBJECTION.—Only holds about 1 oz., far too small an amount.

2. PROBABLY ACTS AS A PRESSURE VALVE, and structure of its epithelium suggests that it absorbs water. After its removal, bile-ducts dilate and pressure is low. Tetra-iodo-phenolphthalein, which is opaque to X rays, is secreted by liver in the bile (after intravenous injection); the shadow becomes denser after 12 hours because the bile in the gall-bladder has become concentrated by absorption of water.

Passage of Bile into the Intestine.—When certain substances enter duodenum, especially proteins, fats or soaps, and magnesium sulphate, gall-bladder contracts reflexly, and sphincter guarding entrance of common bile-duct into duodenum relaxes.

Secretion of Bile.—About 500 to 800 c.c. a day. Flow of bile is more or less continuous, but increased after each meal, due to : (1) Secretin ; (2) Absorption of bile salts, or any agent that causes hæmolysis.

Results of Obstruction of Different Parts of Bile-passages.—

1. CYSTIC DUCT.—Gall-bladder usually distended with a mucoid fluid. No jaundice.

2. COMMON BILE-DUCT.—*Jaundice*, from absorption of bile pigments into blood : skin yellow, urine greenish, stools white or clay-coloured. In old cases, bile colourless.

Methods of Obtaining Bile for Examination.—

1. Gall-bladder in man and animals.
2. Fistula opening from surface into gall-bladder or common bile-duct.

Bile from gall-bladder is very much more concentrated than that from a fistula.

Composition of Bile from Gall-bladder.—Yellowish-green, faintly alkaline, rather viscid fluid. Contains :—

1. Water, about 85 per cent ; 98 per cent in fistula bile.
2. Solids, about 15 per cent ; inorganic salts about 1 per cent.
3. Bile pigments—bilirubin and biliverdin.
4. Bile salts—sodium taurocholate and glycocholate.
5. Mucin and (in the ox) nucleoprotein. Mucin is formed entirely from gall-bladder and bile-passages.
6. Cholesterin and lecithin.

Bile Pigments.—Derived from hæmoglobin by liver cells, or these and endothelial cells of Kupffer (*Fig.* 8). Bilirubin does not contain iron, which is probably stored in liver for manufacture of fresh corpuscles. Recent work shows that bilirubin can be produced after removal of both liver and spleen.

GMELIN'S TEST FOR BILE PIGMENTS.—Addition of drop of fuming nitric acid causes play of colours—i.e., green, blue, violet, red or reddish-yellow. Bilirubin is

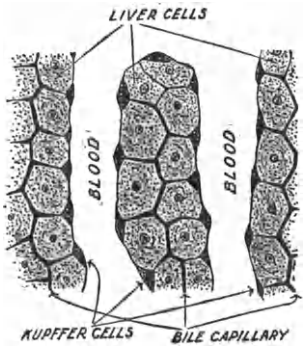


Fig. 8.—Diagrammatic representation of the endothelial cells of Kupffer and their relationship to the liver cells, blood, and bile capillaries.
(*After Evans, 'Recent Advances in Physiology'.*)

Bile Pigments, *continued.*

oxidized to biliverdin (green), bilicyanin (blue), and eventually choletelin (yellow).

VAN DEN BERGH TEST FOR BILIRUBIN IN BLOOD.—Bilirubin in blood gives the diazo test. Two forms, direct and indirect (in the latter, alcoholic extract is used). Jaundiced serum, or bile itself, gives the direct reaction. Bilirubin, and serum in hæmolytic conditions, give indirect. Explanation is obscure.

PROOF THAT BILE PIGMENT ORIGINATES FROM HÆMOGLOBIN.—

1. Bilirubin is identical with hæmatoidin, which occurs as little dark granules in old blood-clot.
2. *Amphioxus*, the only vertebrate with colourless blood, has also colourless bile.
3. In pernicious anæmia, a disease in which there is excessive destruction of red cells, other factors are: (*a*) Excess of bile pigment; (*b*) Increased iron in liver; (*c*) Decreased hæmoglobin in blood.

   A similar condition can be induced by toluylene-diamine poisoning.

Bilirubin is slightly altered by action of bacteria in intestine to stercobilin, the colouring matter in the fæces. Some stercobilin is absorbed into blood-stream, and excreted in urine as colourless urobilinogen, which becomes yellow on standing.

Bile Salts.—Glycocholate and taurocholate of sodium.

Glycocholic acid = glycin + cholalic acid.

Taurocholic acid = taurin + cholalic acid.

Taurin = amino-ethyl-sulphonic acid.

Bile salts are almost entirely absorbed from the intestine and re-excreted in the bile—circulation of bile salts. Only traces are excreted in the fæces. When the bile is diverted by a gall-bladder fistula, the percentage of bile salts is greatly reduced because they are no longer reabsorbed; giving bile by mouth restores them.

TESTS FOR BILE SALTS.—

1. PETTENKOFER'S TEST.—Bile shaken with cane sugar, and concentrated sulphuric acid poured on: purple colour results in the froth, due to formation of furfurol.
2. HAY'S TEST.—Flowers of sulphur normally float on water or urine. Bile salts lower surface tension, and sulphur sinks.

Cholesterin.—A terpene, kept in precarious solution in bile by bile salts. Amount varies greatly, and it may take part in formation of gall-stones.

CRYSTALS OF CHOLESTERIN.—Soluble in ether and hot alcohol, not in water. Rhombic plates which appear to have a chip out of the corner, obtained by crystallizing from hot alcoholic solution.

TEST FOR CHOLESTERIN.—When dissolved in chloroform, and sulphuric acid added, a red colour results in the chloroform and a green in the sulphuric acid.

[ORIGIN OF CHOLESTERIN.—Two theories: (1) It may be excreted by the liver from blood; (2) It may be the product of the inflamed mucosa of the gall-bladder and ducts (the view generally held by surgeons). Other inflamed mucosæ (e.g., middle ear) produce cholesterin.]

Functions of Bile.—

1. Is principally an excretion.
2. Increases rate of action of all the pancreatic ferments, without itself taking any part in reactions. Promotes absorption of secretin, and so aids flow of pancreatic juice.
3. Precipitates unpeptonized protein, thus delaying its progress and facilitating digestion.
4. Aids absorption of fat by: (*a*) Lowering surface tension of cells of villi; (*b*) Solution of fatty acids.
5. *Alleged antiseptic.* Fæces have a more offensive odour when bile is absent, but this may be due to deficient absorption of fat. It checks action of some bacteria, not of others.

ABSORPTION.

Absorption by Stomach.—Water, proteins, and fats are not absorbed. Some sugar may be. Drugs such as cyanides certainly are, because they act so quickly.

Absorption by Small Intestine.—Proteins, fats, and carbohydrates are freely absorbed, but water only to a small extent; it is needed as a flush-through.

Absorption occurs through villi. Each villus consists of core of connective tissue, with blood-vessels and lacteal, covered by a single layer of columnar epithelial cells. Free border is striated.

FATS.—

GENERALLY ACCEPTED THEORY.—Probably they are absorbed as soaps, or as fatty acids dissolved in bile

Absorption by Small Intestine—Fats, *continued.*

and glycerol. These are re-synthetized to neutral fat, enter lacteals as such, and are carried to thoracic duct, and so to venous circulation.

Evidence.—

1. Fat globules occur in deeper part of columnar cells covering villi, not in outer striate border.
2. When no fat-splitting occurs, 80 per cent of fat is excreted in the stools.
3. While a meal is being absorbed, lymphatics of the mesentery become filled with a milky fluid, chyle. Only about 60 per cent of fat taken can be recovered from the chyle, so some probably passes by blood to the liver, where some may be stored.

Fat in blood is united with corpuscles, proteins, etc., so blood does not normally appear milky.

CARBOHYDRATES.—Absorbed as monosaccharides, principally dextrose, directly into blood-stream, and conveyed by portal vein to liver. Much is stored in liver and some in muscles as glycogen.

PROTEIN.—Absorbed as amino-acids into blood-stream. If proteoses or peptones are injected into the blood-stream, they are rapidly excreted by the kidney, being highly toxic substances. Useful acids are built up into tissue proteins, useless ones converted into urea by liver.

PROOF THAT PROTEIN CIRCULATES AS AMINO-ACIDS.—

1. Animal can be kept alive on a diet in which proteins have been replaced by amino-acids, provided vitamins are added.
2. *Increase of amino-acids in portal vein after a meal.*

[Demonstrated by :—

a. Van Slyke's Method.—Based on fact that nitrous acid in presence of amino-acids evolves nitrogen.

b. Vivi-diffusion.—If blood of portal vein is passed through tube of animal membrane, amino-acids diffuse into surrounding fluid.

Serum albumin and globulin are not increased in portal vein after a meal, only the non-protein nitrogen.]

SALTS.—Sodium chloride is rapidly absorbed, sulphates and tartrates only very slowly.

Absorption by Colon.—There are no villi, so apparently any absorption that occurs is through columnar cells of mucous membrane.

WATER.—Contents of lower part of small intestine are very fluid; those of rectum solid.

GLUCOSE.—Absorbed to small extent.

Proofs.—

a. Increased percentage is found in circulating blood after giving glucose per rectum. At same time respiratory quotient rises.

b. In a starving individual, the ammonia nitrogen percentage in the urine is high owing to acidosis, but is decreased on giving glucose per rectum.

Lactose is not absorbed.

PROTEINS and FATS.—These are not appreciably absorbed. Giving amino-acids per rectum in starvation increases urea output (which has dropped) from 5 to about 10 grm. per day.

Composition of Fæces.—

1. UNDIGESTED FOOD RESIDUES.—E.g., cellulose from vegetables, keratin from connective tissue of animals, fragments of fat or starch.
2. SUBSTANCES CONTRIBUTED BY ALIMENTARY GLANDS. — Bile pigments. Cholesterin, epithelium, mucus. Inorganic or mineral salts, chiefly phosphates of calcium, magnesium, and iron.
3. SUBSTANCES FORMED IN BOWEL ITSELF.—Bacteria, which constitute half fæces by weight, most of them being dead. Gases—e.g., nitrogen, carbon dioxide, hydrogen (from lactose), hydrogen sulphide. Organic acids—e.g., indol, skatol, fatty acids.

[**Mechanism of Absorption.**—*Must be vital process, not merely osmotic filtration and diffusion.*

REASONS.—

1. When lining epithelium is living, chlorides, even hypertonic saline, will pass from lumen to blood-vessels, but not vice versa. When it is dead, chloride passes either way according to ordinary laws of osmosis and diffusion.
2. Absorption is accompanied by increased consumption of oxygen and output of carbon dioxide.
3. Dog's bowel will absorb dog's serum from lumen.]

BACTERIAL DIGESTION.

[**Small Intestine.**—Bacteria not numerous; act chiefly on carbohydrates, causing fermentation.

Large Intestine.—Millions of bacteria present, especially *B. coli communis*. Reaction usually alkaline.

Bacterial Digestion, *continued.*

Action of Bacteria.—

1. Cellulose broken down into lower fatty acids, marsh gas, carbon dioxide, and hydrogen.
2. Sugars yield CO_2, hydrogen, lower fatty acids, and alcohol.
3. Proteins are broken down to amines and aromatic indols—e.g., skatol and indol. Hydrogen sulphide may be produced from cystin. Indol, skatol, etc., are partly excreted in fæces; partly absorbed, oxidized to indoxyl and skatoxyl, and excreted in urine as compounds of sulphuric acid.
4. Fats are supposed to be split into fatty acids and glycerol.

Guinea-pigs can be reared on sterile food so that bowel is germ-free. Arctic animals may have germ-free intestines. But chickens, at any rate, thrive better if their intestines contain bacteria.]

CHAPTER IX.

THE ENDOCRINE GLANDS.

An endocrine or ductless gland is characterized by having an internal secretion—i.e., one poured directly into the blood-stream. The ductless glands are the suprarenals, pituitary, thyroid and parathyroid, and possibly pineal and thymus. The ovary, testis, pancreas, liver, and spleen have an internal secretion among other functions.

Methods of Study.—(1) Histology. (2) Morphology. (3) Chemistry. (4) Effects of partial or complete removal in animals, and possibly in man. (5) Results of feeding or injection, using either the gland itself or extracts. (6) Disease in man: (*a*) Hyposecretion; (*b*) Hypersecretion.

THE THYROID GLAND.

Histology.—Closely packed spherical alveoli, lined by single layer of cubical epithelium, containing colloid. Between alveoli are connective tissue and many blood-vessels.

[**Nerve-supply.**—
1. SYMPATHETIC, containing vasoconstrictor fibres and possibly secretory fibres.
2. VAGUS, through superior and recurrent laryngeal nerves.

Secretion of gland is probably controlled primarily through circulation, since portions transplanted to other parts of body continue to function. Stimulation of the sympathetic does not increase thyroxin-globulin (measured by precipitin test) in the blood. Iodine feeding does.]

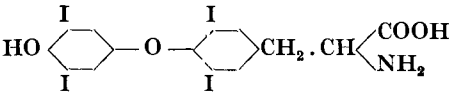
Morphology.—
LATERAL LOBES.—Develop from 4th branchial cleft.
MIDDLE LOBE.—Develops from thyroglossal duct, which grows down from foramen cæcum at back of tongue. Parts of this duct may persist in adult, giving rise to a thyroglossal cyst.

Chemistry.—Contains usual cell constituents—i.e., water, salts (especially sodium chloride), cell albumin and globulin, and nucleoprotein. Active principle is *thyroxin*, containing 65 per cent iodine; it has been isolated as colourless, needle-like crystals, found to produce all the physiological effects of thyroid extracts. Total iodine in gland varies with

The Thyroid Gland—Chemistry, *continued.*

degree of activity of gland, and also in different animals; is high in Orkney sheep, which feed partly on seaweed.

According to Harington, thyroxin is a tetra-iodo derivative of tyrosin. Human thyroid produces 1 mgrm. daily. Formula is



He has recently synthetized it chemically from hydroquinone and tri-iodo-nitrobenzol, and the synthetic thyroxin is active.

Effects of Removal.—Vary in different animals, because: (i) Parathyroids may or may not also be removed; (ii) Animals vary in amount of thyroid they need.

REMOVAL OF WHOLE THYROID GLAND.—

1. In carnivora, nearly always fatal, because parathyroids are embedded in gland.
2. Full-grown animals are often not much affected if parathyroids are uninjured, but there may be diminution of all metabolic processes.
3. In man, and perhaps in monkeys: (*a*) *Myxœdema* develops. Prevented by leaving a piece of gland as big as a walnut. (*b*) Pituitary enlarges and shows increased secretion.

   Symptoms of Myxœdema.—Increased thickness of subcutaneous tissues owing to deposit of embryonic connective tissue containing mucus; gives rise to bloated appearance. Skin dry and coarse. Cheeks flushed. Hair coarse, dry, and scanty. Increased fat. Pulse slow. All metabolic processes subnormal; basal metabolism low. Mental condition dull and apathetic. Sterility occurs, and menstruation ceases.

   Condition usually improved by thyroid feeding.
4. In young animals such as lambs and asses: Stunted growth. Ovary and testis do not develop. Secondary sex characters do not develop. Mental condition dull and stupid. Atheromatous changes in arteries occur early—i.e., calcareous patches in walls of arteries characteristic of old age.

   These animals are called *cretins.*

Effects of Thyroid Injection and Feeding in Man and Animals (thyroxin can be absorbed if given by mouth).—

1. Pulse-rate quickened.
2. All metabolic processes increased.
   - *a.* Increased elimination of nitrogen and phosphates in urine.
   - *b.* Increased oxygen consumption and carbon dioxide output.
   - *c.* Body-weight falls owing to increased metabolism; hence thyroid is a useful treatment in obesity.
3. Symptoms of a common cold may be produced. During thyroid treatment, this condition indicates that too much is being given.
4. Myxœdema and cretinism are relieved, but treatment must be lifelong.
5. Injected into vein of animal, marked fall of blood-pressure occurs owing to vasodilatation.
6. Thyroid extract added to water hastens metamorphosis, but not growth, of tadpoles.

Disease in Man.—

1. HYPOSECRETION (due to atrophy of gland).—

   In Adults: Myxœdema.—Occurs especially in middle-aged women.

   In Infancy: Cretinism.—

   Symptoms.—All the symptoms of myxœdema. Stunted growth. Arrested mental development, resulting in idiocy or feeble-mindedness. Failure of development of sex glands and secondary sexual characters.

   Treatment.—If thyroid feeding is started at an early age, cretins may be restored nearly to normal. Bodily condition is more easily improved than mental.

2. HYPERSECRETION.—

   Graves' Disease, or Exophthalmic Goitre.—Occurs in young women.

   Morbid Anatomy.—Gland enlarged, soft, and vascular. On section, the colloid is watery, and contains increased amount of iodine.

   Symptoms.—Quick pulse. Tremors. Loss of weight. Swelling of thyroid gland. Protrusion of eyes (exophthalmos). Great excitability and irritability. Increased basal metabolism.

The Thyroid Gland—Hypersecretion, *continued.*

Treatment.—Best treatment is to remove most of gland.

ORDINARY GOITRE.—

DEFINITION.—Enlargement of thyroid gland without excess or deficiency of internal secretion.

CAUSE.—Some defect in drinking-water. The water can be rendered harmless by boiling but not by filtering. Goitre can be induced by copious fat-feeding, but not by giving cod-liver oil, which contains iodine.

Theories as to Nature of Defect in Drinking-Water.—

1. Fæcal contamination (McCarrison).
2. Iodine deficiency. Evidence :—
   - *a.* In inland parts of U.S.A. many sheep develop a goitre, prevented by putting a little iodide with their salt.
   - *b.* Administration of small amounts of iodine prevents goitre amongst children in districts where goitre is endemic (e.g., Switzerland).
   - *c.* Iodine added to water in concentration of 1–1,000,000 prevents occurrence of goitre in brook-trout.

Summary : Function.—Conclusions are that thyroid is an important gland secreting an iodine compound into blood-stream which influences general metabolism, growth, genital organs, and intelligence.

THE PARATHYROID GLANDS.

Histology.—Solid columns of cuboidal cells, with intermediate connective tissue. Very vascular.

Morphology.—Outgrowths from 3rd and 4th branchial clefts.

Chemistry.—Unknown. Do not appear to contain iodine.

Effects of Removal.—Removal of parathyroids alone is difficult, but has been done. Results :—

1. Tetany (spasmodic contractions of voluntary muscles), which is often fatal. Thus, hand is held with finger-tips pressed together.
2. Increased irritability of peripheral nerves and muscles to galvanism and mechanical stimulus. A tap on facial nerve induces spasm.

Tetany occurred in rats when parathyroids were destroyed by electric needles.

Parathyroidectomy is nearly always fatal in carnivores, but is averted if great care is taken to avoid intestinal putrefaction. In sheep, tetany and death seldom follow the operation.

Results of Injection or Feeding.—May cure tetany, otherwise no effect.

Theories as to Function.—

1. CONTROL OF CALCIUM METABOLISM.—
   EVIDENCE.—
   a. Administration of calcium salts often cures tetany following accidental parathyroidectomy during thyroidectomy.
   b. Tetany occurs in cases of calcium starvation—e.g., marasmic infants.
   c. It is said that after removal of parathyroids there is increased calcium in urine and fæces, decreased calcium in blood.
2. CONTROL OF GUANIDINE METABOLISM.—
   EVIDENCE.—
   a. Injection of guanidine compounds into animals causes symptoms of tetany.
   b. Accumulation of guanidine and methyl-guanidine in blood and urine occurs after removal of parathyroids and in patients suffering from tetany.
3. MAINTENANCE OF ACID-BASE EQUILIBRIUM OF BODY.—
   EVIDENCE.—After parathyroidectomy there is increase of the alkali reserve in blood.

No theory has as yet been generally accepted, and it cannot be taken as certain that the parathyroids have any separate function at all.

THE PITUITARY GLAND.

Histology.—Shows four parts :—

1. PARS ANTERIOR.—Consists of epithelial cells arranged in tubules in embryo, in solid columns in adult. Cells are of three types : (*a*) Acidophil, stain with eosin ; (*b*) Basophil, stain with methylene blue ; (*c*) Neutrophil, do not stain. Normally, basophils most numerous ; in activity, acidophils ; in exhaustion, neutrophils.
2. PARS INTERMEDIA.—Varies in different animals. In dogs and cats consists of cleft containing fluid, lined by

The Pituitary Gland—Histology, *continued.*

cubical cells. In man is practically non-existent, but region shows nodules of colloid.

3. PARS TUBERALIS.—Around base of stalk. Glandular, with small granular cells. Vascular. Contains colloid.
4. PARS POSTERIOR.—Composed of neuroglia, showing a mass of fibrous tissue with a little colloid, and hyaline bodies. These last may be derived from the breaking down of cells of the pars intermedia.

The hypothalamic region of the brain appears to work with the pituitary gland.

Morphology.—

ANTERIOR LOBE.—Bud of epithelium from nasopharynx, the pouch of Rathke.

POSTERIOR LOBE.—Downgrowth from floor of 3rd ventricle.

Chemistry.—No active principle isolated from either lobe.

Effects of Removal in Animals.—

1. Removal of whole gland is fatal in a few days, with great weakness, but no special symptoms. The latest reports, however, attribute the deaths entirely to brain injury; if this is avoided, removal in dogs is not fatal (Dandy).
2. Removal of anterior lobe alone is fatal (?).
3. Removal of posterior lobe has no effect. Pregnancy and parturition occur normally.
4. Partial removal of anterior lobe, or damaging the stalk, causes :—
   a. In Adult Animals.—Polyuria and thirst—i.e., the clinical syndrome known as diabetes insipidus. Great adiposity. Atrophy of genital organs. Increased tolerance for sugar, which may account for the adiposity. A normal human being cannot take more than 150 grm. of glucose without its appearing in urine; there is a similar threshold for animals.
   b. In Young Animals.—Ovary and testis do not develop. Secondary sex characters do not appear. Body fat increases.

   More recent experiments suggest that similar results, except perhaps genital atrophy, may be attained by lesions of hypothalamic region when pituitary itself is intact.

Effects of Injection.—

1. INJECTION OF ANTERIOR LOBE.—No immediate effect, at any rate in health. Intraperitoneal injection in rats causes gigantism (Evans).
2. INJECTION OF POSTERIOR LOBE.—Marked effect.
   a. RISE OF BLOOD-PRESSURE.—Due to vasoconstriction. Krogh has shown that capillaries are affected even more than arterioles. Effect lasts half to one hour, and a second dose will not usually repeat the effect.
   Heart is slowed, by Marey's law.
   b. STIMULATION OF PERISTALSIS.—It is the best hypodermic purgative.
   c. CONTRACTION OF BLADDER AND UTERUS.
   d. DIURESIS (i.e., increase of urine).—Acts by raising blood-pressure, leaving renal vessels unaffected.
   [Some observers find that this diuretic action is transitory, and that more characteristic result is *diminished* flow of urine.]
   e. INCREASED FLOW OF MILK IN LACTATING BREAST.—Probably due to contraction of unstriped muscle in breast.

General law is that posterior lobe contracts unstriped muscle of body. It acts directly on the muscle-cells apparently, since effects still occur when all nerves to part are cut.

Used in medicine for intestinal paralysis, in midwifery to hasten labour, in diabetes insipidus, and to raise the low blood-pressure of shock. Probably the substance which raises blood-pressure is not the same as that which contracts the uterus.

Disease in Man.—

1. HYPERSECRETION.—

ACROMEGALY.—

Symptoms and Signs.—(1) Increased size of hands, feet, lower jaw, and skull. (2) Headache and neuralgia common. (3) Interference with sex functions, amenorrhœa, and impotence. (4) Glycosuria. (5) Increased basal metabolism.

X Rays.—Usually show dilatation of pituitary fossa, to accommodate enlarged gland.

Morbid Anatomy.—Anterior lobe may be enlarged and full of acidophil granules. Viscera may also be increased in size.

The Pituitary Gland—Hypersecretion, *continued.*

Treatment.—In a few cases of successful removal of pituitary, symptoms have been relieved.

If hypersecretion commences before growth has ceased, *gigantism* results. Skulls of most of the classical cases of gigantism have enormous sellæ turcicæ to accommodate enlarged pituitary. Giants usually suffer from acromegaly as well.

2. HYPOSECRETION.—

FRÖHLICH'S TYPE.—

Morbid Anatomy.—Tumour of gland, or rarely atrophy. Eosinophil granules absent.

Symptoms and Signs.—In the young, patients are of small stature but well shaped. Marked obesity. Secondary sex characters do not appear—i.e., no beard, moustache, or pubic hair; voice does not break; amenorrhœa. Reduced basal metabolism. Increased power of storing sugar. Somnolence.

In adults, sexual functions fail, hair is scanty, and skin may be crinkled.

Treatment.—Feeding with whole pituitary gland extract is probably useless in hypopituitarism.

DIABETES INSIPIDUS (i.e., copious watery urine) is occasionally associated with injury or disease of the hypothalamic region.

THE SUPRARENAL GLANDS.

Histology.—

CORTEX.—Columns of closely packed polygonal glandular cells containing fat globules, and arranged in a radiating manner. Consists of three zones—zona glomerulosa (outside); zona fasciculata; zona reticularis.

MEDULLA.—Scattered cells in a fibrous matrix. Very vascular. Cells may show points, and are *chromaffin*—i.e., stain brown with chrome salts.

Gland is supplied by three arteries, to avoid risk of occlusion.

In some fish the cortex and medulla exist as separate glands.

Morphology.—

CORTEX.—Developed from mesoblastic tissue closely connected with embryonic kidney.

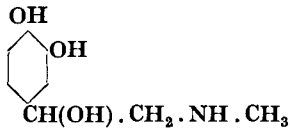
MEDULLA.—Developed from sympathetic nervous system, and appears to correspond to a sympathetic ganglion. Its nerve-fibres, being pre-ganglionic, are medullated.

Chemistry.—

CORTEX.—Contains nothing distinctive, but is rich in lipoid bodies—e.g., lecithin and cholesterin.

MEDULLA.—Contains *adrenalin*, a pyrocatechin derivative, probably arising from tyrosin. It has been synthetized outside body.

Formula of Adrenalin.—Orthodioxyphenyl-ethanol-methyl-amine :—



Effects of Removal in Animals.—

1. REMOVAL OF BOTH GLANDS OR TYING BOTH SUPRARENAL VEINS.—Fatal within a few days, with great prostration and very low blood-pressure.
2. PARTIAL REMOVAL.—Has not thrown much light on function of gland.
3. In those fish in which cortex and medulla exist as separate glands : (*a*) Removal of cortex gland, fatal ; (*b*) Removal of medulla, no effect.

Results of Feeding and Injection.—

FEEDING WITH EXTRACTS.—No effect, adrenalin not being absorbed.

INJECTION OF CORTEX.—No effect.

INJECTION OF ADRENALIN.—

1. Sudden sharp rise of blood-pressure due to contraction of arterioles, lasting only a few minutes. The adrenalin disappears from circulation in a few minutes, and a second dose repeats the effect, thus differing from action of pituitary.

   General law of adrenalin is that it acts exactly like sympathetic. Apparently it acts on some chemical receptor substance in the muscle, since effects are observed when nerves to the part are dead.

   Some arteries escape action of adrenalin, partly or completely—e.g., arteries to heart, lungs, and brain. Action on intramuscular arteries is very slight.

The Suprarenal Glands—Results of Injection of Adrenalin, *continued.*

Adrenalin is dilator to capillaries. Very minute doses are said to dilate arterioles.

Adrenalin applied to mucous membranes arrests superficial hæmorrhage.

2. *Action on the heart.* In practice, in the intact body the heart-rate is slowed; but when vagi are cut or paralysed by atropine, or in the isolated heart, rate is increased. Two conflicting factors exist: (*a*) By Marey's law, rise of blood-pressure causes reflex slowing of heart-rate; (*b*) Like sympathetic, adrenalin quickens heart-rate.
3. *Paralysis of intestinal muscles,* but closure of sphincters.
4. *Contraction of pregnant uterus,* but action is variable.
5. *Dilatation of pupil* of excised eye. With circulation intact this effect is antagonized by internal secretion of pancreas, and instillation of adrenalin only dilates pupil when this secretion is deficient (Loewi's test for pancreatic deficiency).
6. Dilatation of bronchi.
7. Effect on carbohydrate metabolism, causing sugar to appear in urine and increased sugar in blood. Probably due to more rapid conversion of glycogen in liver into glucose.
8. In large doses, adrenalin is distinctly toxic. Intravenously, 1 mgrm. per kilo of body-weight may be followed by rapid paralysis of heart and respiration.

Disease in Man.—There is no evidence of a hyperfunction disease affecting medulla.

HYPOFUNCTION OF MEDULLA.—

ADDISON'S DISEASE.—

Symptoms.—(1) Very low blood-pressure, about 80 mm. instead of normal 120 mm. (2) Great muscular prostration; fainting easily occurs, though patients appear well nourished. (3) Gastro-intestinal symptoms—vomiting and diarrhœa. (4) Bronzing of skin, especially of exposed parts; explanation of this is obscure; may be due to increased vascularity of skin. No bronzing of internal organs.

Treatment.—Adrenalin is a failure. Nearly all patients die in 6 to 20 months.

Post Mortem.—Suprarenals atrophied or destroyed by tuberculosis.

OVERGROWTH OF CORTEX.—Certain symptoms are associated with great overgrowth of cortex in children. They are: (1) Adiposity. (2) Overgrowth and early development of external genital organs, approximating to a male type. Development in a boy of 4 years may be as advanced as it should be at 14 years. In a girl the clitoris may be enlarged and pubic hair developed at 4 years, but she does not menstruate and the uterus is not developed.

Cortical part of suprarenal has been observed to become twice its normal thickness in pregnant rabbits.

Summary of Functions.—

1. CORTEX.—Functions are unknown, and we have only three facts to guide us: (i) Removal is fatal; (ii) The cortex is associated with the genital organs; (iii) The cells contain a lot of fatty material.
2. MEDULLA.—Main function is to secrete adrenalin, but it is doubtful whether this is poured into blood-stream.

Cannon's Theory Regarding Adrenalin.—Adrenalin is continually secreted into blood-stream, and supply is increased in fear, anger, or exercise, owing to reflex stimulation of autonomic system. It is reduced in condition of shock. Consequently, if an animal is frightened, the following effects occur:—

1. Blood is diverted from skin and intestine by vaso-constriction.
2. Better blood-supply is ensured to heart, lungs, brain, and (?) voluntary muscles.
3. Better air-entry owing to dilatation of bronchi.
4. Wide vision owing to dilatation of pupil.
5. Cessation of intestinal peristalsis.
6. Hair stands on end, e.g., in cat.
7. Glycogen is liberated from liver to supply organs with glucose.

EVIDENCE.—

EXPERIMENT 1.—Stimulation of splanchnic nerves causes a double rise of blood-pressure. *First rise* is due to vasoconstriction in abdomen, *second rise* to liberation of adrenalin. If suprarenal veins are tied, second rise does not occur.

EXPERIMENT 2.—If left splanchnic nerves of cat are cut, and animal is then frightened and killed, chromaffin tissue has disappeared on right side, not on left.

The Suprarenal Glands—Cannon's Theory of Adrenalin, *continued.*

EXPERIMENT 3.—If left superior cervical ganglion is removed and animal frightened, pupil on that side will still dilate. Evidently due to chemical and not nervous stimulus, presumably increased adrenalin in blood.

The theory can scarcely be accepted, because: (1) The experiments lack confirmation. The suprarenals of soldiers just dead of shock contain the normal amount of adrenalin (A. R. S.). (2) Stewart and Rogoff find no increase of adrenalin in the suprarenal veins of animals following either fright or nerve stimulation. (3) Such small amounts of adrenalin as get into the blood would probably be vasodilator and not vasoconstrictor.

THE THYMUS.

[Well marked in the fœtus, it usually attains maximum at end of second year of life, and then slowly diminishes. After puberty it rapidly atrophies.

Histology.—Largely lymphoid tissue, characterized by presence of corpuscles of Hassall—i.e., central granular cells surrounded by concentric layers of flattened epithelial cells.

Morphology.—Backward prolongation from 3rd and a little from 4th branchial clefts.

Effects of Removal.—Most recent experiments do not detect any effect on body. Some observers state that ovaries or testes develop precociously after thymectomy in young animals.

Functions.—Unknown. There appears to be some antagonism between this gland and gonads; when it atrophies, they grow.]

THE PINEAL BODY.

[**Histology.**—

IN CHILDREN.—Chiefly epithelial cells. After seven years of age, glandular tissue is gradually replaced by fibrous tissue.

IN ADULTS.—Chiefly fibrous tissue, with some calcareous particles, the so-called brain sand.

Morphology.—Outgrowth from 3rd ventricle. It is said to represent a median unpaired eye, present in *Hatteria.*

Effects of Removal.—In guinea-pigs (Horrax) and cockerels (Foa) there results an accelerated development of sex organs in male.

Effects of Injection of Gland Extract.—Given intravenously, causes definite but transient fall of blood-pressure.

Disease in Man.—A few cases are on record of tumours involving this gland in young children, associated with precocious mental and physical development, especially of sex organs.]

CHAPTER X.

THE SPLEEN.

Histology.—

CAPSULE.—Unstriped muscle, with a little fibrous and elastic tissue.

TRABECULÆ.—Consist of unstriped muscle. Run at right angles to capsule, and branch to form a network.

SPLEEN PULP.—Consists of:—

a. LYMPHOID TISSUE.

b. MALPIGHIAN NODULES, i.e., denser nodules of lymphoid tissue, with central arteriole.

c. SPLEEN PULP CELLS.—Large branching cells which may contain red blood-corpuscles. These cells are homologous with the Kupffer cells of the liver and the endothelial cells of blood-vessels, and form part of the reticulo-endothelial system. Cells of this system ingest particles (dyes, silica, fragmented red corpuscles). Cells breaking loose from it form hyaline leucocytes in the blood.

Accessory Spleens or Hæmolymph Glands.—Small round bodies, situated in hilum of spleen, having a similar structure to spleen.

Chemistry.—Nothing distinctive. Contains: (1) Much nucleoprotein and purine bodies derived from nuclein of nucleoprotein—e.g., guanine, adenine, xanthine, hypoxanthine—and ferments acting on these substances; (2) Fatty acids, fats, and cholesterin; (3) Iron, considerably increased in some anæmic conditions, e.g., malaria.

Effects of Removal of Spleen or Ligature of Splenic Vein.—In both man and animals, little effect.

1. Temporary anæmia, lasting a few months.
2. Enlargement of hæmolymph glands. Cases are known in which an organ like a normal spleen was reproduced in this way.
3. Overgrowth of marrow may occur.
4. Increased resistance of red blood-corpuscles to hæmolytic agents, e.g., saponin. After splenectomy, it is

Effects of Removal of Spleen, *continued.*

difficult to cause hæmolysis or jaundice by injecting hæmolytic agents.

5. Increased excretion of iron in urine and fæces.
6. Various changes in the leucocyte count have been described, but are not constant; e.g., increase of hyalines, and of eosinophils.
7. After removal of a very large pathological spleen, decreased output of uric acid.
8. Increased liability to die from injections of bacteria or toxins.

Result of Injection of Splenic Extract.—Distinct, though temporary, increase in number of red blood-corpuscles.

Disease in Man.—In *splenic anæmia*: (1) Marked enlargement of spleen and anæmia occur; (2) Removal of spleen in early stages cures disease.

Conclusion is that spleen has been destroying too many red corpuscles.

Functions of the Spleen.—

1. DESTRUCTION OF RED BLOOD-CORPUSCLES.—

EVIDENCE.—(*a*) Occurrence of more or less broken-down red blood-corpuscles in spleen-pulp cells. (*b*) Spleen contains excess of iron in blood diseases—e.g., malaria, pernicious anæmia. (*c*) The facts about splenic anæmia just related. (*d*) Structure of spleen: the older, less elastic, corpuscles tend to get entangled in its meshes; the younger slip through. Attempts to show fewer number of red corpuscles in splenic vein than in artery, and free hæmoglobin in former, have failed.

[Recently, however, Rich and Rienhoff, by the Van den Bergh method, have demonstrated much more hæmoglobin in blood of splenic vein than splenic artery in man.]

Other functions are very uncertain:—

2. Formation of red blood-corpuscles in fœtus, not in adult.
3. Formation of some lymphocytes and hyalines.
4. A source of uric acid.
5. Seems to play a part in protecting body against disease by removing micro-organisms.
6. Regulation of blood-flow in portal system.

[EVIDENCE.—On putting organ into an oncometer, it shows arterial pulsation, and slow expansion after a meal, reaching a maximum in about five hours. There is also a rhythmical contraction and

relaxation of the organ occurring about once a minute. Spleen is richly supplied with motor nerves, which, when stimulated, lead to diminution in volume of the organ. If spleen in cat is marked out by tiny metal clips, it can be X-rayed. Shows enormous diminution in size after hæmorrhage.]

[Pulp cells of spleen and hæmolymph glands, lining epithelium of blood-vessels, and Kupffer's cells in liver may all be part of a *reticulo-endothelial system*, which functions, not organ by organ, but as a whole.]

CHAPTER XI.

THE KIDNEY AND EXCRETION OF URINE.

THE KIDNEY AND ITS FUNCTIONS.

Structure of the Kidney.—

THE TUBULES.—Each tubule shows the following construction and course :—

1. BOWMAN'S CAPSULE, which consists of a single layer of flattened epithelium reflected round a bunch of capillaries known as a glomerulus. It is estimated that there are about 2,000,000 glomeruli in the human kidney.

   [Krogh has found on examining kidneys microscopically that the capillaries of some of the glomeruli are dilated, those of others contracted. Probably they take it in turns to function.]

2. FIRST CONVOLUTED TUBULE, lined by cubical, granular cells, striated near lumen. This tube becomes the SPIRAL TUBULE. It then passes into
3. THE LOOP OF HENLE, situated in the medulla. The DESCENDING LIMB of the loop of Henle is lined by flattened epithelial cells, the ASCENDING LIMB by cubical ones.
4. Returning into the cortex, the ascending limb of the loop of Henle passes into the ZIG-ZAG, and then the SECOND CONVOLUTED TUBULE.
5. Ultimately it joins a COLLECTING TUBULE, lined by non-granular cubical epithelium. These tubules pass down through the medulla and unite with other collecting tubules to form
6. A DUCT OF BELLINI, which is lined by columnar cells, and opens on the apex of one of the papillæ into the renal pelvis.

THE BLOOD-VESSELS.—The arteries break up to form ARCHES in the region between the cortex and medulla.

From the convexity of the arches—

INTERLOBULAR ARTERIES pass into the cortex.

AFFERENT GLOMERULAR ARTERIOLES are branches of the interlobular arteries and end in the capillary plexus of the glomeruli.

EFFERENT GLOMERULAR ARTERIOLES have a smaller lumen than that of the afferent one. They break up into a second capillary plexus round the convoluted tubules.

From the concavity of the arches—

TRUE ARTERIÆ RECTÆ arise, arterioles which pass into the medulla, and break up into capillaries round the loops of Henle and collecting tubules.

THE NERVES.—Fibres emerge in the anterior roots of the 11th, 12th, and 13th thoracic nerves in the dog, and pass to the kidney by the splanchnic nerves.

ACTION OF THE NERVES OF THE KIDNEY.—Studied by *oncometer*, a kidney-shaped box, lined by a layer of peritoneal membrane, which is separated from the box by olive oil. At one point of the box, a tube is led off to a tambour. The kidney is enclosed in this box, and every increase in the volume of the kidney leads to an outflow of oil from the oncometer. Or an air plethysmograph may be used. It is found that there are vasoconstrictor and vasodilator fibres to the kidney. On stimulation of the former, diminution in the volume of the kidney occurs; on section, increase in its volume.

Experiments on the Kidney.—

1. REMOVAL.—Removal of one kidney does no harm. Removal of both kidneys leads to death in a week or two without any very striking symptoms. No urine is passed, and there is increase of urea and other metabolites in the blood. There is subnormal temperature, weakness, and drowsiness ending in death.
2. LIGATURE OF THE RENAL ARTERY.—Leads to cessation of the flow of urine. Occluding the artery for 10 seconds leads to cessation of flow for an hour.
3. LIGATURE OF THE RENAL VEIN.—This also stops the flow of urine, because the circulation is arrested.
4. LIGATURE OF THE URETER.—Flow of urine is arrested, the pelvis of the kidney becomes distended, and the kidney gradually atrophies without much harm. If the block is partial or intermittent, there is an abundant secretion of watery urine, and the pelvis of the kidney stretches and may reach an enormous size—i.e., hydronephrosis.

Experiments on the Kidney, *continued.*

5. OXYGEN CONSUMPTION OF THE KIDNEY.—Respiratory exchange of the kidney can be studied by Barcroft's blood-gas apparatus (*see* p. 48). During saline diuresis, there is no increased respiratory exchange by the kidney, but in diuresis due to other drugs such as caffeine, there is a rise in the respiratory exchange.

Chief Differences between Urine and Blood.—

1. Urine lacks the corpuscles and proteins of the blood (albumin may pass into the urine during exercise, and even normally in some healthy young adults).
2. Urine contains hippuric acid and urochrome, which are not present in the blood.
3. Urea, uric acid, and sulphates are more concentrated in the urine. In the plasma the urea is about 0·03 per cent; thus 100 litres of plasma must be drawn on daily to yield the amount of urea in urine.
4. Glucose is present in the plasma, not in the urine.
5. Chlorides and phosphates are not concentrated in the same proportions in plasma and urine.

Hence substances in the urine may be divided into three classes :—

i. Those which are ruthlessly excreted—urea, uric acid, sulphates, poisons.

ii. Those partly excreted, partly retained—chlorides, phosphates, water.

iii. Those entirely retained—glucose. In special cases, chlorides can be entirely retained (e.g., salt starvation, pneumonia).

Saline Diuresis.—Sodium chloride leads to a short sharp diuresis, much chloride being retained. Sodium sulphate leads to a much more prolonged diuresis, because all the sodium sulphate is excreted.

Theories of Urinary Secretion.—

1. BOWMAN'S THEORY.—This supposes that the glomeruli filter off a fluid equivalent to plasma minus albumin, and that the tubules add urea, uric acid, etc.

   EVIDENCE.—Purely that of histological appearances.

2. LUDWIG'S THEORY.—Whole of the plasma minus the protein is filtered through the glomeruli, and water reabsorbed by osmosis.

   This is certainly incorrect, because osmosis would lead to water passing from the blood to the urine.

3. HEIDENHAIN'S THEORY.—This is a revision of Bowman's theory. It supposes that the glomeruli excrete a watery plasma and the tubules add urea.

EXPERIMENTS IN FAVOUR.—

i. *Nussbaum's Experiment.*—In the frog the glomeruli are supplied by the renal artery, the tubules by the renal portal vein.

Ligature of the renal artery results in cessation of flow of urine, but when urea is injected into a vein it is excreted with a little water. Glucose, proteose, and peptone are not excreted when injected intravenously. During the experiment the frog should be kept in an atmosphere of oxygen to help to maintain the functional activity of the renal cells, and the thighs ligatured to prevent return of venous blood from the sciatic and femoral veins.

The experiment has been confirmed by recent observers, but it is not conclusive —the so-called secretion may be merely a transudate.

ii. *Heidenhain's Experiments.*—

a. Sulphindigotate experiment.—Sodium sulphindigotate was used, being of a blue colour. At first all the dye was washed into the ureter. If the flow was reduced by dividing the spinal cord high up, thus lowering the blood-pressure, the glomeruli were unstained and the tubules showed the blue dye.

b. Heidenhain then cauterized the surface part of the kidney, and the glomeruli were destroyed. Blue section was then found below the cauterized area, because the head of water had been cut off. Elsewhere the blue dye was washed into the ureter.

[iii. Leschke stained the kidney to show urea, uric acid, etc., and found them in the convoluted tubules, not in the glomeruli.]

CRITICISM.—

i. Most dyes stain the glomeruli as well as the tubules.

Theories of Urinary Secretion, *continued.*

ii. If most of the water was absorbed by the tubules from a weak solution of the dye, the colour would still be seen in the tubules, not in the glomeruli, because only in the former is it concentrated enough to show it.

Starling's Work.—Starling showed that the glomeruli merely filter and do not forcibly excrete. He showed that blood proteins have an osmotic pressure of about 40 mm. In Bowman's capsule there are therefore two factors at work: (*a*) Blood-pressure; (*b*) Osmotic pressure of the blood proteins. Ordinarily the blood-pressure is far higher than the osmotic pressure of blood proteins, so that urine is excreted; but flow of urine ceases as soon as blood-pressure falls to about 40 mm.—i.e., the osmotic pressure of the blood proteins. If blood-pressure is raised, flow of urine is increased. This shows that the glomeruli merely filter. In confirmation of this fact, during normal saline diuresis the oxygen-carbon-dioxide exchange of the kidneys is not altered.

4. CUSHNY-STARLING THEORY.—This is a modification of Ludwig's, and is widely accepted. The glomeruli filter off, say, 100 litres of plasma minus proteins, but the tubules absorb 98½ litres of the water, most of the sodium chloride and phosphate, and all the sugar, but not urea, uric acid, sulphates, and pigments, which are excreted in 1½ litres of urine. The tubules do vital work in this reabsorption; it is not merely a process of osmosis.

CRITICISM.—Bowman's capsule must filter such a lot of fluid for so little urine. Answers to this objection: (*a*) Tissue fluid in the kidney, derived from the blood, must amount to 100 litres in any case to furnish the daily output of urea; (*b*) In the bird, watery urine passes down the ureters, but nearly all is absorbed in the cloaca, leaving a white paste.

ADVANTAGE OF THE THEORY.—*It does not ask the renal tubules to play the part of a highly trained chemist*, and decide how to deal with each of the countless substances which may appear in the urine. The renal cells have merely to absorb a very simple fluid—water, chloride, phosphate, and glucose (i.e., Locke's fluid)—according to present need. Ordinarily all the glucose is absorbed,

Occasionally, as in diabetes insipidus, the tubules do not absorb any water, but only salts, so that the urine may be more dilute than the plasma.

[EVIDENCE.—*Direct evidence of the theory is almost absent.* The following facts are in its favour :—

1. Nishi has shown that, in cats and dogs, glucose is present in the cortex of the kidney, but not in the medulla.
2. Mercuric chloride will kill the tubules of a frog's kidney, not the glomeruli, and the urine is merely plasma minus protein.
3. Efforts have been made to poison the tubules and glomeruli separately, the tubules by uranium, the glomeruli by cantharides, but not much has been learnt from this. (Schlayer.)]

Functions of the Kidney.—

1. To keep the composition of the blood more or less constant by excreting excess of substances normally present in the blood, and any abnormal substances in the blood. From 0·1 to 0·2 per cent of glucose is normally present in the blood, but if the concentration rises above 0·2 it is excreted in the urine.
2. To regulate the reaction of the blood, any excess acid being excreted as ammonium salts or acid sodium phosphate. During sleep, the respiratory centre is probably less active, and carbonic acid accumulates in the blood. The kidneys counteract this effect by excreting a more acid urine.
3. To form hippuric acid from benzoic acid and glycin. This occurs especially in herbivorous animals.

MICTURITION.

Passage of Urine along Ureters.—The urine is driven down the ureters by the contraction of their muscular coat. Engelmann states that the contractions occur every 10 to 20 seconds, and the peristaltic wave is propagated at the rate of 20 to 30 mm. per second, so that urine enters the bladder in small rhythmical spurts—about one a minute in man. This is observed in human beings with the cystoscope ; also in cases where the anterior wall of the bladder was defective, with exposure of the ureteral orifices (*ectopia vesicæ*). No exact relation exists between the time of flow on the two sides. The entry of the ureters into the bladder is oblique, running for about ½ to ¾ in. in the muscular wall of the bladder, so that backflow of the urine is prevented.

Micturition, *continued.*

Nerve-supply of Ureter.—There is a plexus of nerve-cells and fibres round the muscular coat. The extrinsic nerve-supply is from the splanchnics and inferior mesenteric ganglion, and from the sacral autonomics.

Structure of Bladder.—The muscles of the bladder wall consist of: (1) Outer longitudinal layer, the detrusor urinæ; (2) Middle circular layer, best marked at the base; (3) Inner thin longitudinal layer. At the neck of the bladder, the circular layer is thickened to form the internal sphincter. The compressor urethræ may act as a sphincter after the removal of the prostate, but does not normally do so.

[If sodium iodide solution is injected into the bladder, the shadow is globular without a stalk. So long as the bladder is not too greatly distended, the pressure is kept constant whether it is half or three-quarters full, owing to the tone of the muscle wall. Beyond a certain point the pressure does rise, and creates afferent impulses.]

Epithelium of bladder is of the transitional variety.

Nerve-supply of Bladder.—

MOTOR NERVES.—

1. Sympathetic fibres, originating in 2nd to 5th lumbar nerves, and passing through sympathetic chain to inferior mesenteric ganglion, hypogastric nerves, and plexus, to circular muscle of bladder.

   Result of Stimulation of these Nerves.—In some animals there is a slight contraction of the bladder wall, in others inhibition of it. In the dog there is a strong contraction of the internal sphincter.

2. From 2nd and 3rd sacral nerves, fibres pass by way of the nervi erigentes which contract the detrusor muscle and inhibit the sphincter.

   Result of Stimulation of these Nerves.—Strong contraction of bladder, so that its contents are emptied.

SENSORY NERVES.—Sensory fibres pass up in the first four sacral spinal nerves, especially the 2nd and 3rd.

Urethra probably receives a branch from pudic nerve of sciatic plexus, at any rate in the lower animals.

Mechanism of Act of Micturition.—Accumulation of urine in the bladder stimulates the sensory nerves, leading to reflex stimulation of the internal sphincter. As the amount of urine increases, reflex contractions of the bladder muscle occur, and these contractions give rise to conscious desire to

micturate. If micturition does not occur, the contractions begin to diminish, and finally disappear.

WHEN MICTURITION OCCURS, there is :—

1. *Relaxation of the sphincter*, so that a few drops of urine enter the neck of the urethra, which creates a powerful reflex.
2. Contraction of the detrusor muscle at the same time.
3. Usually assistance by contractions of the abdominal muscle.
4. Compressor urethræ expels last drops of urine from urethra.

REFLEX CHARACTER OF ACT.—The act of micturition may be a pure reflex, as it is in young infants. In the adult it is controlled by the cortex, which up to a certain point can suppress the reflex.

THE REFLEX ARC.—Consists of: (*a*) Afferent path in sacral nerves; (*b*) Centre in lumbosacral region; (*c*) Efferent path by nervi erigentes.

EVIDENCE FOR REFLEX PATH.—Section of nervi erigentes or posterior roots of spinal nerves concerned abolishes act of micturition and leads to distention of bladder. In man micturition occurs when pressure in bladder is about 150 mm. of water.

[MOSSO AND PELLACANI'S EXPERIMENTS.—They measured volume of bladder in women by a catheter connected with recording apparatus. They find the bladder is very sensitive to reflex stimulation, and sensory stimulus is apt to cause contraction or increased tone of the bladder; consequently the amount of urine in the bladder causes greater pressure and more marked stimulation than when the bladder is relaxed.]

Section of the Spinal Cord and its Effect on Micturition.—During spinal shock, the mechanism is completely thrown out of action, both detrusor and sphincter being paralysed. There is total incontinence, urine dribbling away all the time.

In cases where the cord is divided high up in dogs or in man, when spinal shock has passed off there is reflex emptying of the bladder. Micturition occurs at intervals of about 4 to 5 hours, when the pressure exceeds a certain amount, which is found to be constant for the same individual.

THE URINE.

Normal human urine is a yellowish fluid, containing about 4 per cent of solids.

Amount.—Normal amount of urine secreted in 24 hours is 1500 c.c.—i.e., 50 oz.

The Urine—Amount, *continued.*

CAUSES OF INCREASED AMOUNT.—

1. Increased intake of fluids.
2. Increased blood-pressure due to increased force of heart-beat.
3. Constriction of cutaneous arterioles such as occurs in cold weather, leading to reflex dilatation of arterioles in splanchnic area, and consequent rise of pressure in glomerular capillaries.
4. Drugs—diuretics such as pituitary extract, salines, urea, caffeine, etc. Output of urine is also increased by glucose, which stimulates renal cells.
5. Nervous influences—e.g., emotion ; diabetes insipidus.

CAUSES OF DIMINISHED AMOUNT.—

1. Diminished intake of fluid.
2. Increased loss of body fluid in other ways, as in profuse sweating or loss of fluid by the bowel in diarrhœa or hæmorrhage.
3. Low blood-pressure—e.g., in shock.
4. Passive congestion of renal vessels by local compression.
5. Fevers and some types of Bright's disease.

Reaction.—Urine is normally acid to litmus, the pH being 6, i.e., 0·000001 grm. per litre. The reaction depends on the relative amounts of Na_2HPO_4 and NaH_2PO_4 present. Variations in amounts of the two phosphates depend on the selective action of the kidney, by means of which the reaction of the blood is kept constant.

CAUSES OF VARIATION IN REACTION.—

1. Muscular Exercise.—After muscular exercise, lactic acid passes into the blood, the Na_2HPO_4 is retained in the blood to neutralize the acid, and more NaH_2PO_4 is excreted, hence reaction of urine becomes more acid.
2. Nature of the Food.—On animal diet, the acidity of the urine is increased owing to oxidation of the sulphur and phosphorus of the proteins to sulphuric and phosphoric acids. On vegetable diet, the alkaline salts of the vegetable acids result in carbonates when oxidized, hence urine of vegetarians is frequently neutral or even alkaline. Urine of a herbivorous animal is neutral or alkaline, but if the animal is starved its urine becomes acid, since it is living on its tissue proteins.

3. DECOMPOSITION OF UREA INTO AMMONIUM CARBONATE by the *Micrococcus ureæ*, causing the urine to become alkaline. This occurs when the urine stands for some time, and in cases of chronic infection of the bladder.

Specific Gravity.—Varies normally between 1015 and 1025. It is raised when there is much loss of fluid in other ways, or when there is an increased amount of solid in the urine; e.g., in diabetes mellitus it may be raised to 1040 or more. It is lowered in some forms of renal disease, when excess of fluid is being excreted, and in diabetes insipidus, where the solids are unaltered but the water is increased. With normal kidneys, specific gravity varies at different times of the day, whereas in severe renal inefficiency it remains constant.

CALCULATION OF PERCENTAGE OF SOLIDS IN URINE FROM SPECIFIC GRAVITY.—Last two figures of specific gravity are multiplied by 2·2, and result divided by 10. This gives percentage of total solids in the urine.

Composition of the Urine.—

1. WATER.—96 per cent.
2. INORGANIC SALTS.—
   a. Sodium chloride, 1 per cent—i.e., 15 grm. per day.
   b. Phosphates, especially calcium phosphate and acid phosphate of sodium. Potassium acid phosphate and magnesium phosphate also occur.
   c. Sulphates of sodium and potassium.
   d. Carbonates of sodium, ammonium, calcium, and magnesium may occur in an alkaline urine.
3. CALCIUM OXALATE.—Small quantities.
4. ETHEREAL SULPHATES.—Compounds of sulphuric acid with skatoxyl, indoxyl (indican), phenol or cresol, and potassium.
5. NITROGENOUS CONSTITUENTS.—
   a. Urea, 2 per cent—i.e., 30 grm. per day.
   b. Ammonium bodies. Nitrogen excreted in form of ammonia is about 4 per cent of total nitrogen.
   c. Uric acid and purin bodies, about 0·05 per cent.
   d. Creatinine, about 0·08 per cent.
   e. Hippurates, about 0·07 per cent.
6. PIGMENTS.—Urochrome; urobilin; uro-erythrin; hæmatoporphyrin (normally in very minute amounts); indican bodies.

The Urine—Composition, *continued.*

7. DISSOLVED GASES.—
   - *a.* Carbon dioxide. 100 vols. of urine contain 15 vols. of gas, nearly all of which is carbon dioxide.
   - *b.* Nitrogen in small amounts.
   - *c.* A little oxygen (Buckmaster).

Deposits in the Urine (*Fig.* 9).—

1. IN ACID URINE.—
   - *a.* Sodium and potassium biurates; an amorphous, pink sediment.
   - *b.* Uric acid crystals: deep-red, shaped like whetstones or cylinders.
   - *c.* Calcium oxalate crystals: small, square, envelope-shaped.
   - *d.* Rarely, the acid urates of sodium and ammonium: spheroidal masses with projecting spikes.
   - *e.* Very rarely, *cystin*: flat hexagonal colourless plates, soluble in ammonia.
2. IN ALKALINE URINE.—
   - *a.* Earthy phosphates: deposited in amorphous form.
   - *b.* Calcium phosphate: prisms arranged in rosettes.
   - *c.* Triple phosphates—i.e., ammonio-magnesium phosphate: large crystals resembling coffin-lids in shape.

ORIGIN AND DETECTION OF THE URINARY CONSTITUENTS.

Nitrogenous Bodies.—Total nitrogen is about 20 grm. per day, dropping to about 6 grm. after a few days of starvation.

ESTIMATION OF TOTAL NITROGEN.—This is done by Kjeldahl's method. The principle of the method is the conversion of the nitrogen into ammonium sulphate by boiling with concentrated sulphuric acid, neutralizing with strong caustic soda, and distilling the ammonia into standard sulphuric acid.

UREA.—

ORIGIN.—From food and tissue proteins. *See* p. 121.

ISOLATION OF UREA FROM URINE.—Urine is concentrated to one-sixth its bulk by evaporation, and concentrated nitric acid added. Crystals of urea nitrate separate out. They are dissolved in alcohol, and barium carbonate added; carbon dioxide is given off, and barium nitrate and urea formed. The urea can be extracted with alcohol, and purified.

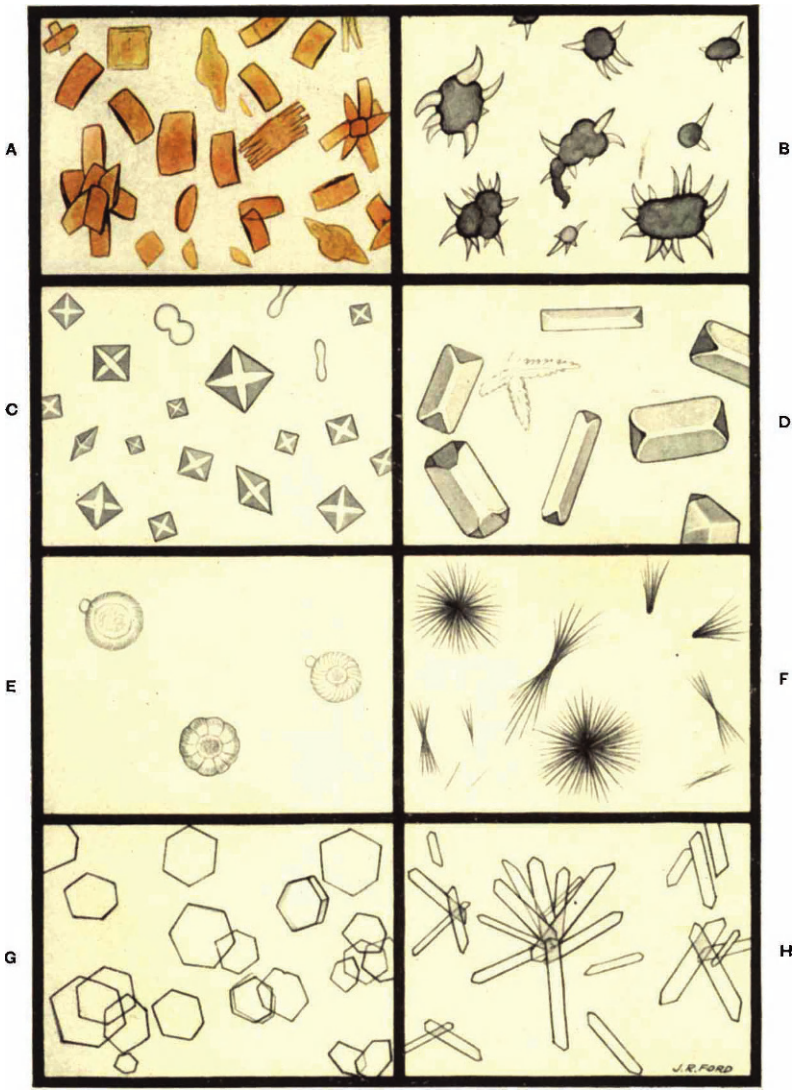


Fig. 9.—Urinary deposits. **A**, Uric acid; **B**, Ammonium urate; **C**, Calcium oxalate; **D**, Ammonio-magnesium phosphate; **E**, Leucin; **F**, Tyrosin; **G**, Cystin; **H**, Stellar phosphates. (*From* '*Pye's Surgical Handicraft*'.)

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TESTS FOR UREA.—

1. Crystals of urea nitrate can be recognized as octahedra under the microscope. If oxalic acid is added, definite prismatic crystals of urea oxalate are produced.
2. Urea crystals are decomposed at 150° C. with evolution of ammonia, and biuret remains, which gives the characteristic rose-red colour with a trace of copper sulphate and excess of 20 per cent caustic potash.
3. Addition of fuming nitric acid to the urine leads to the evolution of carbon dioxide and nitrogen.

ESTIMATION OF UREA.—

1. *Dupré's Method.*—This depends on the fact that urea is decomposed by an alkaline solution. Sodium hypobromite is added, nitrogen being evolved. The nitrogen is collected and the amount of urea present can be estimated.
   Disadvantage : Some nitrogen is evolved from uric acid, creatinine, and ammonia when acted on by sodium hypobromite.
2. *Urease Method.*—Soya bean contains an enzyme, urease, which converts urea into carbon dioxide and ammonia. The ammonia can be drawn over into a known amount of standard acid, and the excess acid titrated with standard alkali.

AMMONIA.—

ORIGIN.—Formed as a result of protein metabolism, and is normally chiefly converted into urea by the liver. A certain amount combines with acids of the blood, chiefly with the CO_2 resulting from oxidative processes. In conditions such as advanced cases of diabetes mellitus, where abnormal acids are formed in the body, there is increased formation of ammonia to combine with them, thus tending to keep the reaction of the blood constant, and the proportion of nitrogen in the form of ammonia in the urine is increased.

[ESTIMATION OF AMMONIA.—

1. *Formalin Method.*—On addition of formaldehyde to neutral solutions of ammonium salts, urotropine (hexamethylenetetramine) is formed, and a corresponding amount of acid set free from the ammonium salt. The acid can be titrated with standard alkali.
2. Add sodium carbonate; draw air through to carry off ammonia; collect and titrate in decinormal acid.]

The Urine—Nitrogenous Constituents, *continued.*

URIC ACID.—

ORIGIN.—From breaking-down of nucleoprotein in the food and tissues, half being exogenous and half endogenous. (*See* METABOLISM, p. 123.)

DETECTION.—

1. Addition of concentrated HCl to the urine, and allowing it to stand for 24 hours, leads to a precipitate of small, pigmented crystals, having a characteristic whetstone shape. They can be purified by dissolving in an alkali and reprecipitating with HCl.
2. *Murexide Test.*—Evaporated with nitric acid and ammonia added, a purple colour occurs owing to the formation of ammonium purpurate or murexide.

[ESTIMATION OF URIC ACID.—

Folin-Shaffer Method.—Based essentially on the fact that ammonium urate is precipitated from the urine on saturation with ammonium sulphate. The urates can then be determined by titration with potassium permanganate.]

CREATININE.—

ORIGIN.—Amount excreted is very constant in health, so that apparently the origin is purely endogenous, especially from muscles. It is increased during fevers, where there is increased breakdown of tissues.

Creatine is not normally present in the urine, but it occurs in women during involution of the uterus, also during starvation. It is normally present to the extent of about 0·5 per cent in the muscles, and to a small extent in the blood.

Creatinine is an anhydrous form of creatine, but their exact relation to one another is uncertain. One view is that they have a common origin, creatine being one of the end-products of tissue break-down, being normally converted into creatinine before it is excreted (Mendel and Ross). Other observers believe that creatinine is formed as an end-product of tissue break-down and excreted as such, while creatine is also formed in the same way, but undergoes a further change, since creatine given to a man by mouth may be excreted either as creatine or creatinine.

TESTS FOR CREATININE.—

1. *Jaffé's Test.*—On addition of a few drops of a

saturated solution of picric acid, and of 20 per cent caustic potash, a deep-red colour is produced.

2. *Weyl's Test.*—On addition of a few drops of sodium nitroprusside solution, and 20 per cent caustic potash, a red colour is produced, which changes to yellow on addition of acetic acid, and, on boiling, the solution becomes green and a prussian-blue precipitate separates out.

[ESTIMATION OF CREATININE.—Folin's colorimetric method is usually employed. This depends on the red colour produced as in Jaffé's test, compared with the colour of a standard solution of potassium bichromate.]

HIPPURIC ACID.—

ORIGIN.—Formed by the synthesis of benzoic acid and glycin. The benzoic acid is derived from aromatics in the food, glycin from the body. It is present in the urine in larger amounts in herbivorous animals, since vegetables contain benzoic acid compounds.

The synthesis occurs in the kidney. Evidence :—

1. Hippuric acid can be formed by minced kidney from benzoic acid and glycin.
2. Perfusion of benzoates through the kidney leads to the formation of hippuric acid.
3. Feeding an animal on benzoates increases the hippuric acid in the urine but not in the blood.

[DETECTION OF HIPPURATES.—A horse's urine is evaporated, and concentrated HCl added ; crystals of hippuric acid are deposited. The crystals are in the form of four-sided prisms arranged in rosettes. On heating to 186° C. the crystals melt, and if they are heated beyond this, the solution becomes red, a white sublimate of benzoic acid occurs, and there is an odour of bitter almonds owing to the formation of hydrocyanic acid.]

Non-nitrogenous Constituents.—

SULPHATES.—

ORIGIN.—From decomposition of proteins in the food and tissues.

Sulphur is present in the urine in three forms : (1) Inorganic. (2) Conjugated sulphates. As a result of the putrefaction of tryptophan in the large intestine, indole, skatole, and phenol are formed. During absorption, they combine with inorganic sulphates to form the relatively harmless products which are excreted in the urine. (3) Neutral sulphur compounds. Nature uncertain.

The Urine—Non-nitrogenous Constituents, *continued.*

CALCIUM OXALATE.—

ORIGIN.—(*a*) Ingestion of oxalates in the food, especially rhubarb, tomatoes, spinach, and strawberries; (*b*) Fermentation of sugar in the stomach in the absence of HCl leads to the formation of oxalic acid.

TEST FOR OXALATES.—They can be precipitated from solution by addition of equal bulk of methylated spirit. The crystals are insoluble in acetic acid, but soluble with difficulty in HCl.

They are the commonest form of urinary calculi. These are more common in India than in this country owing to two facts: (*a*) Increased sweating; (*b*) Eating more coarse vegetables.

INORGANIC SALTS.—

CHLORIDES, CHIEFLY SODIUM CHLORIDE.—

Origin.—Chiefly from the sodium chloride of the food.

Test for Chlorides.—On addition of silver nitrate to the urine which has been acidified (to prevent precipitation of silver phosphate), a white precipitate of silver chloride occurs which is soluble in ammonia.

Estimation of Chlorides.—General principle of the method is the precipitation of the chloride by excess of standard silver nitrate, and estimation of the excess by titration with a standard solution of potassium thiocyanate.

Next to urea, chlorides are the most abundant urinary constituent, but in salt starvation and in pneumonia they are much diminished; in the latter condition plasma exudes into the alveoli of the lungs.

PHOSPHATES.—Earthy phosphates are only very slightly soluble in water, but are normally kept in solution in the urine by the presence of acid sodium phosphate. If the urine becomes neutral or alkaline they are precipitated.

Origin.—(*a*) Exogenous, from protein compounds in the food; (*b*) Endogenous, from nucleoprotein, etc.

Test for Phosphates.—On boiling with excess of nitric acid and ammonium molybdate, a yellow precipitate of ammonio-phospho-molybdate is formed.

[*Estimation of Phosphates.*—The urine plus a little acid sodium acetate solution is warmed to 80° C. and titrated against a standard solution of uranium nitrate, a precipitate of uranium

phosphate being formed. Potassium ferrocyanide is used as an indicator to indicate the presence of free uranium nitrate by the formation of a brown precipitate.]

CARBONATES.—

Origin.—Carbonates of food, and vegetable acids such as citric and tartaric acids. They occur in the urine of vegetarians.

Urinary Pigments.—

1. UROCHROME.—The ordinary straw-coloured pigment. Except that it is allied to urobilin, its relationships are uncertain.
2. UROBILIN.—Formed from bilirubin and thus indirectly from hæmoglobin. Bilirubin is reduced to stercobilin by bacteria in the colon, some being absorbed and excreted by the kidney as urobilinogen. On standing, this is converted into urobilin, which gives the urine a golden colour. Its spectrum shows an absorption band in the blue between the E and F lines.
3. URO-ERYTHRIN.—This gives a red colour to deposits of urates and uric acid.
4. HÆMATOPORPHYRIN.—This is not normally present in the urine, but occurs after poisoning with certain drugs, especially sulphonal, rendering the urine black. Its spectrum shows an absorption band on either side of the D line.
5. INDICAN BODIES.—Indole and skatole conjugated with sulphates.

   TEST FOR INDOLE IN URINE.—Add concentrated HCl, and a little bleaching powder; shake with chloroform: blue colour (indigo).

ABNORMAL CONSTITUENTS OF THE URINE.

Proteins (chiefly albumin).—Usually due to disease of cells of urinary tubules, so that proteins of plasma pass through them.

TESTS FOR PROTEIN.—

1. On boiling top of a long column of urine, the albumin is coagulated, and the urine shows a cloudiness which does not disappear on the addition of acetic acid or heating. Cloudiness may be due to phosphates, but this clears on addition of acetic acid.

   Fallacies. — (*a*) Phosphates. (*b*) Nucleoprotein gives a faint cloud with acetic acid in hot or cold condition. Addition of the acetic acid *before* boiling avoids this fallacy.

The Urine—Abnormal Constituents—Proteins, *continued.*

2. HELLER'S TEST.—When concentrated nitric acid is poured down the side of a test-tube on to urine containing albumin, a white ring forms at the junction of the two fluids.

Fallacies.—(*a*) If urine is concentrated, crystals of urea nitrate may form a cloud. (*b*) If patient is taking drugs containing a resin, cloud may be formed. (*c*) Albumose gives a cloud at the junction, which, however, disappears on heating and reappears on cooling.

ESTIMATION OF PROTEIN.—Esbach's albuminometer is used. A definite amount of urine is poured into a tube, and a certain amount of Esbach's reagent (picric acid, with citric acid and water) added, the fluids are mixed, and left to stand for 24 hours. A yellow precipitate occurs, and the level at which the precipitate stands can be read, the tube being graduated so that it reads the percentage of albumin directly.

Sugar.—Lactose may appear in the urine of lactating women, but the sugar most frequently found in the urine is dextrose or glucose.

TESTS FOR GLUCOSE.—

1. FEHLING'S TEST.—*See* p. 3.

Fallacies of Urinary Origin.—Fehling's solution is also reduced by: (*a*) Uric acid and creatinine, to a slight extent; hence more Fehling's solution must be used than urine. (*b*) Glycuronic acid, which appears in the urine after taking certain drugs—e.g., camphor, chloral, etc. (*c*) Alcapton; distinguished by the urine turning black. (*d*) Lactose; distinguished by formation of the osazone.

2. FERMENTATION TEST.—Yeast converts glucose into carbonic acid and alcohol; and if a tube containing the urine and yeast is inverted over mercury, the carbon dioxide collects at the top of the tube and depresses the urine.

3. FORMATION OF AN OSAZONE.—Phenylhydrazine hydrate and sodium acetate are added to the urine and heated for half an hour. Yellow needle-like crystals of glucosazone are formed. In this way glucose can be distinguished from lactose, which forms lactosazone.

ESTIMATION OF SUGAR.

BENEDICT'S METHOD.—*See* p. 4.

Diacetic Acid and Acetone.—These occur in the condition of acidosis.

TEST FOR DIACETIC ACID.—Sulphuric acid and ether are added to the urine, so that the ether rises to the surface, containing the diacetic acid in solution. On addition of ferric chloride to this ethereal solution a red colour is produced.

TEST FOR ACETONE.—ROTHERA'S TEST: 10 c.c. of urine are saturated with ammonium sulphate, a few drops of a solution of sodium nitroprusside added, and a few c.c. of strong ammonia poured on the surface. A purple ring is formed at the junction of the liquids.

Blood.—Urine is smoky-red or black in colour.

TESTS FOR BLOOD.—

1. GUAIACUM AND OZONIC ETHER.—*See* p. 24.
   Fallacy.—Milk and other substances may give the reaction.
2. BENZIDINE TEST.—The addition of benzidine and glacial acetic acid to the urine, followed by hydrogen peroxide, results in the formation of a blue colour. This test is considerably more reliable than the preceding one.
3. SPECTROSCOPICAL EXAMINATION.
4. MICROSCOPICAL EXAMINATION.—Identification of the red blood-corpuscles under the microscope. In cases known as hæmoglobinuria, as distinct from hæmaturia (blood in the urine), corpuscles are not present.

Pus.—

TESTS FOR PUS.—

1. On addition of 20 per cent caustic potash, the urine becomes stringy.
2. Pus-cells may be seen under the microscope.

Bile.—The urine is a dark-green colour.

TESTS FOR BILE.—

1. BILE PIGMENTS.—Gmelin's test.
2. BILE SALTS.—Hay's sulphur test.

Homogentisic Acid: Alcaptonuria.—The urine turns black on exposure to the air, due to the presence of homogentisic acid, and reduces Fehling's solution. No osazone is formed. It is an inborn defect, occurring in children of first cousins only, and persisting throughout life.

CHAPTER XII.

METABOLISM. DIET. GROWTH. THE LIVER.

Nitrogen and Carbon Equilibrium.—In adult life, intake is regulated normally so that nitrogen equilibrium is maintained. This equilibrium may be established at different levels, e.g., a man may be in nitrogenous equilibrium on a diet containing 10 grm. of nitrogen per day; if nitrogen is increased to 20 grm., it is soon found that 20 grm. is excreted. An individual in nitrogen equilibrium may be either gaining or losing weight. Excess of food may be stored as glycogen or fat; or supply of energy-yielding food may be insufficient, some of body-fat being oxidized. If protein is given to a starved animal, it markedly increases the basal metabolism ('specific dynamic energy' of protein).

Experimental Investigation of Total Metabolic Activity.—First attempted by Voit and Pettenkofer, who performed experiments on men and animals, analysing the nitrogen in urine and fæces and the CO_2 exhaled by lungs. Subjects were kept in small chambers and air was drawn through. Modern experiments attempt to balance not only ingesta and excreta, but income and output of energy. Done by respiration calorimeter.

ATWATER AND BENEDICT RESPIRATION CALORIMETER.—Small room having several walls, so that temperature is kept constant. Heat given off by body is carried away by system of pipes containing water. Knowing rise of temperature and volume of circulating water, number of calories of heat given off by the individual can be estimated. Same air is kept circulating through the room, but CO_2 and water in expired air are absorbed, and fresh oxygen is introduced. Food taken and its calorie value are known; urine and fæces examined as before. Ratio $\frac{CO_2}{O_2}$ (respiratory quotient) serves as an indication of fat and carbohydrate metabolism.

Basal Metabolism.—*See* p. 50.

Composition of Food.—Normally food consists of protein, fats, carbohydrates, vitamins, salts, and water.

Calorie Values of Foodstuffs.—Determined by completely burning a food in a bomb calorimeter. 'Physical' and 'physiological' heat values of protein are not the same, since it does not undergo complete combustion in the body. Fat and carbohydrate do undergo complete combustion.

1 grm. of fat is equivalent to 9·3 calories
1 grm. carbohydrate is equivalent to 4·1 calories
1 grm. protein is equivalent to 4·1 calories (physiological value)

(1 calorie equals amount of heat required to raise temperature of 1000 grm. of water 1° C.)

Energy appears partly as heat and partly as muscular work.

Causes of Increased Metabolism.—

1. MUSCULAR ENERGY.—Energy is provided by increased metabolism of carbohydrates if present in sufficient amount; if not, fats and proteins are used. Relative amounts of food-stuff metabolized are ascertained by observing: (*a*) Nitrogen excretion in urine. Only slightly increased in muscular exercise. (*b*) Respiratory quotient.
2. SIZE OF THE ANIMAL.—The smaller the animal, the greater the metabolic changes. In basal metabolism determinations, analysis of expired air is brought to a standard figure by comparing it, not with body weight, but with body surface.
3. CERTAIN DISEASES.—Fevers and hyperthyroidism increase basal metabolism.

Causes of Decreased Metabolism.—

1. SLEEP.—Decrease in non-protein metabolism; slight or no decrease in protein metabolism.
2. STARVATION.—With animal, at rest, after 3 or 4 days nitrogen output in urine reaches a low level (about ¼ normal), and remains constant until a few days before death, when it may rise again. Uric acid in urine is halved (in man); sulphates are reduced. Creatinine and neutral sulphur are but little affected. Ketone bodies appear; ammonia-nitrogen percentage increases. Store of glycogen in body is used up in 3 days. Loss of weight occurs chiefly at expense of less vital organs such as fat, spleen, and muscle, while heart and central nervous system lose little or none.

Causes of Decreased Metabolism, *continued.*

FURTHER CHANGES IN STARVATION.—Leucocytes diminished. Fæces passed once or twice only. Death follows in about six weeks if water is allowed; one week without water (in adults).

3. MYXŒDEMA.

METABOLISM OF PROTEINS.

Protein is broken down into amino-acids, as described under digestion (Chapter VIII), and absorbed as such by intestine, passing mainly into portal vein.

Fate of Amino-acids.—Amino-acids are utilized in one of two ways :—

1. RE-SYNTHETIZED to form tissue protein—only small proportion in adults. Probably particular amino-acids are combined in much the same way as polypeptides are formed—i.e., by union of OH group of one acid with H of the amino group of another acid.
2. USED AS A SOURCE OF ENERGY.—Exact process is not understood. Following are main points of process known :—
   a. Deaminization, amino (NH_2) group being split off to form ammonia, probably in the liver, and possibly also in other tissues.
   b. Formation of urea from ammonia, and its excretion.
   c. The organic acid resulting from deaminization of amino-acid is oxidized to furnish energy, or built up into sugar and oxidized at some later period.

Formation of Urea.—

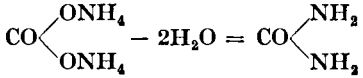
SITE OF FORMATION.—Liver. Evidence :—

1. REMOVAL OF LIVER in frog and dog results in marked decrease in output of urea and increase in that of ammonia.
2. ECK'S FISTULA—i.e., formation of communication between portal vein and inferior vena cava, abolishing portal circulation through the liver. Animals survive this operation for some time. There is decreased urea and increased ammonia in urine, and, later, convulsions occur due to excess of ammonia in blood. If protein is withheld from diet, convulsions do not occur.
3. DISEASE IN MAN.—In acute yellow atrophy of liver, many liver cells become functionless, and there is diminished urea and increased ammonia in urine. Amino-acids (leucin and tyrosin) appear in the urine.

4. SCHRÖDER'S EXPERIMENTS.—Liver was taken from a freshly killed dog, and blood from a starving dog passed through it. There was no increase of urea; but with blood from a well-fed animal urea was increased. Hence, after digestion, blood of an animal contains some substance which can be converted into urea by the liver.
5. SCHÖNDORFF'S EXPERIMENT.—Blood of a fasting dog was irrigated through hind limbs of a well-nourished animal, and no increase of urea in the blood resulted, but when subsequently passed through the liver, there was marked increase of urea.
6. PERFUSION EXPERIMENTS.—Perfusion of solution of amino-acids in saline through the liver results in loss of these bodies and formation of urea.

PRECURSORS OF UREA.—

1. AMMONIUM COMPOUNDS.—Evidence :—
   a. Urea is formed by perfusion of liver with ammonium carbonate or carbamate. Process is one of dehydration, removal of one molecule of water from ammonium carbonate forming ammonium carbamate, while if a second is removed, urea results.



   b. Normally the percentage of ammonia in portal blood is three times greater than that in general circulation. After formation of an Eck's fistula, percentage of ammonia in portal and systemic bloods is the same.
2. MONO-AMINO-ACIDS.—Evidence :—
   a. Feeding animal with glycin, alanin, leucin, aspartic acid, etc., by mouth leads to increased excretion of urea.
   b. Urea is formed by perfusion of liver with mono-amino-acids.

[3. DI-AMINO-ACIDS.—Arginin gives rise to urea by means of conversion of guanidin molecule, not amino group. There is a ferment arginase in various tissues which splits arginin into urea and orthinin.

4. URIC ACID.—Uric acid is converted into urea by an intracellular enzyme present in liver and kidney. Does not occur in man.]

EXOGENOUS AND ENDOGENOUS UREA.—The urea excreted is formed partly from proteins of food (exogenous

Formation of Urea, *continued.*

origin), and partly from the break-down of tissue proteins (endogenous). Evidence :—

1. A marked difference exists between output of urea in a man taking abundant protein and that of a man taking very little. Hence some must be exogenous in origin.
2. In starvation, there is still a small excretion of urea, so that some urea must come from the tissues. Increased work, with consequent increased break-down of tissues, leads to increased excretion of urea the next day.

Urea is derived chiefly from the food under normal conditions.

Functions of Amino-acids.—Amino-acids may be divided into two groups :—

1. THOSE ESSENTIAL TO LIFE.—This class includes tryptophan, tyrosin, arginin, and histidin. They cannot be formed in the body. Tyrosin may be necessary as a precursor of adrenalin.
2. THOSE USED AS A SOURCE OF ENERGY.—Some of these, such as glycin, can be formed in the tissues. Some of them serve as a source of sugar—e.g., glycin, aspartic acid.

OSBORNE AND MENDEL'S EXPERIMENTS ON VALUES OF AMINO-ACIDS.—They fed rats on diet of carbohydrates, fats, inorganic salt, water, and some single protein. Results :—

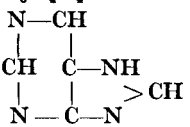
Gelatin or *Zein* was inadequate, and animal died —no tryptophan.

Gliadin sufficed for continuation of life, though growth ceased, probably owing to absence of lysin. If at any time suitable protein was given, growth commenced again. Lysin appears to be necessary for growth.

Casein or *Glutein* was adequate, and growth was normal.

PURIN METABOLISM.

Purin Bodies.—Derived from nucleoproteins. All contain the purin nucleus, $C_5H_4N_4$. Formula :—



PURIN BODIES OF PHYSIOLOGICAL IMPORTANCE.—

1. Oxidation Derivatives of Purin Nucleus.—
   a. Hypoxanthin or monoxypurin, $C_5H_4N_4O$.
   b. Xanthin or dioxypurin, $C_5H_4N_4O_2$.
   c. Uric acid or trioxypurin, $C_5H_4N_4O_3$.
2. Amino Derivatives.—
   a. Adenin or amino-purin, $C_5H_3N_4 . NH_2$.
   b. Guanin or amino-oxypurin, $C_5H_3N_4O . NH_2$.
3. Methylpurins.—
   a. Caffein or trimethylxanthin (in tea and coffee), $C_5H(CH_3)_3N_4O_2$.
   b. Theobromin or dimethylxanthin (in cocoa), $C_5H_2(CH_3)_2N_4O_2$.

Nucleoproteins.—Occur in cell nuclei. Broken down during digestion into protein and nucleic acid. On hydrolysis, nucleic acid yields: (1) *Purin bases*, adenin and guanin; (2) *Pyrimidine bases*, cystosine, thymine, and uracil; (3) *Carbohydrate*, a pentose or hexose; (4) *Phosphoric acid.* Adenin and guanin may be in part excreted as such, but are chiefly oxidized to oxypurins by the ferments adenase and guanase. Oxypurins are further oxidized to uric acid.

Origin of Uric Acid.—From nucleoproteins of tissues or food—i.e., of endogenous or exogenous origin. Half is normally endogenous, half exogenous (in man).

ENDOGENOUS URIC ACID.—Originates from break-down of cell nuclei due to ferments found especially in spleen, liver, and other organs.

Nucleases of several kinds convert nuclein into guanin and adenin.

Adenase converts adenin into hypoxanthin.

Guanase converts guanin into xanthin.

Oxydase converts xanthin and hypoxanthin into uric acid (only in the liver of man).

Endogenous uric acid can be estimated by putting an individual on a purin-free diet—i.e., milk, bread, and eggs. It is increased by severe or unwonted muscular exercise, or fever, owing to increased catabolism of body tissues.

EXOGENOUS URIC ACID.—Sources in food:—

1. Methylpurins.—Caffeine and theobromine in tea, coffee, and cocoa (in practice very little).
2. Xanthin and Hypoxanthin.—In soups, gravies, and meat extracts. Advertised beef extracts contain no

Purin Metabolism—Origin of Uric Acid, *continued.*

protein, some sugar, fat, salts, and useless substances like creatin; they are valueless as foods, and act merely owing to xanthin and hypoxanthin.

3. COMBINED PURINS.—E.g., nucleoproteins in liver, sweetbread, or any substance rich in cell nuclei.
4. Purins occur to a less extent in fish and a few vegetables, especially peas, beans, and lentils, and to a small extent in mushrooms. Small amount present in beer.

Uric acid which passes through the liver is converted into urea (not in man).

Action of Purin Bodies.—Stimulants to flow of gastric juice, and also increase strength of heart-beat, and improve circulation. Unlike alcohol, they are not followed by a depressing effect. Bovril increases rate of growth of young animals to greater extent than can be accounted for by amount of nitrogen in it. Probably acts by facilitating digestion and absorption. To some people purin bodies act as poisons, giving rise to headache and premature degeneration of the arteries.

METABOLISM OF CARBOHYDRATES.

Sources of Carbohydrates.—

1. STARCH, in potatoes, bread, etc.
2. DISACCHARIDES, e.g., lactose in milk, sucrose in cane sugar, maltose in yeast.
3. MONOSACCHARIDES, e.g., glucose in fruits, honey, etc., and fructose in various fruits.

Absorption of Carbohydrates.—All are broken down by digestive juices into monosaccharides, and absorbed into blood as such, chiefly as glucose, but a little as lævulose and galactose. Absorption is mainly from small intestine, but can occur to some extent from rectum.

Blood-sugar.—Estimated by MacLean's method, picramic acid method (red colour with picric acid), or Folin's method. (*Folin's method:* Precipitate proteins from oxalated blood by sodium tungstate + H_2SO_4. To filtrate add alkaline $CuSO_4$. Heat. Add phospho-tungstic acid + phospho-molybdic acid + Na_2CO_3. Blue colour. Estimate by colorimetry.) Present as α and β glucose, perhaps the γ glucose.

Amount of sugar in general circulation is constant in health, and even in prolonged starvation. Before food it is 0·08 per

cent; after carbohydrate meal it rises in half an hour to 0·18, then soon falls, owing to outflow of insulin. In certain diseases it may be increased to 0·2 per cent, but above this point excess sugar is excreted in the urine. If it falls too low, convulsions occur (in animals).

Amount in portal vein varies—i.e., from 0·05 per cent in advanced starvation to 0·4 per cent after meal rich in carbohydrates.

Formation and Function of Glycogen.—

GLYCOGENIC FUNCTION OF THE LIVER.—Glucose can be stored in the liver as glycogen or 'animal starch'. Glycogen can be converted into glucose by various enzymes, or by hydrolysis with acids.

DEMONSTRATION OF PRESENCE OF GLYCOGEN IN THE LIVER.—Liver of a well-fed animal is hardened in alcohol. Sections show cells containing substance which stains port-wine colour with iodine.

ESTIMATION OF AMOUNT OF GLYCOGEN IN THE LIVER.—Liver is removed soon after a carbohydrate meal, is cut up into small pieces, and thrown into boiling water for 2 to 3 minutes (to kill ferment). It is then pounded with sand, boiled for a few minutes in slightly acidified water, and filtered into alcohol, which precipitates the glycogen. Amount of glycogen in liver is very variable, the maximum being 150 grm. [About 150 grm. of glycogen is stored in the muscles (in man).]

EVIDENCE THAT GLUCOSE IS CONVERTED INTO GLYCOGEN IN LIVER.—

1. Difference between portal and systemic blood-sugars, showing that sugar must be stored in the liver in some form.
2. Glycogen in liver may be raised from normal 1 to 4 per cent to 17 per cent in dog after a diet rich in carbohydrates.
3. Grübe circulated defibrinated blood containing glucose through excised liver of a dog, and found an increase of glycogen.
4. Starch analogy in plants.

Protein can give rise to glucose, hence it must be able to produce glycogen. It is uncertain whether glycogen can be formed from fats; probably it is not formed from fatty acids, but Cremer has furnished apparent proof that the glycerol part of fats can be converted into glycogen or sugar.

Metabolism of Carbohydrates, *continued.*

FUNCTION OF GLYCOGEN.—

1. CLAUDE BERNARD'S VIEW (generally accepted).—Glycogen is a means of storing sugar, being reconverted into sugar as the body needs it. Thus, as sugar is used up in muscular work, systemic blood-sugar would fall; but glycogen is then converted into sugar, which enters the circulation and maintains constant level.

   Evidence for Bernard's View.—Freshly excised liver contains only a very small amount of sugar, but in a short time glycogen becomes markedly diminished and disappears, while sugar increases. Conversion of glycogen into glucose is probably due to an enzyme in the liver. In starved animals, blood-sugar remains constant, while at death glycogen is almost absent from liver. If liver is removed, blood-sugar falls. In death after severe exercise there is very little glycogen in liver, in death from diabetes none.

[2. PAVY'S VIEW.—He considered formation of sugar from glycogen was a purely post-mortem phenomenon, and believed glycogen was built up into fat. Possibly some glycogen is used in this way.]

Fate of Sugar.—Finally oxidized to CO_2 and water, with production of energy, but intermediate stages are unknown. Methyl-glyoxyl is probably one, and lactic acid another; it occurs in muscles during activity. Glycuronic acid may be formed from sugar, and is usually combined with injurious substances, e.g., phenols. It may be a protective substance or a member of a normal series of metabolites of sugar. A certain amount of sugar is stored in muscles as glycogen, and some is converted into fat for storage.

Functions of Carbohydrates.—

1. SOURCE OF ENERGY, especially for muscular work.

   EVIDENCE:—

   a. Starling found, using heart-muscle preparation, that normal heart used up 4 mgrm. of sugar per grm. of heart muscles per hour.

   b. Contracting muscle takes up more sugar from blood perfused through it than does resting one.

   [If nerve to a limb is cut so that limb is paralysed, glycogen is present in larger amounts in these muscles than in normal ones. It has been shown that muscular tissue cannot readily use the sugar unless it has first been perfused through the pancreas, or insulin has been added.]

c. When a muscle contracts, glycogen disappears from it, and during muscular exercise glycogen eventually disappears from liver.

2. SOURCE OF HEAT.
3. PROTECTION OF PROTEIN.
   EVIDENCE.—Nitrogen equilibrium can be maintained on very much smaller amount of protein if carbohydrate is freely supplied.
4. FORMATION OF FAT, if excess of carbohydrate is taken. It may take part in other constructive processes—e.g., formation of nucleic acid and cerebrosides.
5. PREVENTION OF KETOSIS.—*See below.*

Causes of Glycosuria (i.e., sugar in urine).—

1. ALIMENTARY.—In a healthy man, if more than 150 grm. of glucose is eaten, more sugar is carried to the liver than it can deal with. Hyperglycæmia results—i.e., increased sugar in systemic blood—and excess of sugar is excreted by kidneys.
2. INJECTION OF PHLORIDZIN (glucoside from bark of cherry-tree, etc.).—Causes glycosuria, but the blood-sugar is not raised, and may even be lower than normal. Acts even when there is no glycogen in liver, so that sugar is formed from protein. Apparently acts on kidney, causing increased permeability of renal cells to sugar. Phloretin, which is sugar-free, has same effect. Either will act on the excised kidney.
3. ADRENALIN GLYCOSURIA. — Injection of adrenalin results in rise of blood-sugar and glycosuria.
4. DIABETIC PUNCTURE (Claude Bernard's *piqûre*).—Puncture of floor of 4th ventricle gives rise to hyperglycæmia and glycosuria, occurring in about 2 hours. Only occurs if there is glycogen in the liver, if splanchnic nerves are intact, and if suprarenals are present.

   [Two theories as to mode of action: (*a*) Stimulation of nerve-fibres in splanchnics to liver; (*b*) Reflex stimulation of suprarenals leading to increased output of adrenalin, and glycosuria.]

   Glycosuria sometimes follows a head injury in man.
5. PANCREATIC GLYCOSURIA.—Removal of whole of pancreas in dogs causes severe glycosuria, and death in a week or two; after death, glycogen has almost disappeared from liver. Four-fifths of pancreas may be removed without ill effect, but seven-eighths causes mild symptoms, which closely resemble those of diabetes in

Pancreatic Glycosuria, *continued.*

man. They are: (*a*) Glycosuria, which persists in severe forms even on carbohydrate-free diet, sugar being formed from food and body protein. (*b*) Polyuria, i.e., increased flow of urine to wash out the sugar. (*c*) Thirst, due to the polyuria. (*d*) Wasting, due to breaking down of tissue proteins. (*e*) Rise of blood-sugar. (*f*) Urinary changes besides glycosuria: (i) High specific gravity. (ii) In severe cases, when sugar is being formed from protein, increased nitrogen and sulphur excretion, the $\frac{\text{dextrose}}{\text{nitrogen}}$ ratio being constant. (iii) Presence of β-oxybutyric acid, diacetic acid, and acetone, probably intermediate products of fat metabolism, since in diabetes the metabolism of fats is affected. Accumulation of these bodies in the blood gives rise to diabetic coma. (iv) Increased percentage of ammonia nitrogen, where acids just mentioned are in excess. This is a protective mechanism, acids in blood being neutralized by ammonia.

MILD CASES.—Glycosuria disappears on carbohydrate-free diet. These patients are fat, excessive sugar in blood being stored as fat.

CAUSE OF DIABETES IN MAN.—Usually due to disease of islets of Langerhans in the pancreas. (It may be that the blood-sugar in diabetes is an isomer of the normal blood-sugar.) Evidence:—

1. Removal of pancreas leads to glycosuria, but if a small piece is left or grafted into abdominal wall, glycosuria is prevented.
2. Ligation of pancreatic duct leads to atrophy of the acini, but the islets persist, and glycosuria does not occur. The islets produce an internal secretion which enables tissues to assimilate glucose. When it is absent the glucose is not used and runs to waste.
3. Occasionally in diabetes the islets are diseased and the acini normal.

Insulin.—This is an extract of the islets of Langerhans, first obtained by Banting, Best, and Macleod in 1921 by ligating the pancreatic duct and waiting until the acini degenerated, or from the fœtal pancreas; it is now extracted from normal pancreas with 90 per cent alcohol. (In ordinary pancreatic extracts it is destroyed by ferments.) It has recently been

obtained in crystalline form by Abel. Injection of insulin lowers the blood-sugar; if this is greatly reduced, hypoglycæmia is produced, and death may ocur, with hunger, faintness, delirium, convulsions, and coma; this may be averted by giving sugar. Insulin removes the symptoms of diabetes, and can cause recovery from diabetic coma. It is standardized by the dose required to reduce blood-sugar in a rabbit.

[Fate of Sugar after Insulin Administration.—Partly taken up by muscles as glycogen; partly oxidized.

Thyroid and Insulin.—In hyperthyroidism, tiny doses of insulin may reduce sugar to convulsive level.

Suprarenals and Insulin.—Injection of adrenalin causes outflow of insulin, and injection of insulin causes outflow of adrenalin.]

METABOLISM OF FAT.

Absorption of Fat.—Absorbed as fatty acids and glycerol, resynthetized into neutral fat, and passes as chyle by lacteals to thoracic duct and so into blood-stream, being gradually removed by the tissues. In some regions of the body, fat is stored (especially in subcutaneous tissues and the great omentum), until it is needed for conversion into energy. Apparently some fat is absorbed straight into portal vein and carried to liver. Fat droplets are found in liver-cells during absorption.

Sources of Body Fat.—

1. FROM FAT IN FOOD.—

   Proofs.—(*a*) Animals are fed on abnormal fats, e.g., spermaceti, rape-seed oil, or linseed oil; these can afterwards be recognized in adipose tissue. (*b*) Hoffman starved a dog until its fat stores were used up, then fed it on bacon fat: fats laid down in fat depôts had same properties as bacon fat.

2. FROM CARBOHYDRATE IN FOOD.—Known from universal experience. Herbivorous animals can be fattened more easily on a diet rich in carbohydrates than on one rich in fats. Reverse is true of carnivora.

   Lawes and Gilbert's Proof.—They took a litter of young pigs, killed a few, and estimated the body fat. The rest were then fed on a diet containing a little protein, a little fat, and much carbohydrate. After four months they had put on so much fat that, even assuming that fat had been formed from protein, there was still some which must have been formed from carbohydrate.

Sources of Body Fat, *continued.*

FAT IS PROBABLY *NOT* FORMED FROM PROTEIN.—

EVIDENCE.—If a dog is fed on a purely protein diet for many months, it survives, but no fat is found in the body.

EVIDENCE THAT HAS BEEN ADDUCED IN FAVOUR OF FORMATION OF FAT FROM PROTEIN.—In some diseases—e.g., phosphorus poisoning—fatty degeneration of the tissues occurs. It was suggested that protein had been directly converted into fat; but chemical analysis shows little or no increase of fat, only that previously invisible fat becomes visible. If a dog is fed with spermaceti, and then poisoned with phosphorus, fat in the liver contains spermaceti, so that it has been derived from the fat of the food.

Functions of Fat.—

1. Supplies energy which is liberated as heat and as muscular work when fat is oxidized in the tissues to CO_2 and water.
2. By its storage in fat depôts it forms a source of energy on which the body can draw in time of need. A fat animal, when starved, survives longer than a lean one.
3. Acts as a non-conductor of heat, and so diminishes heat loss from body. In some regions acts mechanically, protecting organs.
4. As a component of lipoids, fat plays an important part in formation of cell membranes.
5. According to some workers, it may be a source of sugar. Probably this does not normally occur.

Chemical Changes in Fats during Metabolism.—Probably fatty acids are first broken down into unsaturated fatty acids, and these are further broken down by oxidation, two molecules of carbon being lost at each stage. Process probably occurs in the liver, fat in fat depôts not being able to be used directly.

EVIDENCE.—(1) Liver contains far more unsaturated fats, and fatty acids lower in the series, than the fat depôts; (2) All the fatty acids in the body contain an even number of carbon atoms, except propionic acid, which contains three; (3) Phenomena of ketosis (*see below*).]

Ketosis.—In this condition, β-oxybutyric acid ($CH_3.CHOH.CH_2.COOH$) and diacetic acid ($CH_3.CO.CH_2.COOH$) are present in the blood, and these and acetone are excreted in the urine. Acetone is also excreted by the lungs. The condition is due essentially to deficiency in carbohydrates—e.g., in absence of carbohydrates from the diet, starvation,

persistent vomiting and diarrhœa, and severe diabetes. These bodies are formed from fats, so that giving fats in diabetes makes the condition worse. Probably β-oxybutyric acid and diacetic acid are normally formed in metabolism of fats, but in absence of carbohydrates they pass into blood-stream, and instead of undergoing further oxidation are converted into acetone.

DIET AND DIETETICS.

Accessory Food Factors.—

INORGANIC SALTS.—Chiefly chlorides, phosphates, and carbonates of sodium, calcium, magnesium, and potassium, also iron.

RESULTS OF ASH-FREE DIET.—Dogs fed on a diet of ash-free fat and carbohydrate, and protein which had been extracted with water until the salts had been much reduced, were moribund in 26 to 36 days. They die sooner than if starved completely. Wild animals, especially herbivores, travel great distances for salt.

FUNCTION OF INORGANIC SALTS.—

1. To maintain osmotic pressure of blood more or less constant.
2. Specific functions for different bases :—

Sodium.—Essential for preservation of muscular irritability. Very important for maintaining osmotic pressure of blood. Deprivation of NaCl in the days of heavy salt taxation gave rise to œdema and weakness.

Potassium.—Promotes muscular relaxation.

Calcium.—(*a*) Promotes muscular contraction, and stops heart in systole (authorities differ, however) ; (*b*) Takes part in clotting of the blood ; (*c*) Takes part in clotting of milk in stomach ; (*d*) Calcium salts are concerned with growth of skeleton, they and phosphorus being essential for proper formation of bone.

VITAMINS.—Substances of unknown composition, present in minute quantity in a proper dietary, and essential for health. Young animals fed on mixture of pure protein, fat, carbohydrate, salts, and water in adequate proportions will not thrive. In young rats, addition of only a teaspoonful of

Diet and Dietetics—Vitamins, *continued.*

milk a day results in growth (Hopkins). *Three vitamins are definitely recognized* :—

1. VITAMIN FAT-SOLUBLE A.—Occurs in cod-liver oil, butter, and almost any animal fat except lard, in green vegetables, but not in vegetable fats. It is eventually derived from grass, and is absent from lard partly because the pig does not eat grass. Destroyed by bubbling air through a solution, but not by boiling unless solution is alkaline or boiling prolonged.

   Function.—Essential for growth. Rats fed on diet deficient in this vitamin develop a diseased condition of the eyes known as xerophthalmia—cured by cod-liver oil or butter. The Mellanbys have shown that puppies fed on a diet poor in vitamin A always develop rickets and the teeth are badly formed, and that giving plenty of fat prevents and cures the conditions.

   [McCollum finds that if air is bubbled through cod-liver oil for 12 hours, it will no longer prevent xerophthalmia, so that it must have lost its vitamin A, but it will still cure rickets. Hence he considers its efficiency in curing rickets is due to another vitamin, known as vitamin D. (Rickets does not apparently depend entirely on vitamin deficiency; it is partly due also to too much cereal food, and deprivation of sunlight.) Partial deficiency of this vitamin predisposes to respiratory infections. Amount present in cow's milk is increased if cow is kept in sunlight. Irradiation of pure cholesterin will produce vitamin D.]

2. VITAMIN WATER-SOLUBLE B.—Occurs in cereals in the germ and just beneath the pericarp (outside membrane); in eggs, vegetables, yeast, and to some extent in milk. Very resistant, and not destroyed by drying or cooking if not too prolonged.

   Function.—Diet deficient in this vitamin produces beri-beri, a disease in which there is neuritis, paralysis, anæsthesia, and wasting, and in some types marked dropsy.

   Evidence: (*a*) Amongst Orientals who live largely on rice, limiting the diet to polished rice gives rise to beri-beri; if unpolished rice is eaten, disease does not occur. (*b*) When pigeons are fed on polished rice, they

develop a condition similar to beri-beri; cured by giving rice with the husk on, or altering the diet.

Partial deficiency causes atony of intestines and constipation.

3. VITAMIN WATER-SOLUBLE C.—Occurs in fresh vegetables and some fruits, especially lemons, oranges, tomatoes, in germinating peas, and to some extent in milk and fresh meat. Lime-juice contains very little. Ordinary methods of food preservation usually destroy it.

Function.—Prevents scurvy. Scurvy used to be very common on long voyages, when no fresh fruit or vegetables could be obtained. Nansen has shown that fresh meat in large quantities will prevent scurvy. Bottle-fed infants occasionally develop scurvy as a result of excessive boiling of the milk. Prevented by: (*a*) Raising temperature of milk only just to boiling point; (*b*) Giving orange- or grape-juice regularly.

[VITAMIN X.—Occurs in lettuce, meat, cereals, liver, and egg yolk. According to Evans and Bishop, female rats fed on a diet deficient in this factor were sterile. Addition of these food-stuffs resulted in a return to normal fertility.]

Dietetics.—A mixed diet is considered the most beneficial.

FUNCTIONS OF DIET.—

1. TO SUPPLY THE BODY WITH ENERGY, by fat, carbohydrate, or protein; carbohydrates are chiefly used for this purpose, owing to economy and ease with which they are used by the body.

2. TO CONSTRUCT PROTOPLASM to replace break-down of tissue protein, and in young animals for growth. Proteins or amino-acids are essential, and probably also inorganic salts and vitamins.

CALORIE VALUE OF DIET.—For basal metabolism—i.e., at rest asleep in bed—a man of average weight (70 kilo.) requires 1600 to 1700 calories per day, or 40 calories per hour per square metre of skin surface. Opinions differ as to the calorie value necessary for a man doing average muscular work, and also amount of protein required. Total energy required depends on amount of muscular work done. Much less is needed for brain work. Diet values constructed for average work are:—

Dietetics—Calorie Value of Diet, *continued.*

	Ranke's Diet		*Voit's Diet*	
	grm.	calories	grm.	calories
Protein	100	410	118	483
Fats	100	930	56	520
Carbohydrate ..	240	984	500	2050
Total calories	..	2324	..	3053

[During the late war, the Interallied Food Commission recommended a diet of 3300 calories for a man of average weight doing an average amount of muscular work for 8 hours a day. Children and young animals require excess of protein for growth. In animals which grow rapidly, maternal milk is rich in proteins—e.g., a new-born baby doubles its weight in about 180 days, and maternal milk contains barely 2 per cent of protein; while a kitten doubles its weight in 7 days, and its food contains 9·5 per cent of protein. A diet deficient in protein gives rise to the disease pellagra.]

Chittenden finds that nitrogenous equilibrium on moderate muscular work can be maintained on 60 grm. of protein, and any excess merely throws extra strain on excretory organs. Hindhede kept a laboratory attendant in health for 150 days on a diet of potatoes, margarine, and onions, only 4·425 grm. of nitrogen per day, but a total calorie value of 4000. The races of Bengal which take little protein are relatively less efficient mentally and physically than those that take more.

CRITERIA OF AN ADEQUATE DIETARY.—It must: (*a*) Maintain body weight; (*b*) Maintain mental and physical efficiency; (*c*) Provide for the average daily heat loss; (*d*) Maintain nitrogenous equilibrium.

FACTORS CONTROLLING GROWTH.

1. **Diet.**—

QUANTITY.—Must be adequate.

QUALITY.—

a. AMINO-ACIDS.—Certain amino-acids are essential for growth—e.g., lysin and cystin. Tyrosin and tryptophan are essential for life.

Evidence.—Animals fed on zein, the protein from maize, which does not contain lysin, do not grow. On addition of small amount of lysin, growth occurs.

b. VITAMINS.—Fat-soluble A and water-soluble B are essential. Both occur in milk. Hopkins fed young rats on adequate amounts of pure protein, fat, carbohydrates, salts, and water. Growth did not occur, but on addition of only a teaspoonful of milk a day, growth occurred normally. Winter milk contains less than summer milk. Human milk will not make rats grow.

Fat starvation of children in Austria and Germany during the War led to much stunting of growth as well as rickets.

2. **Endocrine Glands.**—

THYROID.—Deficiency by disease in children or removal in young animals causes arrest of growth. Restored more or less to normal by thyroid feeding.

PITUITARY.—Increased internal secretion in youth leads to gigantism ; decreased secretion to stunting.

3. **Race.**—Certain races of mankind tend to be very small or very tall, but otherwise normal. Cause is unknown ; probably lies in the fertilized ovum.

4. **Disease.**—Stunted growth may be due to various diseases.

THE LIVER AND ITS FUNCTIONS.

Contents of Liver-cells.—(1) *Glycogen*, which in alcohol-hardened liver stains brown with iodine. (2) *Organic iron compound*, demonstrated by treating liver with dilute hydrochloric acid (to liberate iron from organic combination) and potassium ferrocyanide ; Prussian blue colour results (hæmosiderin reaction). (3) *Fat* ; with osmic acid, fat granules stain black.

Functions of Liver.—

1. Bile formation (*see* p. 78).
2. Glycogen formation (*see* p. 125).
3. Urea formation (*see* p. 120).
4. Uric acid formation in birds and reptiles.

Proof.—Perfusion of amino-acids or ammonium lactate through a bird's liver results in formation of uric acid.

In man, uric acid is formed in the liver by action of oxydase on various purins.

5. Desaturation of fatty acids.

The Liver and its Functions, *continued.*

6. Destruction of red blood-corpuscles.
   Evidence.—(*a*) Presence of hæmoglobin crystals and of red blood-corpuscles in Kupffer cells. If Kupffer cells are choked with colloidal silver, hæmolytic agents (AsH_3) no longer cause jaundice. (*b*) Increased amount of iron in diseases such as pernicious anæmia, where there is increased breaking-down of red blood-corpuscles.
7. Possibly production of antithrombin. Blood repeatedly passed through the liver is said not to clot.
8. Possibly formation of creatinine.
9. Production of antibodies.
10. Formation of proteins of blood-plasma.
11. Heat production, owing to marked metabolic processes in liver.

Results of Removal of Liver.—Mann and other workers at the Mayo Clinic have succeeded in removing the whole liver by multiple operations, in a large number of dogs, and by taking special measures have kept animals alive for days. They tend to die in a few hours from convulsions due to rapid fall in blood-sugar; this is prevented by intravenous injections of glucose. It is unknown what these dogs eventually die of; but they get jaundice, showing that bile-pigments can be formed in the absence of the liver. Presumably they are formed from the spleen, but even after splenectomy some bilirubin is formed.

CHAPTER XIII.

BONE.

Chemistry.—Bone consists of two-thirds inorganic and one-third organic matter.

INORGANIC OR MINERAL MATTER.—Chiefly calcium phosphate. Small amounts of magnesium phosphate, and calcium carbonate and fluoride.

ORGANIC MATTER.—Obtained by dissolving out mineral matter with acid. Consists chiefly of *ossein*, a scleroprotein allied to collagen of cartilage. On boiling it yields gelatin, which gives protein tests except those depending on benzene ring—e.g., Millon's and glyoxylic reactions.

Histology.—

1. COMPACT BONE.—Shows concentric lamellæ surrounding central marrow cavity and parallel to the periosteal surface. Tunnelled by Haversian systems.

   STRUCTURE OF HAVERSIAN SYSTEM.—

   Haversian Canal.—Central canal, running parallel with the long axis of the bone, about 0·05 mm. in diameter. Each contains a minute artery, vein, nerve filaments, and lymphatics. It is surrounded by concentric *lamellæ*.

   Lacunæ.—Tiny spaces between the lamellæ. *Canaliculi* connect the lacunæ with one another and with the central canal, but do not usually communicate with adjacent systems. Supply lymph to bone-cells.

   Bone-cells.—Flattened branched cells occupying the lacunæ.

2. CANCELLOUS BONE.—Shows numerous cavities containing marrow, enclosed in thin bony walls, with lacunæ arranged concentrically to the cavities.

Blood-supply.—

1. FROM PERIOSTEUM.—Branches pass into Haversian canals.

Blood-supply of Bone, *continued.*

2. NUTRIENT ARTERY.—Enters medullary cavity, and gives twigs to the Haversian canals, anastomosing with arteries from periosteum.

Nerve-supply.—Numerous small twigs enter from periosteum; also a nerve enters nutrient foramen.

Bone-marrow.—

YELLOW MARROW.—In adults occupies shafts of long bones. Scanty in children.

STRUCTURE.—Consists of connective tissue, fat-cells, blood-vessels, and a few myelocytes.

RED MARROW.—Occurs in short and flat bones such as ribs and vertebræ, and in upper ends of humerus and femur (in man); also in ends of long bones (in animals).

STRUCTURE.—

1. Small amount of connective tissue, a few blood-vessels, and fat-cells.
2. Large number of *myelocytes*—large, nucleated, granular cells, precursors of leucocytes.
3. *Erythroblasts*, nucleated cells, precursors of red blood-corpuscles. Protoplasm may be red-tinted.
4. Multinucleated cells, *myeloplaxes or megakaryocytes*, said to be source of blood-platelets.

Periosteum.—Consists of fibrous tissue, blood-vessels, and nerves. In young animals a layer of cells called osteoblasts is present between it and surface of bone (cambium layer).

Development of Bone.—

1. IN MEMBRANE (e.g., vault of skull).—Radiating fibres appear, along lines of which bone-corpuscles lay down calcium salts. Network of bone is formed, in meshes of which are blood-vessels, connective tissue, and osteoblasts. Later a diploë is eaten out by osteoclasts.
2. IN CARTILAGE.—(i) Blood-vessels enter the rod of cartilage, and there is multiplication of the cartilage cells, which lay down calcium salts in the matrix. Thus calcified cartilage is produced. (ii) Calcified cartilage is invaded by *osteoclasts* or bone-destroyers, large multinucleated cells which eat away calcified cartilage, and by *osteoblasts* from the perichondrium, which lay down lamellæ of bone. Haversian canals are formed by osteoclasts excavating tunnels in the bone, which are partly filled in by rings of bone laid down by osteoblasts.

Growth of Bone.—

INCREASE IN GIRTH.—Rings of bone are laid down beneath periosteum.

EVIDENCE.—

1. If growing animal is fed for a time on madder (which stains bone yellow), a yellow ring is seen in the bone.
2. *Duhamel's silver ring experiment.* A silver ring was inserted round the bone just beneath the periosteum; in time, it became completely buried in bone.

New bone is laid down by osteoblasts on the surface of the bone —i.e., the cambium layer—not by periosteum as was formerly supposed. Periosteum probably limits production of bone.

EVIDENCE.—

1. If a strip of periosteum is removed from a growing bone and implanted in the neck, a projecting ridge forms on the bare area of bone, but no bone forms in the neck.
2. After a fracture, union can occur even if bone is denuded of its periosteum. Osteoblasts near the fracture divide, pass out into the blood-clot between the two ends, and lay down calcium salts. After a few weeks they become enclosed, and cease to form new bone.
3. Bone-grafts will live and unite even if devoid of periosteum.

EVIDENCE THAT WAS PRODUCED IN FAVOUR OF FORMATION OF BONE BY PERIOSTEUM.—

1. *Duhamel's silver ring experiment.* This experiment, however, has been performed after complete removal of periosteum, and exactly the same condition was found.
2. In the disease known as periostitis, the periosteum becomes separated from the bone by pus; in a few months a sheath of new bone is laid down beneath the periosteum. The explanation is probably that the cambium layer has become adherent to the periosteum owing to the inflammatory process.

INCREASE IN LENGTH.—Occurs at ends of bones, cartilage between epiphysis and shaft being constantly transformed into bone, while at the same time there is multiplication

Growth of Bone, *continued.*

of cartilage cells. These arrange themselves into rows at right angles to the bone-cartilage junction, with a clear space (lacuna) around each cell.

EVIDENCE.—

1. *Hunter's experiment.* Two lead shot were inserted one inch apart in shaft of tibia of young pig. When growth was complete, they were still one inch apart.
2. If shaft of bone is removed, and tinfoil fitted over the sawn extremities, epiphyses grow so freely that the two ends come together. Occurs whether periosteum is removed or left.
3. If epiphysis is destroyed, growth ceases at that end of the bone.

CHAPTER XIV.

SKIN. BODY TEMPERATURE.

SKIN.

Structure.—

EPIDERMIS.—Non-vascular. Consists of 4 layers :—

1. STRATUM CORNEUM OR HORNY LAYER.—Especially marked in palm of hand and sole of foot. Flattened, non-nucleated cells, surrounded by envelope of keratin, a scleroprotein. Constantly being shed.
2. STRATUM LUCIDUM.—Two or three layers of flat, clear, refractive cells not completely cornified.
3. STRATUM GRANULOSUM.—Marked where horny layer is well marked. Two or three layers of fusiform cells, containing granules of eleidin, a precursor of keratin.
4. STRATUM MALPIGHII OR RETE MUCOSUM.—Lies on papillæ of dermis. Polygonal, nucleated cells, connected with one another by protoplasmic bridges, i.e., 'prickle cells.' Those of the deepest layer are columnar and pigmented. From these the skin is renewed, and regenerated after loss. Minute lymph spaces and non-medullated nerves occur between cells.

DERMIS.—Contains blood-vessels, lymphatics, and nerves. Consists of connective tissue with some elastic tissue. Two layers :—

1. PAPILLARY LAYER.—Dense fibrous tissue with numerous vascular papillæ, arranged in ridges, two rows of papillæ on each ridge, the duct of a sweat gland opening between them. Some papillæ contain tactile corpuscles.
2. RETICULAR LAYER.—Meshwork of connective tissue, containing connective-tissue corpuscles, fat-cells, and sweat glands. In some parts, dermis contains a little unstriped muscle—e.g., scrotum, nipple, etc.

Appendages of Skin.—

NAILS.—Thickenings of stratum lucidum, resting on stratum Malpighii (nail-bed). Dermis of nail-bed is thrown into longitudinal ridges. Growth in length is due to proliferation

Appendages of Skin, *continued.*

of cells of stratum Malpighii at root of nail, growth in thickness from stratum Malpighii beneath the lunula.]

HAIRS.—Each hair consists of shaft and root, ending in an enlargement, the hair bulb surrounded by the hair follicle. Projecting into the hair bulb is a vascular papilla from the dermis. Destruction of papilla leads to cessation of growth. Hair bulbs are well supplied with nerves.

STRUCTURE OF A HAIR.—

1. *Medulla* in centre, consisting of polygonal cells with spaces in between. Absent in fine hairs.
2. *Cortex* of spindle-shaped, pigmented cells.
3. *Cuticle*, a single layer of flattened cells, overlapping one another from below upwards.

[STRUCTURE OF A HAIR FOLLICLE.—

1. *Outer Coat.*—(*a*) Longitudinal connective-tissue coat. (*b*) Circular connective-tissue coat. (*c*) Hyaline membrane, present in deeper parts of follicle only.
2. *Inner Coat.*—(*a*) Outer root sheath, corresponding to stratum Malpighii. (*b*) Inner root sheath, consisting of: (i) Cuticle, next to hair; (ii) Huxley's layer of flattened nucleated cells; (iii) Henle's layer of flattened non-nucleated cells.]

ARRECTOR PILI MUSCLE is attached to each hair follicle. Plexus of nerve fibrils is present round each follicle.

SEBACEOUS GLANDS.—Occur in upper parts of dermis, connected with hair follicles. Absent in palms of hands and soles of feet. Consist of sacculated follicles lined by cubical epithelium on basement membrane, and containing cells, which in the centre are disintegrating, forming a fatty secretion, the *sebum*. Show practically no lumen.

DUCT.—Lined by stratified epithelium.

SWEAT GLANDS.—Occur in dermis or subcutaneous tissue. Each gland consists of a coiled tube lined by cubical epithelium, outside which is a layer of unstriped muscle, and a basement membrane. Lumen relatively large.

DUCT.—Lined by cubical epithelium.

CERUMINOUS GLANDS.—Modified sweat glands present in skin of external auditory meatus.

Functions of Skin.—(1) Protective. (2) Sensory. (3) Heat-regulating, by varying vascularity, and by sweating. (4) Excretory.

The Sweat.—

COMPOSITION.—

Reaction usually neutral or alkaline; may be just acid owing to acid sodium phosphate and fatty acids.

Contains *water*, 99 per cent; *sodium chloride*, 0·4 per cent; traces of sodium phosphate, potassium chloride, and fatty acids; *urea*, 0·08 per cent.

AMOUNT.—About 700 c.c. are formed in twenty-four hours, some being evaporated at once—*insensible perspiration*—some remaining for a time as drops of fluid—*sensible perspiration*.

MECHANISM OF SWEATING.—Independent of vascularity of skin; cf. 'cold sweat' in fear.

1. AFFERENT IMPULSES from stimulation of mucous membrane of mouth and stomach by hot substances and painful stimuli.
2. SWEAT CENTRE in medulla, and subsidiary ones in grey matter of lower cervical and upper lumbar regions of spinal cord.
   Stimulated by rise of temperature, increased CO_2 in blood, and drugs, e.g., opium, pilocarpine.
3. EFFERENT IMPULSES in white rami communicantes from 1st dorsal to 4th lumbar nerves to sympathetic ganglia, thence by grey rami communicantes in spinal nerves.

BODY TEMPERATURE.

Poikilothermic or cold-blooded animals have a temperature which varies directly with that of the surrounding medium—e.g., invertebrates, reptiles, fish, amphibians, and embryo birds and mammals.

Homoiothermic animals have a practically constant temperature, due to active oxidation and heat-regulating mechanism——e.g., mammals and birds.

Hibernating animals are usually homoiothermous, but become poikilothermous during hibernation.

Body Temperature in Man.—Normally about 98·4° F.; about half a degree higher in rectum. The hottest organ in the body is the liver. The blood *distributes* the heat.

Normal Variations in Temperature.—

1. *Diurnal variation* of about 1° F.—highest about 6 p.m., lowest about 3 a.m. In individuals who work by night and sleep by day, rhythm is reversed.
2. Slight rise with muscular exercise.
3. Slight rise after food, most marked about 1½ hours after a meal.

Body Temperature, *continued.*

Mode of Heat Production.—Caused by metabolic changes in food and tissues, especially in liver and muscles during exercise. These changes are almost entirely oxidations, practically no heat being liberated by hydrolysis, synthesis, etc. (For heat value of different food-stuffs, *see* METABOLISM, p. 119.)

Ways in which Heat is Lost.—

1. From skin by evaporation, radiation, convection, and conduction—about 87·5 per cent of total loss.
2. By expired air: (*a*) Evaporation of water from lungs—7 per cent; (*b*) Warming expired air—3·5 per cent.
3. By urine and fæces—2 per cent.

MEASUREMENT OF HEAT LOSS.—Calorimeter is used.

1. FOR ANIMALS, REICHERT'S WATER CALORIMETER.—Double-walled box, with known weight of water between the walls, and enclosed in a box packed with shavings to prevent heat loss by radiation. There are tubes for entrance and exit of air, and rise in temperature of expired air is noted. Calorimetric equivalent of apparatus is known—i.e., heat necessary to raise temperature of apparatus 1° C.
2. FOR HUMAN BEINGS, ATWATER-BENEDICT CALORIMETER.—*See* METABOLISM, p. 118. A bicycle may be introduced into the apparatus, and heat loss during muscular work noted.

Heat Regulation.—

REGULATION OF HEAT PRODUCTION.—By increased or decreased oxidation, depending upon :—

1. Amount of food ingested—e.g., appetite is increased by cold.
2. Muscular contractions. Increased voluntary muscular activity counteracts effects of cold.

   Shivering is a series of small muscular contractions in response to stimulation by cold, and increases heat production.

   Paralysis of muscles by curare or section of all motor nerves by section of spinal cord, converts a warm-blooded animal into a cold-blooded one.

REGULATION OF HEAT LOSS.—

1. EXTERNAL MEANS.—In man, by clothes, and heating of rooms, thus controlling evaporation and radiation.
2. SWEAT AND VASOMOTOR MECHANISMS.—In warm

weather, secretion of sweat is increased, so that more heat is used in evaporating it. Blood-vessels in skin are dilated, more heat being lost by radiation, convection, and conduction, provided temperature of air is below that of blood. Alcohol lowers body temperature by dilating cutaneous vessels. External cold causes constriction of cutaneous blood-vessels by stimulating vasomotor centre.

3. RESPIRATORY MOVEMENTS.—Increased during exercise, thus slightly increasing heat loss. Important in dogs, because sweat nerves are absent, and loss by radiation is limited by hairy coat. Evaporation occurs from tongue during panting.

HEAT CENTRE.—There is probably a heat centre in the corpus striatum. *Evidence:* (1) Injury to corpus striatum causes rise of body temperature; (2) Heating corpus striatum causes fall of body temperature, cooling it a rise of temperature (Barbour).

In fevers, and in prolonged exposure to high temperature (heat-stroke) or undue cold, action of heat centre becomes upset, temperature is widely altered, and death may occur.

May be subsidiary heat centres in pons, since hæmorrhage in this region causes rise of temperature.

In babies, and some higher mammals, heat-regulating mechanism is not perfectly developed at birth. Babies born prematurely have no power of heat regulation.

CHAPTER XV.

MUSCLE.

Structure of Muscle.—

STRIPED MUSCLE.—Composed of fibres up to 36 mm. long, with diameter from 0·1 to 0·01 mm. On each fibre is a motor end-plate.

STRUCTURE OF A FIBRE.—

1. *Sarcolemma*, a nucleated sheath.
2. Numerous groups of fibrils known as *sarcostyles*, consisting of alternate light and dark bands. In the middle of the clear band is a membrane, Krause's membrane.
3. Jelly-like granular material, *sarcoplasm*, in which the sarcostyles are embedded.

[Both sarcostyle and sarcoplasm seem to be contractile, sarcostyles probably being used for quick contractions, sarcoplasm for tonic ones.

Boeke has recently described certain nerve-endings in muscle fibre, supplied by very fine or non-medullated nerves. Sarcoplasm is supposed to be controlled by these fibres; sarcostyles by the motor end-plates.]

UNSTRIPED MUSCLE.—Composed of small spindle-shaped cells, having a single rod-like nucleus, and containing fine fibrils passing through cells from one to another. Occurs in walls of hollow viscera—e.g., alimentary canal, ureter, bladder, uterus, trachea, bronchi, and blood-vessels.

Chemistry of Muscle.—Contains :—

1. WATER.—About 75 per cent.
2. PROTEINS.—20 per cent. (*a*) Paramyosinogen and myosinogen, which yield myosin after death. Myosinogen is more abundant. Paramyosinogen clots direct to myosin; myosinogen via soluble myosin. (*b*) Myoalbumin and myoglobulin. (*c*) Nucleoprotein in small amounts. (*d*) Myohæmatin, a pigment derived from hæmoglobin.
3. CARBOHYDRATES.—(*a*) Glycogen. (*b*) Glucose. Glucose is converted into glycogen in muscles. Glucose may be present as hexose-phosphate.

4. FATS.—Present both in and between fibres, but usually in an invisible form. Pork contains rather a large amount of visible fat, making it indigestible.
5. INORGANIC SALTS.—Especially potassium phosphate.
6. EXTRACTIVES.—(*a*) Creatine (methyl-guanidine-acetic acid). (*b*) Purin bodies—xanthin and hypoxanthin. (*c*) Carnosin—probably a histidin derivative. (*d*) Inosite, an aromatic substance ($C_6H_{12}O_6$). (*e*) Sarcolactic acid, always present in dead muscle; small quantities in fresh muscles, increased by fatigue.
7. VITAMINS.—Water-soluble B and C, in small amounts.

Changes in a Muscle during Simple Contraction.—

1. PHYSICAL.—Muscle becomes shorter and thicker, though volume remains the same.

   CHARACTERISTICS OF CONTRACTION.—(*a*) *Latent period*, i.e., period between application of stimulus and commencement of muscle contraction—about 0·01 sec. with frog's nerve-muscle preparation. (*b*) *Contraction period*—about 0·04 sec. (*c*) *Relaxation period*—about 0·05 sec.

   MUSCLE TONE.—Normally muscle is in a state of partial contraction—i.e., tone—depending on integrity of reflex arc. Hence muscle at rest is in condition to contract, no time being lost in taking in slack.
2. HISTOLOGICAL.—There is some change in relations of light and dark bands to one another, but nature of change is uncertain. Dim band is probably active agent in contraction.
3. CHEMICAL.—
   a. Diminution of glycogen, said to be proportional to functional activity and to amount of lactic acid formed.
   b. Formation of lactic acid and probably of phosphoric acid.
   c. Reaction becomes acid.
   d. Formation of CO_2 and consumption of oxygen.
      Proofs.—
      i. Expired air during exercise contains more CO_2 and less oxygen.
      ii. Nerve-muscle preparation placed in confined space in atmosphere of oxygen uses up oxygen and exhales CO_2; on contraction the exchanges are greater.

Changes in a Muscle during Simple Contraction—Chemical, *continued.*

iii. Analysis of blood coming to and going from muscle.

Method.—A few c.c. of blood are drawn off from the artery and from the vein, oxygen evolved by potassium ferricyanide, and CO_2 by 25 per cent tartaric acid. Estimated in Barcroft's apparatus.

Chemical Mechanism of Contraction.—Contraction can take place in absence of oxygen, by running up an oxygen debt, to be repaid later. Contractions can be got till lactic acid reaches such a figure that rigor ensues; the muscle can be rescued by oxygen. If oxygen is freely supplied, no debt is run up.

Weight of glycogen lost in muscle contraction corresponds well with oxygen consumption; therefore, in the last resort, it is to burn the glycogen that oxygen is needed. Much more lactic acid is produced than the oxygen intake could burn; evidently about four-fifths of the lactic acid is reconverted into glycogen, and one-fifth or one-sixth burnt to CO_2 and H_2O.

[Probably the lactic-acid precursor is hexose-phosphate. Such a compound can be isolated. It is derived from glycogen. The highest lactic-acid content is obtained in muscle when phosphates are present; PO_4 increases in urine after exercise. Contraction is said to be due to surface-tension effect of the acid on surface of sarcostyles; adding lactic acid to a muscle in Ringer's solution throws it into rigor.

If exercise is severe in human muscle, lactic acid may rise to 0·3 per cent, and more work is impossible. In quieter exercise, a 'steady state' is reached in which oxygen intake just balances oxidation of lactic acid, and oxygen debt is small.]

In active exercise, some lactic acid escapes into blood and urine.

Respiration of Contracting Muscle.—R.Q. before exercise, 0·8; during exercise, 1·002; after exercise, (*a*) 1·17, (*b*) 0·9, (*c*) 0·76 (varies, however). The high figures are due to CO_2 being pushed out by the lactic acid reacting with bicarbonate; also by increased pulmonary ventilation. This goes on *after* the high oxygen requirements begin to tail off. The low final figure is due to re-formation of bicarbonate. For the *total period*, R.Q. = 1; therefore a carbohydrate furnishes the energy for muscular contraction.

4. THERMAL.—Measured by a thermopile—e.g., gold-nickel junction generating an electric current.
   There are four stages of heat evolution—namely, during (*a*) onset, (*b*) maintenance, (*c*) relaxation, (*d*) recovery. The first three are the same whether oxygen is present or absent, and are due to 'explosion' of the lactic-acid precursor; the fourth is much larger in presence of oxygen, and is due to oxidation of lactic acid and re-formation of glycogen.
   Maximum efficiency (i.e., proportion of work done to total energy output) is 25 per cent.
5. SOUND.—There may be an audible sound—e.g., the 1st heart-sound. It is possible to hear one's own masseter contracting.
6. ELECTRICAL.—Active or damaged muscle becomes electronegative to resting muscle. The law of animal electricity is that current flows from active to inactive regions. Contracting part is electronegative to quiescent one, hence current flows from contracting to quiescent. Hence :—
   a. NEGATIVE VARIATION.—Apply non-polarizable electrodes to a damaged and an undamaged area of muscle, and complete circuit: galvanometer shows deflection. Stimulate muscle to contract: galvanometer swings back to zero.
   b. DIPHASIC VARIATION.—Apply non-polarizable electrodes to curarized sartorius of frog; stimulate one end. As wave of contraction sweeps along it, galvanometer swings first in one direction, then in the other.

Factors affecting Muscle Curve.—

1. STRENGTH OF STIMULUS.—Stronger stimulus results in stronger contraction up to certain point, at which a maximum is reached.
2. NUMBER OF STIMULI.—
   a. STAIRCASE EFFECT.—Contractions increase with first few stimuli, showing beneficial effect of contraction.
   b. SUMMATION.—Muscle shortens more if second stimulus is given during contraction due to first stimulus.
   c. TETANUS.—Results from muscle receiving stimuli so rapidly that it remains in contracted state.
3. FATIGUE.—*See below.*

Factors affecting Muscle Curve, *continued.*

4. TEMPERATURE.—Affects strength and duration of contraction.
   Cold leads to longer latent period and contraction. Below 0° C., irritability is entirely lost.
   Warmth leads to shorter latent period, stronger and quicker contraction. Above 42° C., heat rigor occurs owing to coagulation of muscle proteins.
5. DRUGS.—*See* p. 151.

Fatigue.—Studied by repeated stimulation of nerve-muscle preparation.

MUSCLE CURVE IN FATIGUE.—Shows: (1) Longer latent period; (2) Smaller contraction; (3) Prolonged contraction and relaxation.

CAUSE OF FATIGUE.—

1. LACTIC-ACID FORMATION.
   Evidence.—(*a*) With circulation intact, fatigue is long delayed; (*b*) Muscle, perfused with normal saline to wash out lactic acid, recovers to large extent; (*c*) Perfusion with lactic acid causes immediate fatigue.
2. INORGANIC SALTS may play some part. Potassium salts induce rapid fatigue; calcium salts, permanent contraction in systole.

MOSSO'S ERGOGRAPH.—Used for experimenting on fatigue of single muscle in man. Method is for one finger to raise a weight until it is unable to lift it, i.e., is completely fatigued. On stimulation of corresponding nerve, finger flexes briskly.

SITE OF FATIGUE.—Might theoretically be in: (1) Muscle itself; (2) Myoneural junction; (3) Nerve-fibres; (4) Anterior-horn cells; (5) Cortical cells. Note that: (*a*) Stimulation of cortical motor centre of a finger in a chimpanzee causes movement of finger, but fatigue soon occurs; if cortex is sliced away and underlying region stimulated, movement occurs. (*b*) When movement ceases, stimulation of pyramidal tract in cord will give rise to it again. (*c*) When pyramids are fatigued, stimulation of peripheral nerve causes contraction. (*d*) Fatigue is not in muscle, because in nerve-muscle preparation, when stimulation of the nerve ceases to give contraction, a response occurs if electrodes are applied to the muscle. Fatigue, then, is primarily cortical, and can be delayed to some extent by excitement or drugs—e.g., caffeine, cocaine, alcohol.

Structures are fatigued in following order: (1) Cortical cells; (2) Anterior-horn cells of spinal cord; (3) Motor end-plate; (4) Muscle. Nerve-fibres are never fatigued. If nerve of nerve-muscle preparation is stimulated for hours with nerve blocked by freezing, contraction occurs when the block is removed.

Action of Drugs on Muscular Contraction.—

VERATRINE.—(1) Relaxation greatly prolonged. (2) Curve shows two summits: (*a*) Short contraction; (*b*) Slower contraction, following brief relaxation.

CURARE.—Paralyses myo-neural junction.

PROOFS.—

1. Injection subcutaneously into pithed frog causes paralysis.
2. In nerve-muscle preparation from curarized frog, stimulation of nerve gives very feeble or no contraction, stimulation of muscle normal response.
3. One limb is ligatured, omitting the nerve, before injection of curare. Stimulation of that nerve gives normal response.

[NICOTINE.—(1) Causes contraction of muscle. (2) Applied to curarized muscle, no contraction. (3) If nerve to muscle has degenerated, application of nicotine still causes contraction. Hence nicotine and curare do not act on motor end-plates, but on a *chemical receptor* substance, which may link nervous messages to the chemical molecule, explosion of which provides energy for muscular contraction (much as fulminating mercury is required to detonate a charge of trinitrotoluol).]

Rigor Mortis.—A state of rigidity and loss of power of contractility of all muscles, occurring usually 3 hours after death, though it may be instantaneous, especially after sudden death. Passes off in 3 days, owing to autolysis.

CHEMISTRY OF PROCESS.—Coagulation of muscle proteins into insoluble *myosin*. Acid reaction (owing to production of lactic acid), and evolution of CO_2. Abundance of oxygen delays onset, owing to lessened lactic-acid formation. Calcium salts are necessary for coagulation of myosinogen.

Physiology of Muscular Exercise.—

SUMMARY.—Oxygen must be supplied, and CO_2 and lactic acid rapidly got rid of.

1. RESPIRATORY CHANGES.—Increased depth and rate of respiration.
2. CIRCULATORY CHANGES.—
   a. General.—(i) Increased heart-rate and output per beat; (ii) Rise in blood-pressure.
   b. Local.—In muscles.

Physiology of Muscular Exercise, *continued.*

3. INCREASED SWEATING.—A reflex to get rid of heat produced by muscular contraction.
4. Flushing of skin.
5. Rise of temperature with violent exercise.
6. May be slightly increased output of nitrogen, uric acid, and lactic acid in urine.
7. May be increased output of adrenalin.

RESPIRATORY CHANGES.—Amount of respiratory exchange may be increased four-fold. In violent exercise in man, 4 litres of oxygen per minute may be taken in, necessitating a cardiac output of 200 c.c. per beat.

CAUSES OF INCREASED RATE AND DEPTH.—

1. Increased concentration of hydrogen ions in blood (due to CO_2 and lactic acid) stimulates respiratory centre.
2. *Psychic.* Anticipation of exercise causes involuntary increase in respiration.

CIRCULATORY CHANGES.—

INCREASED HEART-RATE.—In early stages, probably due to stimulation of sympathetic. Later, due to *Bainbridge's Law*—i.e., rate of heart varies with amount of blood entering auricle. Owing to muscular activity and increased respiratory movements, more blood enters auricles. Depression of vagal centre may also be a factor.

INCREASED OUTPUT PER MINUTE.—*Starling's Law* states that force of contraction of heart muscle is proportional to degree of stretching of cardiac muscle fibres. Heart is better filled with blood during exercise and contracts more powerfully. Stretching of heart muscle is limited by pericardium. Increased output in man is demonstrated by nitrous-oxide or ethyl-iodide method. (*See* p. 35). X rays, however, show no marked increase in size of heart.

RISE OF BLOOD-PRESSURE.—

Causes.—(1) Increased strength of heart-beat; (2) General vasoconstriction, especially in splanchnic area, due to action of liberated H ions on vasomotor centre. *Adrenalin* may be a factor.

Increased blood-pressure in aorta results in better supply of blood to heart muscle by coronary arteries. Untrained heart responds chiefly by change in rate, trained heart by change in output. The heart of an athlete is often rather large.

LOCAL CHANGES IN MUSCLES.—Dilatation occurs of many capillaries in muscle, and many previously collapsed ones fill and become visible. Due to diffusible substances (lactic acid, etc.) liberated which act on capillaries.

Final result of these changes is that partial pressure of oxygen and CO_2 in plasma round muscle is kept the same in activity as at rest, in spite of increased respiratory exchange. The liberated CO_2 and lactic acid cause the HbO more readily to part with its oxygen. (*See* p. 51.)

ADRENALIN.—If it is true that more adrenalin enters the blood during exercise, it assists by the following phenomena : (*a*) Vasoconstriction of all vessels, except those of brain, lung, heart, and contracting muscle ; (*b*) Cessation of peristalsis ; (*c*) Increase in rate and strength of the heart ; (*d*) Mobilization of glycogen from liver.

'SECOND WIND'.—Signifies the passing off of the first distress in a trained athlete so that he can continue in comfort. Used to be explained by action of depressor nerves, but more probably is due to all the above aids to oxygen-supply to the muscles coming into action.

Characteristics of Involuntary Muscle.—

1. Generally not under control of will.
2. Contractions very sluggish, principal function being to maintain tone. For this purpose the muscle does not require a further supply of oxygen nor give out more CO_2, and gives out no extra heat.
3. Cannot be fatigued.
4. Scarcely responds to single stimulus, but is easily tetanized. Long latent period.
5. Supplied by sympathetic nerve-fibres.
6. Effect of drugs :—
   Curare or veratrine has no effect.
   Atropine paralyses nerve-endings.
   Pilocarpine and muscarine stimulate nerve-endings.
   Pituitary contracts muscle itself.

[7. *Experiments of Uexhill.*—Stimulation of adductor muscles of a mollusc (*Pecten*) shows a sort of 'catch mechanism'—i.e., muscle can settle down to steady contraction at any given length without doing any work.]

CHAPTER XVI.

NERVE.

Structure of a Nerve Trunk.—A bundle of cords, each cord surrounded by dense fibrous tissue, *perineurium*, which may be covered with pavement endothelium. Each cord consists of nerve-fibres supported by processes of connective tissue, *endoneurium*.

Histology of a Nerve-fibre.—

1. NON-MEDULLATED.—Shows AXIS CYLINDER and NEURILEMMA. These fibres arise in sympathetic ganglia and mainly supply viscera.
2. MEDULLATED.—
   - *a*. AXIS CYLINDER in centre, composed of sheath and nerve fibrils.
   - *b*. MYELIN SHEATH, made of peculiar fatty material, interrupted at regular intervals, the *nodes of Ranvier*.
   - *c*. NUCLEI, one to each internode or segment.
   - *d*. NEURILEMMA, a delicate elastic sheath.

Function of Myelin Sheath.—

1. INSULATION OF AXIS CYLINDER.
   EVIDENCE.—(*a*) In disseminated sclerosis, a disease where myelin sheath is lost, impulses intended for one group of muscles affect another, and intention tremor occurs; (*b*) Myelin sheath is lost after nerve enters tissue to which it is to be distributed.
2. SOURCE OF NUTRITION TO AXIS CYLINDER.
   No definite evidence.

Medullated fibres are more easily stimulated than non-medullated ones.

Chemistry of Nervous Tissue.—

1. LIPOIDS.—In myelin sheath—e.g., lecithin ($C_{44}H_{90}NPO_9$), cholesterin ($C_{27}H_{46}O$), sphingomyelin.
2. PROTEINS.—Cell albumin and globulin, nucleoprotein, neurokeratin.
3. GALACTOSIDES.—Especially cerebrin.

4. INORGANIC SALTS.—Chlorides (and so show a cross at the nodes of Ranvier when stained with silver nitrate). Potassium salts are common in myelin sheath.

Functions of Nerve-fibres.—To conduct impulses, and thus produce any of following effects :—

1. Production of muscular contraction.
2. Control of muscular tone.
3. Conveyance of conscious and unconscious sensory impulses.
4. Control of secretions.
5. Trophic function possibly.

Methods of Artificial Stimulation of Nerve.—

1. CHEMICAL.—By concentrated solutions of acids or alkalis.
2. MECHANICAL.—E.g., tapping or cutting.
3. THERMAL.—Sudden change of temperature affects sensory but not motor nerves, unless very extreme and sudden.
4. ELECTRICAL.—By means of constant galvanic current (i.e., current taken direct from a battery), or induced interrupted current from secondary coil of induction apparatus (faradic).

Mechanical or electrical stimulation of a sensory nerve in man produces pain. To obtain other sensations, nerve-endings must be stimulated.

Electrical Phenomena in Nerves.—

Stimulated point becomes galvanometrically negative to normal one, and current flows *from* the negative point.

[ELECTROTONUS.—A term indicating the changes in a nerve at the poles resulting from the passage of a constant current : (*a*) Changes round anode and kathode setting up currents; (*b*) Change in excitability and conductivity—increased at kathode, decreased at anode.

PFLÜGER'S LAW.—Contractions in a muscle on stimulation of the nerve vary with strength and direction of current. Results obtained constitute Pflüger's Law.

Strength	Descending Current		Ascending Current	
	Make	*Break*	*Make*	*Break*
Weak	C	—	C	—
Moderate	C	C	C	C
Strong	C	—	—	C

Ascending current flows from muscle—i.e., anode is nearest muscle.

Descending current flows towards muscle.

When current is made, impulse arises at kathode; when broken, at anode.]

Normal Reaction to Electrical Stimulation in Man.—

STIMULATION OF NERVE OR MUSCLE BY FARADISM.—Produces contraction of muscle all the time that current is passing.

STIMULATION OF NERVE OR MUSCLE BY GALVANISM.—Produces contraction of muscle at make-and-break of current. When current is made, contraction at kathode is greater than that at anode—i.e., K.C.C. > A.C.C.

Reaction of Degeneration.—

1. STIMULATION OF NERVE.—No response to faradism or galvanism.
2. STIMULATION OF MUSCLE DIRECTLY.—(*a*) No contraction to faradism; (*b*) Much more sluggish contraction to galvanism; (*c*) On making current, contraction at anode is greater than at kathode—i.e., A.C.C. > K.C.C.

Results of Section of a Mixed Nerve (e.g., sciatic).—

1. Flaccid paralysis of muscles supplied.
2. Loss of sensation over area exclusively supplied.
3. Trophic changes.
4. Loss of reflexes, superficial and deep.
5. Muscular wasting and reaction of degeneration (R.D.).
6. Paralysis of sweat and pilomotor nerves.
7. At first, vasodilatation with flushing; later, vasoconstriction.
8. Degenerations: chromatolysis in the nerve-cell; Wallerian degeneration in the nerve distal to point of section.

These changes are not necessarily permanent if ends of nerve are brought into apposition.

Trophic Lesions.—

MANIFESTATIONS.—

1. After Section of Sensory Nerves.—Ulcers, gangrene of the fingers and toes; glossy skin, and slowly healing sores.
2. After Removal of Gasserian Ganglion.—May be ulceration of cornea and destruction of eye.
3. After Section of Both Vagi High in the Neck.—Death of animal about a week later from septic pneumonia, due to aspiration of infected mucus and food into lungs through anæsthetic and paralysed larynx.
4. After Transection of Spinal Cord in the Mid-dorsal Region.—Cystitis (infection of the bladder) and bed-sores—may cause death.

CAUSE OF TROPHIC CHANGES.—

1. OLD EXPLANATION.—Interference with special trophic nerve-fibres having sole function of maintaining nutrition of part. Contains an unnccessary assumption. No real evidence exists of purely trophic fibres.
2. MODERN EXPLANATION.—Due to two factors: (*a*) *Anæsthesia of the part.* In an anæsthetic area, small injuries are unnoticed. If eye is kept covered after removal of Gasserian ganglion, trophic changes are largely prevented. (*b*) *Loss of vasomotor reflex.* Normally, if a few germs enter a crack in the skin, an increased amount of blood and of leucocytes is brought to the part, owing largely to a vasomotor reflex. If this reflex is lost, germs may give rise to considerable damage.

The Neuron.—The nerve-cell with all its processes.

STRUCTURE OF THE NEURON (*Fig.* 10).—Shown by special stains (*see* p. 160).

1. CELL BODY.—(*a*) Large, spherical nucleus, relatively poor in chromatin. (*b*) Neurofibrils running through dendrons, cell, and axon. (*c*) Nissl's granules, which stain with methylene blue (artefacts: not seen in living cell); present in dendrons, not in axon.
2. AXON.—The axon is single and does not branch, and generally becomes the axis cylinder of a nerve-fibre.
3. DENDRONS.—Arise from angles of cell body; usually short, and show marked branching. Studded with 'thorns' (Golgi stain).

THREE TYPES OF NEURON.—

1. UNIPOLAR.—In posterior root ganglia. Axon and one

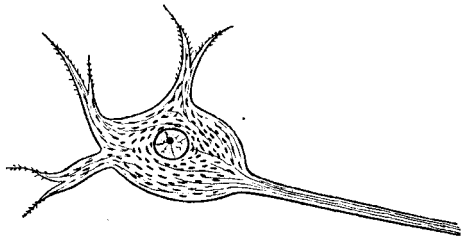


Fig. 10.—Normal multipolar nerve-cell, with dendrons and axon.

The Neuron, *continued.*

dendron arise together, so that cell appears to be unipolar, but process divides later in T shape.

2. BIPOLAR.—In ganglia of eighth nerve. Show axon and one dendron.
3. MULTIPOLAR.—In brain and spinal cord and sympathetic ganglia. Axon and several dendrons.

THE NEURON DOCTRINE.—Each neuron is complete in itself. Axon ends in contact with dendrons of another neuron, forming an arborization known as a *synapse.* No actual continuity.

LAW OF FORWARD DIRECTION.—Impulse always passes same way in neuron—i.e., dendrons to cell body, then by axon to another neuron, or cell in some tissue.

EVIDENCE FOR NEURON DOCTRINE.—(1) With Golgi and other stains, numerous branches are seen, but neurons appear discontinuous; (2) Wallerian degeneration does not *usually* spread beyond synapse.

OBJECTIONS TO NEURON DOCTRINE.—Apathy and others have shown that, in invertebrates, fine filaments pass from one neuron to another.

Histological Results of Nerve Section.—

1. CHANGES PERIPHERAL TO LESION.—After a few days Wallerian degeneration sets in, due to nerve being cut off from its trophic centre, i.e., the nucleus of the cell from which it arises.

CHANGES IN WALLERIAN DEGENERATION.—(*a*) Myelin sheath breaks up into fatty droplets, eventually removed by leucocytes; (*b*) Axis cylinder breaks up into short lengths; (*c*) Nuclei of neurilemma proliferate.

Broken-up myelin sheath and axis cylinder are later removed by phagocytes, and after a time nothing is left but fibrous tissue and nuclei.

CHEMICAL CHANGES.—*Lecithin* is split up into: choline; phosphoric acid; glycerol; fatty acid. Choline and phosphoric acid are removed by circulation, glycerol and fatty acid remaining as fat, for a time.

2. CHANGES IN NERVE CENTRAL TO LESION.—At first, no change, though part immediately contiguous to lesion may degenerate as rapidly as peripheral nerve. This degeneration may extend slowly.
3. CHANGES IN NERVE-CELL.—*Chromatolysis* or *Nissl's degeneration* commences 24 to 48 hours after injury, and

increases for about 18 days, after which cells usually regain normal appearance, though in some cases degeneration is permanent.

CHANGES IN CHROMATOLYSIS (*Fig.* 11).—(*a*) Granules disappear—cells staining diffusely with methylene blue. (*b*) Cell becomes swollen; dendrons may be lost. (*c*) Nucleus assumes an eccentric position, and may be lost.

Regeneration of Nerve.—With clean wound, and cut ends of nerve in apposition, some degree of recovery usually takes place in 6 to 24 months. For a motor nerve, recovery may be complete; for a mixed nerve—e.g., ulnar—only rarely.

HISTOLOGY OF REGENERATION.—Neurilemmal sheath in peripheral part forms a nucleated band of protoplasm—an 'embryonic fibre'. Down-growth takes place from central end of divided nerve into embryonic fibre, owing to chemical attraction, probably of substance formed from break-down of myelin.

[If a tube of brain emulsion, and one of liver emulsion, are presented to central end of a divided nerve, all the sprouting fibres pass into the one containing brain emulsion.]

EVIDENCE.—

a. Nerve-cells can be picked out of a tadpole's spinal cord, and growth of the nerve-fibres watched (Ross Harrison).

b. If upper end of peripheral part of a cut nerve is enclosed in a rubber cap, no axis cylinder is found in the degenerated nerve.

c. Cajal and Marinesco and others have observed down-growth histologically.

d. If nerve is cut, sutured, and allowed to regenerate, second section at same place results in degeneration of fibres peripheral to injury, so their centre of origin must be proximal to lesion.

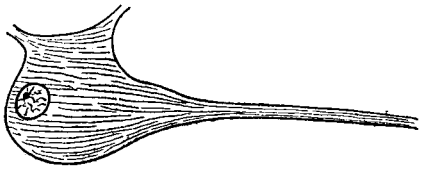


Fig. 11.—Nerve-cell showing chromatolysis after nerve section.

Regeneration of Nerve, *continued.*

[UNION OF DISSIMILAR NERVES.—

1. UNION OF CENTRAL PART OF ONE MOTOR NERVE TO PERIPHERAL PART OF ANOTHER.—Good result may ensue. In cases of facial paralysis, part of spinal accessory nerve has been sutured. Facial movements occur, but accompanied by shrugging of shoulders.
2. UNION OF PURELY MOTOR WITH PURELY SENSORY NERVES.—Histological but not functional regeneration.

Nerve anastomosis in paralysed limbs has not been a success.

NERVE GRAFTING.—If there is so marked a gap between ends of a nerve that they cannot be opposed, piece of another nerve (e.g., internal cutaneous) may be sutured in position. Nerve grafting may succeed, but is not very reliable.

LANGLEY'S EXPERIMENT.—Vagus and sympathetic nerves divided in a cat, and vagus sutured into sympathetic. When regeneration had occurred, swallowing was accompanied by effects of stimulation of cervical sympathetic on that side—i.e., dilated pupil, protrusion of eye, retraction of nictitating membrane, bristling of hair, pallor of ear, and quickening of heart-beat.]

Stains for Normal and Degenerated Nerve Tissue.—

a. FOR NERVE-ENDINGS.—

1. GOLD CHLORIDE.—Soak fresh tissue in lemon-juice, then in 1 per cent gold chloride. Reduce with formic acid in the dark. Section is purple and nerve-endings are black, from reduced metallic gold.
2. EHRLICH VITAL METHYLENE BLUE.—Injection of 1 per cent methylene blue in saline into tissues of a living or freshly killed animal. Tissues are at first white, having used up the oxygen in the dye. On exposure to air, become blue again.

b. FOR NERVE-CELLS.—

1. NISSL'S METHYLENE BLUE.—Overstain with hot methylene blue, and decolorize with aniline oil and alcohol.
2. GOLGI.—(i) Soak in Müller's fluid (potassium bichromate and sodium sulphate); (ii) soak in 0·75 per cent $AgNO_3$ in the dark. A precipitate of silver chromate forms in the neuron. Mount in Canada balsam with no cover-glass.

c. FOR DEGENERATED NERVES.—

1. MARCHI (for recent lesions).—(i) Soak fresh nerve in Müller's fluid; (ii) soak in Marchi's reagent (Müller's fluid + 1 per cent osmic acid). Normal nerve stains yellowish-brown colour, degenerated nerve black. Useful in tracing tracts; useless after fat droplets have been absorbed.

[*Lecithin* of normal nerve will stain with osmic acid, but not in presence of potassium bichromate; *olein* will.]

2. WEIGERT-PAL (for old-standing degenerations).—(i) Overstain with acid hæmatoxylin, and transfer to Pal's bleaching solution (sodium sulphite, oxalic acid, and water); (ii) then $KMnO_4$. It is a stain for myelin. Normal white matter stains bluish-black; degenerated white matter and grey matter are unstained.

Nature of Nerve Impulse.—Not accurately known. Probably an interchange of electrical charges between ions in axis cylinder and those in sheath.

[LILLIE'S THEORY OF NERVE IMPULSE.—A surface film of unstable reducible material is present in the fibre, readily destroyed by stimuli, with production of an electronegative area, and consequently passage of an impulse, with destruction of a new portion of surface film. Reduction of surface film is followed by return to normal, oxygen being needed for this purpose.

EVIDENCE.—During activity, a nerve-fibre probably uses up oxygen and gives out CO_2.]

Müller's Law.—A nerve-fibre, however stimulated, carries only one kind of message—e.g., cutting optic nerve gives sensation of light. Probably true, though not universally accepted.

Direction of Conduction of Nerve Impulse.—A nerve can conduct in both directions, although in synapse the law of forward conduction is observed—i.e., from axon of one neuron to dendron of another.

PROOF.—

AXON REFLEXES (*Fig.* 12).—*Example*: Inferior mesenteric ganglion is isolated from its connections with central nervous system. If one hypogastric nerve is cut and its central end stimulated, bladder contracts. If nerves running across aorta are cut and allowed to degenerate, contraction does not occur. Therefore it is not a true reflex, but an axon reflex due to arborization of pre-ganglionic fibres round various cells in ganglion.

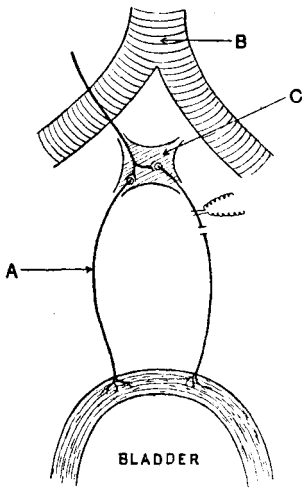


Fig. 12.—Diagram to show axon reflex. A, Hypogastric nerve; B, Aorta; C, Inferior mesenteric ganglion.

Velocity of Nerve Impulse.—
In motor nerves, about 30 metres per second in frog, 125 metres per second in human being, at average room temperatures. Velocity in sensory nerves is not accurately known.
METHOD OF DETERMINATION.—Nerve is stimulated close to and far away from a muscle. The distance between the two points and difference in refractory period are noted. In man, myograph is held between thumb and fingers, and median nerve at bend of elbow is stimulated, then brachial plexus just below clavicle.

Fatigue of Nerve.—Normally a nerve cannot be fatigued.
PROOF.—Two nerve-muscle preparations A and B are stimulated, the impulses being prevented from reaching muscle of B by freezing small section of nerve. Stimulation is continued until muscle of A will not respond. Electrodes are moved to muscle, and it responds, therefore fatigue is not in the muscle. B is now thawed, and stimulation of nerve of B causes contraction of muscle, therefore fatigue is not in nerve. Must be in myo-neural junction.

Factors Influencing Conduction of a Nerve.—
1. TEMPERATURE.—Conduction is increased by slight rise of temperature, decreased by cooling, abolished by freezing.
2. ELECTROTONUS.—Impulse may be increased, decreased, or suspended entirely.
3. DRUGS.—Conduction is decreased by carbon dioxide, alcohol, chloroform, ether, or absence of oxygen.]

CHAPTER XVII.

THE SPINAL CORD.

STRUCTURE OF CORD AND CONDUCTION OF NERVE IMPULSES.

Grey Matter.—Consists of nerve-cells and their processes either non-medullated or very finely medullated, with much connective tissue known as neuroglia.

White Matter.—Consists chiefly of medullated nerve-fibres having no neurilemma, and a little neuroglia.

Central Canal.—Lined by columnar ciliated epithelium. Contains cerebrospinal fluid.

Cross-section of Different Regions of Spinal Cord (in man) (*Fig.* 13).—

1. CERVICAL REGION.—Oval. Large amount of white matter. Anterior horn broad, posterior horn narrow.
2. THORACIC REGION.—Circular. Anterior and posterior horns both narrow. Lateral horn present.
3. LUMBOSACRAL REGION.—Circular. White matter scanty. Anterior and posterior horns both broad.

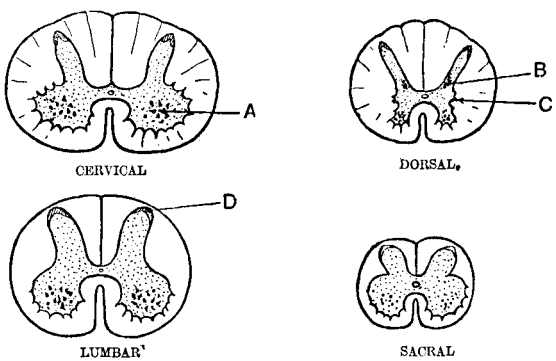


Fig. 13.—Cross-section of different regions of spinal cord. A, Anterior horn cells; B, Clarke's column; C, Lateral horn; D, Gelatinous substance of Rolando.

Arrangement of Cells in Grey Matter.—

1. ANTERIOR HORN CELLS.—These are multipolar, with axons passing out as anterior roots of spinal nerves; a few pass to anterior horn cells of opposite side.
   SYNAPSES.—Formed with fibres from: (*a*) Posterior root ganglia, mostly of same side; (*b*) Posterior horn cells, mostly of same side; (*c*) Crossed pyramidal tract of same side; (*d*) Direct pyramidal tract of opposite side, decussation of fibres occurring in white commissure; (*e*) Rubrospinal and antero-lateral descending tracts of same side.
2. CLARKE'S COLUMN CELLS.—Situated at inner angle of posterior horn, from 7th cervical to 3rd lumbar. Cells are bipolar, axons ascending in dorsal cerebellar tract of same side and ventral cerebellar tract of both sides.
   SYNAPSES.—Formed with fibres of: (*a*) Posterior horn cells; (*b*) Collateral fibres from tracts of Goll and Burdach.
3. INTERMEDIO-LATERAL GROUP.—Situated in lateral horn. Cells are multipolar, axons passing out in anterior roots as white rami communicantes, ending in ganglia of sympathetic chain.
   SYNAPSES.—Formed with fibres from antero-lateral ground bundle.
4. POSTERIOR HORN CELLS.—Situated at base of posterior horns. Widespread connections.

Anterior Nerve Roots.—Axons of anterior horn cells. Also contain vasomotor fibres from 2nd thoracic to 2nd lumbar. May also contain pupillo-dilator, pilomotor, and cardio-accelerator fibres.

RESULTS OF SECTION.—

1. FUNCTIONAL.—
   i. Paralysis of parts supplied.
   ii. Loss of reflexes.
   iii. Muscular wasting.
   iv. Reaction of degeneration.
   v. If several thoracic roots are cut, signs of sympathetic paralysis.
2. STRUCTURAL.—
   i. Wallerian degeneration of fibres peripheral to lesion.

ii. Degeneration of white rami communicantes as far as sympathetic ganglion cells in which they end.

iii. Chromatolysis of anterior horn cells.

Posterior Nerve Roots.—

RESULTS OF SECTION.—Stimulation of central end—reflexes are obtained; of peripheral end—vasodilatation. Section of one posterior nerve root produces no obvious results. Section of all roots to a limb in man or monkey produces the following changes :—

1. FUNCTIONAL.—

i. Total anæsthesia of area supplied.

ii. Ataxia of corresponding limb. Movements wild and disorderly.

iii. *Trophic lesions*, e.g., shiny skin, painless ulcers. These always accompany loss of protopathic sense.

iv. Loss of tone, with marked flaccidity of corresponding limb.

v. Practically paralysis. Animal will not use limb, though reflex movements may occur.

vi. Loss of reflexes.

[Eloesser has shown that bone and joint disease similar to Charcot joints occurring in locomotor ataxia can be produced in cats by bruising or crushing the joints, after section of all posterior nerve roots to a limb, but not if sensory nerves are intact.]

2. STRUCTURAL.—

a. Section Peripheral to Ganglion.—

i. Wallerian degeneration extending to periphery, and degeneration of sensory end-organs.

ii. Chromatolysis of cells in posterior root ganglia.

iii. Disuse chromatolysis of anterior horn cells at same level.

b. Section Proximal to Ganglion.—

i. Degeneration of columns of Goll and Burdach and tract of Lissauer.

ii. Chromatolysis of anterior horn cells and cells in posterior root ganglion.

iii. Downward degeneration of comma tract.

[Section of posterior nerve roots may be performed for relief of severe root pains or spasticity of old paralysed limbs. When many nerve roots are cut, one or two must be left intact or ataxia may result.]

Main Sensory Neuron.—Unipolar nerve-cell in posterior root ganglion. Axon on entering spinal cord divides in T-shaped manner into :—

a. SHORT DESCENDING BRANCH.—Helps to form *comma tract*, ending in cells at base of posterior horn, situated in cervical region between Goll and Burdach ; similar tracts are present in lower parts of cord. This, and also the ascending branch, give off finely medullated fibres at various levels to end in grey matter of cord ('collaterals').

b. ASCENDING BRANCH.—Impulses may be conducted by fibres ending in one of three ways :—

TYPE 1.—Runs in outer division of the nerve-root. Short non-medullated fibres ending in posterior horn cells at different levels. From these stations, fibres arise which cross at once and ascend as spinothalamic tract.

TYPE 2.—Runs in inner division of the nerve-root. Very long medullated fibres passing up in *columns of Goll and Burdach* on same side, terminating in cells of nucleus gracilis and nucleus cuneatus. Fibres at first enter postero-external column of Burdach, those rising low down passing later into column of Goll; hence Goll carries fibres chiefly from leg, Burdach from arm.

TYPE 3.—Certain short fibres and collaterals of Type 2 ending in cells of Clarke's column. From these cells, fibres pass to cerebellum by *dorsal* and *ventral cerebellar tracts*.

[LISSAUER'S TRACT.—Situated at tip of posterior horn. Consists of fibres from posterior root ganglion to posterior horns a few segments higher.

Section of outer division of posterior nerve-root abolishes evidences of pain (e.g., struggling, pressor vasomotor reflex, and quickened breathing) in lightly anæsthetized animal when sensory nerves are stimulated. Section of inner half of root has not this effect. The outer non-medullated part may be path for pain and temperature sense.]

THUS THERE ARE TWO PATHS FOR SENSATION :—

1. By medium-length fibres and spinothalamic tract, crossing in cord from 2 to 6 segments above level of entry, finally joining mesial fillet and ending in optic thalamus. They carry sensations of heat, cold, and pain. Pain fibres cross almost at once, temperature ones about 5 segments higher up.
2. By long fibres forming tracts of Goll and Burdach,

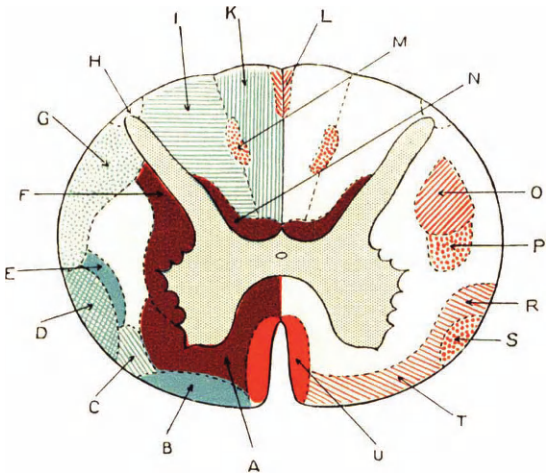


Fig. 14.—Diagram of conducting tracts in spinal cord. The ascending tracts are shown in blue, the descending tracts in red, the association tracts in purple. **A**, Anterior ground bundle; **B**, Spinothalamic tract (anterior); **C**, Spinotectal tract; **D**, Ventral cerebellar tract; **E**, Spinothalamic tract (posterior); **F**, Lateral limiting layer; **G**, Dorsal cerebellar tract; **H**, Tract of Lissauer; **I**, Column of Burdach; **K**, Column of Goll; **L**, Septomarginal tract; **M**, Comma tract; **N**, Cornu-commissural tract; **O**, Crossed pyramidal tract; **P**, Rubrospinal tract; **R**, Tectospinal tract; **S**, Olivospinal tract; **T**, Vestibulospinal tract; **U**, Direct pyramidal tract.

To face page 167]

which are uncrossed. They carry sense of weight and position, stereognosis, and tactile discrimination. Touch sensations may travel by either path.

EVIDENCE.—

1. *Brown-Séquard Phenomenon : Result of Hemisection of Cord in Man.*—(*a*) Loss of heat, cold, and pain sense on opposite side of body ; (*b*) Loss of tactile discrimination, stereognosis, and muscle sense on same side as lesion.
2. *Syringomyelia.*—Cavities are formed in cord, especially in central part, spinothalamic tract being commonly destroyed at its origin, with loss of sensations of pain and temperature, but maintenance of other sensations.

Tracts of Cord (*Fig.* 14).—Classified as: (1) *Short or association tracts.* (2) *Long tracts*: (*a*) Ascending or sensory ; (*b*) Descending or motor.

ASSOCIATION TRACTS.—Include septo-marginal and cornu-commissural tracts (in posterior columns) ; lateral limiting layers ; and antero-lateral ground bundle. Fibres extend for one only or for many segments in cord, ending round another neuron in grey matter, but do not leave the cord. May be ascending or descending.

Function.—To connect different segments of cord, and associate their various activities.

SENSORY OR ASCENDING TRACTS.—

1. COLUMNS OF GOLL, BURDACH, AND LISSAUER.
2. DIRECT OR DORSAL CEREBELLAR TRACT OF FLECHSIG.—Arises in cells of Clarke's column, starting in lower thoracic region, and travels up on same side of cord, through medulla, and enters cerebellum by inferior peduncle to end in superior vermis.

   Function.—To convey impulses from muscles, tendons, and joints concerning position of limbs ; impulses do not rise into consciousness.
3. ANTERO-LATERAL ASCENDING TRACT OF GOWERS.—Situated in antero-lateral region of cord, anterior to direct cerebellar tract. Endogenous in origin. Consists of :—

   a. Ventral spino-cerebellar tract, arising in cells of posterior horn on both sides of the cord. Enters cerebellum by superior peduncle, and ends in anterior part of superior vermis.

   Function.—Same as direct cerebellar tract,

Tracts of Cord—Sensory, *continued.*

b. Spino-thalamic and spino-tectal fibres, arising in cells of posterior horn of opposite side. Spino-thalamic fibres join mesial fillet in medulla, and end in optic thalamus; they carry pain and temperature sense. Spino-tectal fibres end in anterior corpus quadrigeminum.

MOTOR OR DESCENDING TRACTS.—

1. Pyramidal Tract, Crossed and Direct (only in mammals).—The main descending tract. Arises in large cells of Betz in pre-Rolandic area of cortex. Fibres pass through internal capsule, occupying genu and anterior two-thirds of posterior limb; in mesencephalon, they occupy middle three-fifths of crusta of crura cerebri; in pons, they run as scattered bundles of fibres in anterior region; they continue down in anterior region of upper medulla, then divide into (*a*) crossed and (*b*) direct pyramidal tracts.

a. Crossed Pyramidal Tract.—Formed by decussation of greater part of fibres in lower part of medulla. Fibres pass down in lateral column of opposite side of cord, to end by arborizing round cells of anterior horns (or Clarke's column, according to Sharpey-Schafer).

b. Direct Pyramidal Tract (only in man and great apes).—A few fibres continue on same side on either side of antero-median fissure, and gradually cross in anterior white commissure to end in anterior horn cell of opposite side. About 1 per cent of pyramidal fibres are uncrossed all the way. The direct pyramidal tract ends in the lower thoracic region.

Before reaching medulla, pyramidal tract gives off a few fibres which, crossing mid-line, end in cells of origin of cranial nerves.

Function.—To govern voluntary movements and inhibit muscle tone. Evidence: Damage to pyramids in internal capsule causes paralysis of opposite half of body (hemiplegia), with great increase of muscle tone.

2. RUBROSPINAL TRACT, PRE-PYRAMIDAL TRACT, OR MONAKOW'S BUNDLE.—Arises in red nucleus in midbrain, crosses almost immediately, and descends on opposite side of pons and medulla to cord. Passes down in lateral columns, anterior to crossed pyramidal tract, to cells of posterior part of anterior horns. Tract can be traced to sacral region.

   Function.—A primitive motor path controlling stock movements, e.g., standing and walking.

3. ANTERO-LATERAL DESCENDING TRACT OF LÖWENTHAL.—Consists of :—

   a. Tecto-spinal Tract.—From anterior corpus quadrigeminum of opposite side.

   b. Vestibulo-spinal Tract.—From Deiters' nucleus of same side. Fibres pass down in antero-lateral region of cord to end round anterior horn cells.

   Function.—Probably convey co-ordinating impulses.

[4. COMMA TRACT (*see* p. 166).

5. OLIVO-SPINAL TRACT, OR HELWEG'S BUNDLE.—Occurs at periphery of cord anterior to Gowers' tract, in cervical region only. Arises in cells of olivary nucleus in medulla.

6. Possibly fibres arise in cells of medulla, pons, and midbrain.

Extra-pyramidal tracts are of considerably more importance in animals than in man. (1) In dogs, section of pyramidal tracts is not followed by complete paralysis; (2) After section of pyramidal tracts in monkeys, there is only transient loss of voluntary movement.]

Methods of Tracing Tracts in Spinal Cord.—

1. EMBRYOLOGICAL OR FLECHSIG MYELINATION METHOD.—Nerve-fibres have at first no myelin sheath, and acquire one at different periods of development. Stain used is Pal-Weigert. Myelin sheath is acquired first in sensory tracts, in pyramidal tracts only just before or after birth, and last in association fibres connecting up various parts of cortex cerebri.

2. DEGENERATION OR WALLERIAN METHOD.—Consists in tracing tracts which degenerate after injury or disease of nervous system. Stain usually used is Marchi (which stains degenerated areas black) for recent degenerations, Pal-Weigert for old ones.

3. PHYSIOLOGICAL.—Stimulation or destruction of certain nerve-cells or fibres, and observation of resulting symptoms.

REFLEX ACTION.

Definition.—Reflex action is involuntary production of activity in some peripheral tissue resulting from stimulation of *afferent* nerve-fibres. May be conscious or unconscious.

Reflex Arc.—The structures concerned in the production of reflex action.

ELEMENTS OF REFLEX ARC.—

1. AFFERENT PATH.—(*a*) Sensory end-organ or receptor; (*b*) Afferent nerve-fibre.
2. CENTRE.—Consists of one or more neurons of the spinal cord or lower-level centres of the brain.
3. EFFERENT PATH.—(*a*) Efferent nerve; (*b*) Effector organ, usually muscle or gland.

VARIETIES OF REFLEX ARC.—

1. SIMPLE.—Consists of sensory neuron with cell in posterior root ganglion, and motor neuron with cell in corresponding anterior horn of same side.
2. INTERCALATED.—One or more intermediate neurons between sensory and motor ones.
3. CROSSED.—Intermediate neuron is connected with an efferent neuron of opposite side.
4. COMPLEX.—Axon of sensory neuron passes up to medulla, but gives off collaterals at various levels. A sensory fibre passing to cortex and giving rise to conscious sensation may also give rise to reflex action—e.g., painful stimulation of muscle results in conscious sensation of pain and also reflex vasoconstriction in muscle through vasomotor centre in medulla.

Types of Reflex Action.—

1. SIMPLE.—A single muscle is affected—e.g., winking.
2. CO-ORDINATED.—Several muscles affected, but result is an orderly purposive movement.
3. CONVULSIVE.—A number of muscles affected, and result is disorderly and useless movements—e.g., convulsive movements caused by tickling. Due to either or both of following factors: (*a*) Very intense or especially effective sensory stimulation; (*b*) Increased irritability of central nervous system—e.g., after administration of strychnine, hydrophobia, tetanus.

Methods of Studying Reflex Action.—Best studied in a frog whose brain has been destroyed, after it recovers from shock—i.e., the spinal frog. Can also be studied in mammals—e.g., dog—but if cord is divided high up, animal

usually dies of shock. Sherrington, after removal of head of anæsthetized cat, has kept the animal alive for some hours. Spinal cord may be divided below origin of phrenic nerves and animal live for years. In man, reflexes can be studied in cases of injury to spinal cord (*see below*).

IN SPINAL FROG.—Initial stage of shock, during which reflexes are absent—lasts a few minutes. No spontaneous movements.

Reflexes obtained are chiefly co-ordinated ones: (*a*) If toe is pinched, foot is withdrawn. (*b*) Stimulation of small areas of skin by pieces of paper soaked in acetic acid causes movements of leg on same side so as to brush off the paper; if this leg is held, movements of the other leg occur.

IN SPINAL DOG.—Shock lasts about a day. Afterwards dog shows:—

1. *Scratch reflex.* Stimulation between scapulæ by tickling results in scratching movements with hind leg.
2. Stimulation of foot produces flexion of leg.
3. *Extensor thrust.* Pressure on pad of hind foot causes extension of limb—i.e., dog kicks out.
4. *Mark-time movements.* When animal is held up so that hind legs hang free, they extend by their weight, then flex. Stimulus is probably due to stretching of skin and tendons by weight of limbs.

Characteristics of Reflex Action.—

1. DEPENDENT ON RECEPTOR.—
   - *a.* Specificity of Stimulus.—There must be a particular variety of stimulus for a particular reflex response—e.g., rise of blood-pressure is caused by dilatation of bile-duct by passage of a gall-stone, but not by mechanical or electrical stimulation of duct.
   - *b.* Co-ordination of Reflex.—Depends on stimulation of normal sensory endings; stimulation of the nerve leads to disorderly reflex movements.
2. DEPENDENT ON SYNAPSE.—
   - *a.* Reduced Reflex Time.—The time taken in transmission of impulse through neurons of central nervous system.

     Total reflex time is time taken in passage of impulse from receptor to affector organ. The reduced reflex time is very short with strong stimuli; it rapidly increases with diminution in strength of stimulus, or fatigue. Reduced

Characteristics of Reflex Action, *continued.*

reflex time in man for winking is about 0·0555 sec. (Exner). In frog, reduced reflex time is about 0·01 sec.

b. Reflexes are very readily Fatigable.—Seat of fatigue is apparently in synapse.

c. Temporal Summation or Cumulation.—A weak stimulus may have no effect, but, repeated a number of times, it may be adequate.

d. Inhibition.—Reflexes are normally moderated by the brain.

Evidence.—

i. If a frog's brain is removed and exposed surface of cord stimulated by crystals of sodium chloride, reflexes are greatly depressed. On removing stimulus by washing away crystals, reflexes are normal.

ii. In a disease, lateral sclerosis, where the lateral columns, including pyramidal tracts, are degenerated, reflexes are increased.

e. Effect of Drugs.—Anæsthetics depress or abolish reflex excitability, while strychnine increases it.

Some reflexes take precedence over others, the strongest being pain, then sexual.

Reciprocal Innervation.—Contraction of group of muscles acting on a movable organ results in relaxation of opposing group—e.g., when elbow is bent by contraction of flexor muscles, extensor muscles are relaxed. This depends on reciprocal innervation.

EXAMPLES.—

1. Sherrington's Hamstring Experiment.—After cutting insertion of hamstring muscles and stimulating them, quadriceps extensor relaxes, and tibia drops by its own weight.
2. Cut left 6th cranial nerve. Stimulate cortex to turn eyes to left. Left eye still turns, by relaxation of internal rectus.

EXPLANATION OF RECIPROCAL INNERVATION.—Probably tension produced in a muscle during contraction acts on its sensory end-organs, with passage of impulse to cord, spreading up or down by association tracts, depressing motor cells of opposing group. Strychnine abolishes this inhibitory effect.

Conditioned or Acquired Reflexes.—*See* p. 188.

Reflexes in Man (*Fig.* 15).—

CLASSIFICATION.—

1. SUPERFICIAL.—Muscular contraction resulting from stimulation of skin.
2. DEEP OR TENDON REFLEXES.—Obtained by tap on tendon of slightly stretched muscle.
3. VISCERAL.

REFLEXES OF CLINICAL IMPORTANCE.

Reflex	*Method of Obtaining*	*Result*	*Spinal Segment Involved*
SUPERFICIAL:—			
Plantar	Stroking sole of foot	Flexion of toes normally. In babies, and in disease of pyramids, extension of big toe	Sacral 1 and 2
Cremasteric	Stroking inner side of thigh	Drawing up of testicle	Lumbar 1 and 2
Epigastric	Stroking down chest from nipple	Retraction of same side of epigastrium	
Conjunctival	Touching cornea	Winking	Nuclei of 5th and 7th cranial nerves
Pupillary	Flashing light into eye	Contraction of pupil	Nucleus of 3rd cranial nerve
DEEP:—			
Knee-jerk	Tapping patellar tendon	Kicking forward of leg	Lumbar 3 and 4
Ankle-jerk	Tapping tendo Achillis	Plantar flexion of foot	Sacral 1 and 2
Biceps-jerk	Tapping biceps tendon	Flexion of forearm	Cervical 5 and 6
Triceps-jerk	Tapping triceps tendon	Extension of forearm	Cervical 8, dorsal 1 (?)
Wrist-jerk	Striking extensor tendons just above wrist	Jerking up of hand	Cervical 8 (?)

ANKLE-CLONUS.—Obtained by suddenly dorsiflexing foot and maintaining pressure on sole. Result is a series of rhythmical contractions. Absent in health.

VISCERAL REFLEXES.—(1) Deglutition; (2) Defæcation—sacral 5; (3) Micturition—sacral 3 and 4. Many others. In adults, these reflexes are normally under voluntary control.

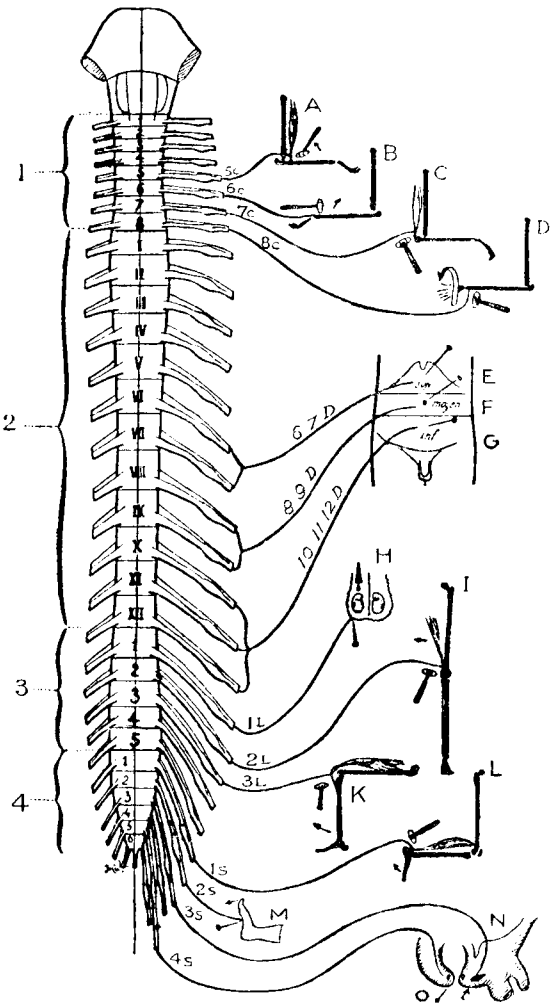


Fig. 15.—Scheme of the principal spinal reflexes. 1, Cervical cord; 2, Dorsal cord; 3, Lumbar cord; 4, Sacral cord. Reflexes: A, Biceps; B, Supinator; C, Elbow-jerk; D, Pronator; E, F, G, Upper, middle, and lower abdominal; H, Cremasteric; I, Adductor-jerk; K, Knee-jerk; L, Ankle-jerk; M, Plantar; N, Bulbocavernosus; O, Anal. (*From the 'British Journal of Surgery'—after Lévy-Valensi.*)

KNEE-JERK.—Obtained by tapping patellar tendon with quadriceps extensor under slight tension—e.g., by crossing knees or letting leg hang freely over edge of chair.

REINFORCEMENT OF KNEE-JERK.—Knee-jerk can be greatly augmented by a voluntary movement of the individual—e.g., clenching hands—or if a sensory stimulus is given when tendon is struck. If reinforcing act precedes blow by more than about 0·5 sec., jerk is inhibited; if by more than about 2·5 seconds, it has no influence.

[*Explanation of Reinforcement.*—

1. *Overflow theory.*—Supposes that motor impulses from cortex concerned in voluntary action 'overflow' to lower part of cord, increasing irritability of the neurons.
2. *M'Dougall's drainage theory.*—Supposes that neurons contain a store of energy during rest. When voluntary action occurs, energy flows from all other neurons to those concerned in the action, the resistance of those governing the knee-jerk is lowered, and the reflex is more easily elicited.]

IS THE KNEE-JERK A TRUE REFLEX OR MERELY A TWITCH DUE TO MECHANICAL STIMULATION?—Generally accepted that it is a true reflex.

Evidence.—

1. Its elicitation depends on integrity of reflex arc. (But muscle tone is essential even for a twitch, and this is lost when reflex arc is broken.)
2. Tapping tendon on one side may result in knee-jerk on opposite side.
3. The smaller the animal, the shorter is the latent period: evidently there is some factor besides the latent period of the muscle.

Objections.—Most have been satisfactorily answered.

1. *The response is too rapid,* i.e., the latent period is too short. Accepting the newer figures for velocity of nerve impulses, however, the time is just long enough for a reflex action, too long for a direct one.

[2. Knee-jerk is a simple twitch, while motor centres in cord when stimulated usually give a series of twitches, a tetanus. But stimulation of central end of cut sciatic nerve in frog gives a reflex contraction which is a twitch.]

USE OF REFLEXES IN DIAGNOSIS.—

Absent in lesion of any part of reflex arc.

Exaggerated in disease of pyramidal tracts, since normally these fibres inhibit the reflex arc.

Reflexes in Man—Use in Diagnosis, *continued.*

Segments of cord on which various reflexes depend are known, so that level of lesions can be located.

Lesions of central nervous system are divided into :—

1. Upper Motor Neuron Lesions.—Those which involve cortical Betz cells or pyramidal tracts.
2. Lower Motor Neuron Lesions.—Those which involve spino-muscular neuron, either anterior horn or medullated fibres of peripheral nerve.

Results of Lesions.

Upper Motor Neuron Lesion	*Lower Motor Neuron Lesion*
1. Paralysis, spastic type	1. Paralysis, flaccid type
2. Deep reflexes exaggerated Knee-jerk increased Ankle-clonus present Plantar reflex extensor	2. Reflexes absent
3. No wasting (except from long disuse)	3. Wasting
4. No reaction of degeneration	4. Reaction of degeneration

The Double Motor Path.—The motor path appears to be double throughout.

EVIDENCE.—

1. For Double Path from Brain to Anterior Horns.—
   - *a.* Fœtus or baby can move limbs before pyramids are myelinated.
   - *b.* After hemiplegic stroke, stock movements such as standing and walking may persist although fibres of pyramids are almost entirely destroyed.
   - *c.* In animals, extensive lesions of pyramids or motor cortex do not produce lasting paralysis.
   - *d. Phenomena of Spasticity.*—After a hemiplegic stroke in internal capsule, there is marked rigidity of paralysed side. Transection of the mid-brain in an animal leads to decerebrate rigidity, abolished by second transection below 4th ventricle, or section of posterior nerve-roots. Hence there must be another innervation for muscles besides pyramids, which is responsible for the spasticity.

[*Probable Path of Tonic Impulses.*—Opinion varies. One view is

that the tonic impulses originate in region of Deiters' nucleus, and are inhibited by the red nucleus and rubrospinal tract.

Tracts inhibiting Muscular Tone.—(i) Pyramidal; (ii) Fronto-pontic; (iii) Temporo-occipito-pontic. Lesion of cortex is frequently flaccid because cortico-pontic tracts are spared.

2. For Double Path from Anterior Horns to Periphery.—There are end-plates for non-medullated as well as for medullated nerve-fibres in striped muscle (Boeke), and many non-medullated fibres in peripheral nerves, shown by silver pyridine stain (Ranson).

Two paths suggested :—

i. Rubrospinal and antero-lateral descending tracts, fine and non-medullated nerve-fibres, Boeke's end-plates, and sarcoplasm.

ii. Pyramidal tract, coarsely medullated nerve-fibres, ordinary end-plates, and sarcostyles. This is a newer mechanism and concerned with quicker movements.

After facial paralysis, tone may recover before voluntary movement.]

Spinal Man: Results of Complete Section of Spinal Cord.—Three stages. In all stages there are :—

1. Paralysis below lesion.
2. Total anæsthesia below lesion.
3. Trophic lesions.
4. Loss of control of bladder and rectum.

STAGE 1.—*Stage of spinal shock.* Lasts 1 to 3 weeks. Features :—

1. Absence of reflexes.
2. Flaccidity of muscles.
3. Bladder fills up passively, and when quite full overflows, so that urine dribbles away all the time. Capacity of bladder becomes less and less.
4. Blood-pressure low owing to vasodilatation.

STAGE 2.—*Stage of recovery.* Cord recovers its irritability and may be hyper-irritable. In man this stage may last weeks or years, or never appear at all. Features :—

1. Return of reflexes, which may be exaggerated. 'Mass reflex' may be shown—i.e., stroking inner side of thigh results in flexor spasm of thigh and abdominal muscles, so that knees are drawn up on to chest, sometimes accompanied by emptying of bladder and profuse sweating. In complete section of cord, reflex spasms are always flexor.
2. Ankle-clonus present.
3. Plantar reflex extensor.
4. Reflex emptying of bladder. Fills up completely, then empties itself periodically but without knowledge or control of patient.

Results of Complete Section of Spinal Cord in Man, *continued.*

STAGE 3.—*Stage of degeneration.* Cord below lesion degenerates and ceases to function. Features :—

1. Loss of reflexes.
2. Loss of muscle tone and great wasting.
3. Trophic changes more marked.
4. Bladder reverts to condition in first stage.

Patients usually live from three months to three years, dying generally from toxic absorption from bed-sores, or from a septic condition of the bladder which spreads to the kidneys. If patient is pregnant, pregnancy is unaffected, and painless labour occurs at the normal time.

[**Removal of Spinal Cord.**—Gatz has removed the spinal cord by degrees in animals, except the cervical and upper thoracic regions, and some lived for long periods. Muscles of hind limbs and trunk atrophied completely, and blood-vessels were paralysed, but later recovered their tone.]

CHAPTER XVIII.

THE BRAIN.

THE CEREBELLUM.

Anatomy.—Shows a vermis and two lateral hemispheres. Three peduncles unite it to mid-brain, pons, and spinal cord. Consists of:—

1. Outer layer of grey matter, the *cortex*.
2. Central *white matter*.
3. Several ganglionic masses: (*a*) *Dentate nucleus*, in centre of each hemisphere; (*b*) *Nucleus fastigii*, *nucleus globosus*, and *nucleus emboliformis* near centre of vermis.

Structure of Cortex.—

1. OUTER OR MOLECULAR LAYER: (*a*) *Basket cells*, axons terminating round body of Purkinje's cells; (*b*) Small neuroglial cells; (*c*) Dendrons of Purkinje's cells, axons of small cells in granular layer, and termination of afferent fibres in white matter.
2. SINGLE ROW OF PURKINJE'S CELLS.—Flask-shaped cells, having an axon passing from the base through internal layer into white matter, and dendrons branching profusely in molecular layer. Round body of each Purkinje's cell is an arborization of two sets of fibres: (*a*) Afferent fibres from spino-cerebellar tracts; (*b*) Fibres from basket cells.
3. INNER OR GRANULAR LAYER.—

[(*a*) Numerous small nerve-cells, whose axons pass into molecular layer, and divide in T-shaped manner, the divisions running parallel with surface; (*b*) A few large cells of Golgi-II type; (*c*) Neuroglia cells; (*d*) Moss fibres of Cajal, afferent fibres which break up in granular layer.]

Subjacent White Matter consists of 3 sets of fibres.—

1. AXONS OF PURKINJE'S CELLS, which run to nucleus dentatus.

[2. MOSS FIBRES of Cajal, which break up in granular layer. They are afferent.

3. TENDRIL FIBRES, also afferent, and ending round cells of Purkinje.]

Tracts Connecting Cerebellum and other Parts of Central Nervous System.—

A. AFFERENT CONNECTIONS.—

1. WITH SPINAL CORD.—

Direct cerebellar tract, and *antero-lateral ascending tract of Gowers,* from spinal cord by inferior and superior cerebellar peduncles to vermis. Convey impulses from muscles and joints regarding sense of position and movement.

2. WITH PONS AND MEDULLA.—

a. Dorsal and ventral external arcuate fibres, former arising in nucleus gracilis of same side, latter in that of opposite side. They may carry impulses from skin indicating where weight is being borne.

b. Fibres from olivary bodies on both sides. Function unknown.

c. Vestibular fibres from Deiters' nucleus of opposite side. Carry impulses from semicircular canals of opposite side.

[*d.* Fibres from nuclei of 5th, 10th, and 11th cranial nerves of same side.]

All enter cerebellum by inferior peduncle.

3. WITH CEREBRUM AND MID-BRAIN.—

a. Cortico-ponto-cerebellar fibres, arising in pyramidal cells in frontal and temporal cortex, having cell station in pons, and entering cerebellum by middle peduncle of opposite side.

[*b. Occipito-cerebellar fibres,* having cell station in anterior corpus quadrigeminum, entering by superior peduncle. Function: To carry visual impressions.]

B. EFFERENT CONNECTIONS.—The only efferent cells in the cortex are Purkinje cells, from which fibres pass to dentate nucleus. Thence :—

1. From dentate nucleus by superior peduncle to red nucleus of opposite side, then by rubrospinal tract, which decussates, so that cerebellum influences anterior horn cells of same side.

[2. From dentate nucleus and nucleus fastigii to Deiters' nucleus of same side of pons, thence to antero-lateral descending tract.

3. A few fibres to optic thalamus by superior peduncle.]

Effects of Removal in Animals (dogs, pigeons, etc.)—

IMMEDIATE EFFECTS.—Partial removal of lateral lobe has no effect. Removal of whole or large part of cerebellum

produces inability to stand or move. No true paralysis, but a total lack of muscular co-ordination, any attempt at movement causing violent disorderly contractions that frequently result in somersaults in birds. The head is retracted and twisted. If removal is unilateral, animal rolls towards affected side.

PERMANENT SYMPTOMS.—After about 4 weeks animal makes more or less successful attempts at standing and walking, but shows :—

1. ATAXIA, i.e., unsteadiness of gait. Especially affects hind limbs.
2. ASTHENIA, i.e., muscular weakness.
3. ATONIA, i.e., lack of muscular tone.
4. TREMOR of muscles during action.

If lesion was unilateral, these symptoms appear on operated side.

Effects of Disease in Man.—Symptoms are similar to later effects in dogs. Inco-ordination manifested in arms, as well as ataxic gait : e.g., inability to place finger on tip of nose, or to pronate and supinate forearms rapidly (dysdiadochokinesis). May also be : (1) Vertigo (i.e., giddiness) ; (2) Nystagmus (i.e., oscillating movements of eyes). If cerebellum is damaged very slowly, may be no symptoms.

Results of Stimulation of Cerebellum.—Electrical stimulation of cortex caused definite movements of head, limbs, or eyes, according to part stimulated. These indications of localization have been strengthened by results of ablation of various parts of cerebellum. Dentate nucleus is more excitable than cortex.

Functions of Cerebellum.—

1. FLOURENS' THEORY.—Suggests that cerebellum co-ordinates voluntary movements, especially complex movements, e.g., those of equilibration (is " head ganglion of the proprioceptive system "—Sherrington). Afferent impulses are brought from skin, muscles, tendons, eyes, and labyrinths. Efferent impulses pass to red nucleus, thus influencing motor tracts. When muscles and joints are moved, fresh afferent impulses pass to cerebellum, efferent impulses are modified, and muscle tone is altered. When one side of cerebellum is injured, impulses from this side predominate, causing disturbance of equilibrium.

   OBJECTION.—No explanation of almost complete disappearance of symptoms, unless other cerebral centres are assumed to take on functions of cerebellum.

Functions of Cerebellum, *continued.*

2. MITCHELL-LUCIANI THEORY.—Suggests that cerebellum augments tone of voluntary muscles. Early symptoms supposed to be due to irritation from removal of organ, permanent ones being essentially muscular weakness and loss of tone.

   OBJECTION.—No explanation of absence of symptoms in some slowly produced lesions.

Neither theory is wholly satisfactory, and it can only be said that the cerebellum exerts some influence on the neuro-muscular apparatus.

THE CEREBRUM.

Cortex.—Thickness varies from 2 to 4 mm.

STRUCTURE.—Consists of 5 layers :—

1. OUTER FIBRE OR MOLECULAR LAYER.—

   [Consists of medullated nerve-fibres, running parallel to surface (termination of afferent fibres, and dendrons from deeper layers), neuroglial cells, and small nerve-cells, including horizontal cells of Cajal, whose processes run parallel with surface, and end in this layer.]

2. OUTER CELL LAYER.—Pyramidal cells, chiefly small and medium-sized. Apices point upwards, and dendrons pass from them into outer fibre layer ; axons pass down from base of cell.
3. MIDDLE CELL LAYER OR GRANULAR LAYER.—Small stellate cells with short branching axons ending in outer cell layer ; small pyramidal cells ; and a band of nerve-fibres running parallel to surface, the *external band of Baillarger.*
4. INNER FIBRE LAYER.—Nerve-fibres running parallel to surface, the *internal band of Baillarger.*
5. INNER CELL LAYER.—Fusiform and polymorph cells, with dendrons passing into outer cell layer.

VARIATIONS IN STRUCTURE OF CORTEX IN DIFFERENT REGIONS.—

1. MOTOR AREA.—Characterized by numerous large pyramidal (Betz) cells in inner fibre layer.
2. SENSORY AREA.—Well-marked development of middle-cell layer.
3. VISUO-SENSORY AREA. — (*a*) Middle-cell layer much hypertrophied, and divided into two parts by a thick layer of medullated nerve-fibres, the white line of Gennari ; (*b*) A few solitary cells of Meynert in inner fibre layer.

4. VISUO-PSYCHIC AREA.—Outer cell layer is nearly twice as thick as in visuo-sensory area.

White Matter.—Contains 3 sets of fibres: (1) *Projection system*, i.e., fibres connecting cortex with underlying parts of central nervous system; (2) *Association system*, i.e., fibres from cortex of one convolution to that of another convolution in same cerebral hemisphere; (3) *Commissural system*, i.e., fibres connecting the two cerebral hemispheres.

1. PROJECTION SYSTEM.—
   - *a.* AFFERENT FIBRES.—
     - i. *Thalamo-cortical.*—Upward continuation of the mesial fillet.
     - ii. *Auditory Radiations.*—Fibres from the posterior corpus quadrigeminum and internal geniculate body through internal capsule to temporal convolution.
     - iii. *Optic Radiations.*—From external geniculate body to occipital lobe.

     [iv. *Cerebello-cerebral Fibres.*—Emerging from cerebellum by superior peduncle.]
   - *b.* EFFERENT FIBRES.—
     - i. *Pyramidal Tract.*—*See* p. 168.
     - ii. *Fronto-pontine.*—Lies in front of pyramids in internal capsule, internal to them in mid-brain.
     - iii. *Temporo-pontine.*—Behind pyramids in internal capsule, external in mid-brain.
     - iv. *Occipital Bundle.*—To anterior corpus quadrigeminum.

     Last three conduct impulses to cerebellum.
2. ASSOCIATION SYSTEM.—Two types of fibres:—
   - *a.* SHORT ASSOCIATION FIBRES.—Unite adjacent convolutions.
   - *b.* LONG ASSOCIATION FIBRES.—Unite distant lobes.
3. COMMISSURAL SYSTEM.—
   - *a.* CORPUS CALLOSUM.
   - *b.* ANTERIOR COMMISSURE.—Connects the two temporal lobes.
   - *c.* HIPPOCAMPAL COMMISSURE.—Connects the two hippocampal convolutions.

Differences in Structure of Cortex in Man and Animals.—Surprisingly little difference in structure considering marked difference in function.

Differences in Structure of Cortex in Man and Animals, *continued.*

1. Inner cell layer develops first, and is probably concerned with organic and instinctive activities; well developed in all but helpless idiots.
2. Outer cell layer only appears late in phylogeny of vertebrates, and reaches greatest development in man. Probably concerned with higher psychical processes.
3. Greater mental development appears to be associated with greater complexity of endings of neurons.
4. Greater development of association areas occurs in human brain, especially in frontal lobe.

Effects of Removal of Cerebrum.—

1. IN BONY FISH.—No apparent result; fish can distinguish between a worm and a thread.
2. IN FROGS.—
   REMOVAL OF CEREBRAL HEMISPHERES ONLY.—No effect, when immediate results of operation have worn off. Posture and equilibration are normal, and frog continues to feed itself by catching passing insects.
   REMOVAL OF CEREBRAL HEMISPHERES AND OPTIC THALAMI.—Frog becomes a purely reflex animal, and if not stimulated will remain in same position till it dies.
3. IN PIGEON.—Bird becomes lethargic and reacts only when stimulated. It will not eat voluntarily (though if hungry it may walk about and peck aimlessly at ground), and shows no sexual or maternal instincts. Equilibration is normal, and animal reacts to stimuli—i.e., is awakened by a loud noise if dozing—but shows no signs of fear.
4. IN DOG.—Difficult operation in mammals, owing to hæmorrhage. Goltz has removed whole cortex in dogs in several stages, and in the most successful experiment animal lived for 1½ years. After immediate effect of operation had passed off, animal could perform reflex actions and complicated acts like standing and eating, but showed no signs of intelligence, nor emotions.
   REMOVAL OF ONE CEREBRAL HEMISPHERE.—Motor and sensory disturbances occur, chiefly on opposite side, but intelligence seems normal.
5. IN MONKEYS (*Macacus*).—One lived 26 days. They are reduced to automata, but react to bright lights or noises.

There is a case on record (Edinger and Fischer) of a child who lived four years, with no signs of intelligence, and showed post-mortem total destruction of cerebral hemispheres.

Functions of Cerebrum.—

1. Reception of stimuli.
2. Combination of effects of present stimuli with those of past ones. Psychical processes.
3. Giving out efferent impulses based on such stimuli.

Localization of Function in Cerebrum.—

Only in anthropoid apes is pattern comparable to human.

Chief Methods of Study.—(1) Electrical stimulation of cortex ; (2) Removal of certain parts of cortex ; (3) Disease in man, comparing functional derangements during life with results of post-mortem examination ; (4) Histological, noting endings of various tracts.

MOTOR AREA.—Situated in front of fissure of Rolando in ascending frontal convolution and adjacent parts of 1st, 2nd, and 3rd frontal convolutions. Divided into areas representing different parts of the body, from above downwards : (1) Leg (toe area being highest). (2) Trunk. (3) Arm (shoulder being highest). (4) Face and neck ; in front of this area in 2nd frontal convolution is area for eye movements. (5) Tongue, lips, larynx ; just in front of these in posterior part of 3rd frontal convolution is Broca's speech area, found only on left side in right-handed people.

EVIDENCE OF ITS MOTOR FUNCTION.—

1. Shows Betz cells, in which pyramidal tract originates.
2. *Electrical stimulation.*—Weak current causes movement of corresponding area of body on opposite side. With strong current, reaction spreads to more muscles on opposite side and some of same side ; may be convulsions. In movements, such as respiration, where muscles of two sides act together, there is bilateral innervation—i.e., centre on each side of brain controls movements on both sides of body. *Movements*, not *muscles*, are represented in cortex, and size of area is not in proportion to musculature of part of body it governs, but to delicacy and variation of movement of that part. Thumb area is larger than trunk area. There are separate centres for movements of flexion and extension.

Localization of Function in Cerebrum, *continued.*

3. *Experimental Removal.*—Produces paralysis. In dog, paralysis clears up in a few hours; in monkeys in a few weeks, though in anthropoids it may persist longer. In man it is permanent. Slight sensory changes are described.
4. *Disease in Man.*—
   a. *Irritative*, e.g., Jacksonian epilepsy. Convulsions start in a particular group of muscles and spread in a definite order. It is often found that corresponding area in cortex is being irritated, e.g., by spicule of bone.
   b. *Destructive*, such as follows a hæmorrhage. There is paralysis of opposite side of body, of upper motor neuron type.

[Apraxia.—Inability to perform some voluntary movement in response to a command, though there is no actual paralysis and patient understands what is required. The movement may be carried out by accident or under influence of emotion. Occurs commonly in left arm in right hemiplegia, but rarely in left hemiplegia. In such cases lesion is cortical. Centres which consciously initiate voluntary movement are therefore confined to left side of cortex in right-handed people, probably in precentral convolution or anterior to it.

Lesion of anterior part of corpus callosum causes apraxia of left arm.]

Frontal Eye Area.—Concerned with co-ordination of eye movements. In man and higher monkeys it is separated from precentral area by a strip of inexcitable cortex.

SENSORY AREAS.—

1. *Tactile, Kinæsthetic, or Body-sense Area.*—In ascending parietal convolution behind fissure of Rolando.
2. *Auditory Area.*—In superior temporal convolution and island of Reil. (*See* p. 209.)
3. *Taste and Smell Area.*—In uncinate and hippocampal regions. (*See* p. 200.)
4. *Visual Area.*—(*a*) *Visuo-sensory* on inner surface of occipital lobe; (*b*) *Visuo-psychic* on outer surface of occipital lobe. (*See* pp. 225, 226.)

Body-sense Area.—Concerned with purely sensory functions (sensory representation of leg, trunk, arm, face, in the same order as in motor area)—i.e., muscle sense, pressure, temperature, appreciation of passive movements, tactile discrimination, appreciation of size,

weight, form, and texture of an object, including stereognosis.

Evidence.—

1. Removal in apes: no obvious effect.
2. Stimulation in animals at first causes no movement, but with stronger stimuli reflex muscular movement occurs, though latent period is longer than when precentral area is stimulated.
3. Stimulation of this area of cortex in conscious patients gave rise to localized sensations of numbness and tingling. Incision in the area was quite painless, but gave rise to some numbness to all forms of sensation in hand (Cushing).
4. *Disease in man.*—Lesions of postcentral region showed more or less marked hemi-anæsthesia, without any paralysis. Anæsthesia was especially for tactile discrimination, most positive sign being astereognosis; only partial loss of temperature sense occurred, and pain sense was hardly affected.
5. *Myelination method* shows that mesial fillet path ends in this region.

[Slight loss of sensation may be due to lesion of precentral gyrus, much more if combined with lesion of postcentral gyrus. There is some loss with lesion of parietal convolution just behind postcentral gyrus and angular gyrus. Lesions of precentral cortex affect especially spatial sense, those of postcentral region judgements of weight and size. Lesion in angular gyrus affects tactile or perhaps temperature sense.]

SPEECH CENTRES.—Older writers describe three or four, all in left brain. Some modern writers only recognize one.

MOTOR APHASIA.—Loss of power of speech, though vocal organs and muscles of phonation are normal. Speech centre in cortex is a memory centre for combination of movements necessary to form appropriate words. According to Broca, it is situated in 3rd left frontal convolution. Denied by Marie, who maintains that clinical experience does not fit the theory.

SENSORY APHASIA.—Inability to understand spoken or written language. Probably due to damage of a large diffuse centre in left temporoparietal region. There was supposed to be a centre for spoken language in the superior and middle temporal convolutions, for written language in the angular gyrus; but this does not accord with results of disease.

Localization of Function in Cerebrum—Speech, *continued.*

Marie considers all patients with aphasia are mentally defective.

ASSOCIATION AREAS.—Besides the motor and sensory areas of the cortex are much larger areas, 'silent areas'. Probably centres of complex activities.

Evidence.—(1) Fibres of association areas are myelinated later than those of sensory areas, so presumably acquire their function later; (2) They have no projection fibres linking them up with underlying parts of central nervous system, but show connections with one another.

FRONTAL CORTEX.—

a. Extirpation of this part of cortex in dogs results in changes in character.

b. Tumours and injuries involving this region in man are frequently, though not invariably, accompanied by changes in character.

c. In idiots this area may be under-developed, and atrophy of it has been found in insanity.

POSTERIOR PART OF PARIETO-OCCIPITAL REGION is probably concerned with memory of sense impressions.

[*Evidence.*—Disease of this area has been found associated with incoherence of ideas. If destroyed on left side, patient cannot identify objects shown him.]

Some observers contend that the whole cortex is to some extent concerned with higher mental processes.

CONDITIONED REFLEXES.—If a dog is trained to associate a sound, an object shown, or other stimulus, with feeding, eventually the stimulus will cause salivation, apart from feeding. This reflex becomes very constant, unless the animal is purposely 'muddled'. Does not occur after extirpation of whole cortex, or of the visual, auditory, or other area involved. May be used to show that dogs cannot distinguish colours; that their range of audition is much higher than human; that destruction of part of cochlea gives results in accordance with Helmholtz theory. Puppies fed solely on milk, and a conditioned reflex developed, show no salivation when shown meat, even if allowed to smell. Shows non-inheritance of an acquired character.

Basal Ganglia.—

OPTIC THALAMUS.—Cell station for all sensory tracts, receiving fibres of optic tract, mesial fillet, and those from

dentate nucleus of opposite side of cerebellum. From it, fibres pass to cerebral cortex. Fibres also run from cerebral cortex to lateral nucleus of thalamus.

FUNCTIONS OF THALAMUS.—

1. Relay station for all sensory impressions.
2. Seat of primitive sensations—e.g., touch, temperature, and especially pain (Head and Holmes). It is concerned with degrees of sensation, while cortex tends to inhibit these sensations.
   Evidence.—(*a*) Lesion of postcentral convolution does not cause complete anæsthesia to touch, pain, and temperature, while one of thalamus does, and also blindness of same half of each retina; (*b*) Damage to lateral nucleus causes pain sense to become keener.
3. *Primary centre for emotional expression.* Normally it is under control of cortex, but in disease or injury of cortico-thalamic fibres there may be paroxysmal attacks of laughing and crying. In disease of thalamus there may be automatic screaming, forced laughter and crying, etc. When pyramidal tract is injured, as in hemiplegia, voluntary movements of face are impaired, emotional ones are not; in damage to thalamus, the reverse holds.

CORPUS STRIATUM.—Made up of: (1) Caudate nucleus; (2) Internal capsule; (3) Lenticular nucleus; (4) External capsule.

LENTICULAR NUCLEUS.—Connected with red nucleus and thus with rubrospinal tract.

Functions.—(1) Production and control of automatic movements; (2) Maintenance of muscles in condition for prompt performance of automatic acts.

Evidence.—Atrophy of this region results in symptoms of paralysis agitans—i.e., increased tone, tremors, and suppression of automatic associated movements (Hunt).

CAUDATE NUCLEUS.—Said to inhibit action of lenticular nucleus.

Meyer and Barbour suggest that anterior part of corpus striatum represents a heat-regulating centre. Marked changes of temperature follow lesions of caudate nucleus.

INTERNAL CAPSULE (*Fig.* 16).—Three parts: (1) Anterior limb; (2) Genu; (3) Posterior limb.

Corpus Striatum—Internal Capsule, *continued.*

1. *Anterior limb* contains from before backwards :—
   - *a.* Fronto-pontic fibres.
   - *b.* Pyramidal fibres for eye and head.
2. *Genu* contains : Pyramidal fibres for mouth and tongue.
3. *Posterior limb* contains :—
   - *a.* In the anterior two-thirds : Fibres for arm, trunk, and leg from before backwards.
   - *b.* In the posterior third : (i) Temporo-pontic fibres ; (ii) Thalamo-cortical fibres ; (iii) Auditory radiation ; (iv) Optic radiation.

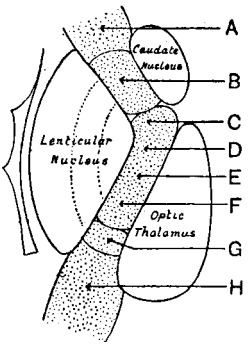


Fig. 16.—Diagram of internal capsule. A, Sensory fibres ; B, Fronto-pontic fibres ; C–F, Pyramidal fibres ; C, Head and eye ; D, Arm ; E, Trunk ; F, Leg ; G, Temporo-pontic fibres ; H, Optic radiations.

PHYSIOLOGY OF SLEEP.

Conditions of Various Systems during Sleep.—

1. NERVOUS.—Partial or complete loss of consciousness, power of making voluntary movements being first lost, auditory sensations lasting longest.
2. RESPIRATORY.—Respirations become slower and deeper. Costal respiration predominates over abdominal. Snoring, from relaxation of soft palate.
3. CIRCULATORY.—Pulse becomes slower. Blood-pressure falls slightly. Mosso has found in patients with a trephine hole in skull that volume of brain diminishes during sleep while that of limbs increases, presumably owing to vasodilatation of these regions and more blood passing to them, while less goes to the brain. Shepherd finds contradictory results.
4. URINARY.—Amount of urine diminished.
5. GLANDULAR.—Secretions are all diminished, with probable exception of digestive ones.
6. METABOLISM.—Physiological oxidations appear to be diminished.

Intensity of Sleep.—Estimated by intensity of sensory stimulus necessary to cause awakening. Reaches a maximum in about one hour, and from about third hour onwards it is very slight.

[There may be a second increase in intensity about fourth or fifth hour. In children of four years, Czerny found a marked increase towards morning. There are large individual variations.]

Amount Required.—7 to 8 hours; some do with 5. Children need 10; babies 16 to 20. Insomnia prolonged for weeks may lead to sudden collapse.

Theories of Causation of Sleep.—

1. TOXIN THEORIES.—Assumption is that acid waste products, or toxins, are formed during waking hours and finally accumulate in sufficient quantities to cause sleep.

   EVIDENCE.—Dogs kept awake for 30 to 300 hours show evidence of a toxin by changes in cortical cells of frontal region. Injection of their blood or cerebro-spinal fluid into 4th ventricle of another animal produces a condition of somnolence and similar changes in cortical cells (Piéron).

2. NEURON THEORY.—Duval, Cajal, and others, assuming that dendrons are contractile, suppose that sleep is caused mechanically by retraction of these dendrons and breaking of synapse.

3. ANÆMIA THEORIES.—Experimental interference with blood-supply to brain brings on unconsciousness almost at once.

4. HOWELL'S THEORY.—Supposes rhythmical loss of tone in vasomotor centre due to fatigue from continued activity, with diminished vasoconstriction of the body blood-vessels (especially of skin), and a consequent poorer blood-supply to the brain. Cessation of normal stimuli also diminishes activity of this centre.

   Hill advocates a similar view, but considers the control is chiefly through the splanchnic vessels. This probably explains drowsiness following a heavy meal.

Sleep Centre.—It has been suggested that there is a sleep centre near the 3rd ventricle. When this region is diseased in man (e.g., tumours, encephalitis lethargica), there is persistent drowsiness.

BRAIN-STEM.

Grey Matter of Brain-stem.—

NUCLEI OF CRANIAL NERVES (*Fig.* 17).—

MOTOR NUCLEI.—

1. Inner column, close to mid-line, continuous with base of horns, giving rise to 12th, 6th, 4th, and 3rd cranial nerves.
2. Outer column, continuous with head of anterior horn, giving rise to 10th, 9th, 7th, and 5th nerves.

SENSORY NUCLEI.—

1. Inner column, continuous with base of posterior horns, forms nuclei of 9th and 10th nerves.
2. Outer column, continuous with apex of posterior horns, forms nucleus of 5th nerve.

Nuclei of 8th nerve are at junction of pons and medulla (*see* p. 208).

OTHER MASSES OF GREY MATTER IN BRAIN-STEM (*Figs.* 18–21).—

IN MEDULLA.—

Nucleus gracilis and *nucleus cuneatus* in which posterior columns end. From them, fibres pass as: (1) Internal arcuate fibres to form the fillet; (2)

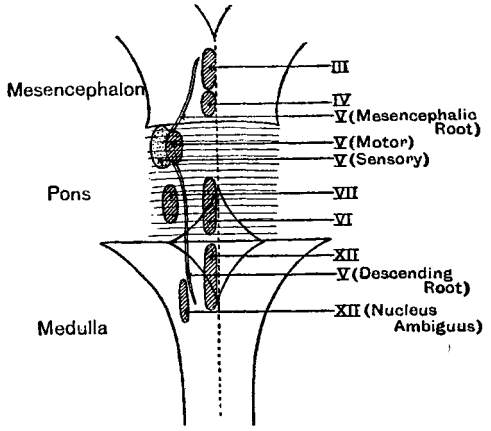


Fig. 17.—Cranial nerve nuclei in brain-stem.

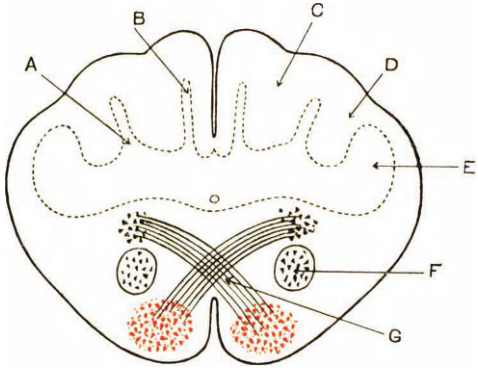


Fig. 18.—Diagram of lower medulla. **A**, Nucleus cuneatus; **B**, Nucleus gracilis; **C**, Column of Goll; **D**, Column of Burdach; **E**, Gelatinous substance of Rolando; **F**, Anterior horn; **G**, Decussation of pyramids.

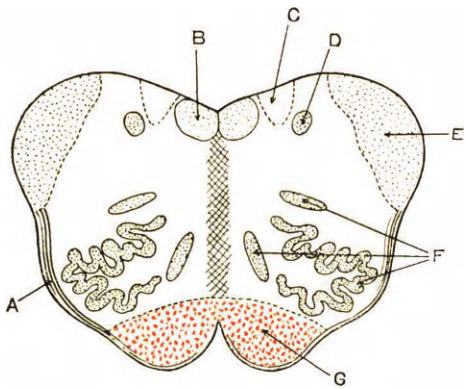


Fig. 19.—Diagram of middle medulla. **A** Arcuate fibres; **B**, Hypoglossal nucleus; **C**, Vagus nucleus; **D**, Funiculus solitarius; **E**, Inferior cerebellar peduncle; **F**, Inferior olive and accessory olives; **G**, Pyramidal fibres.

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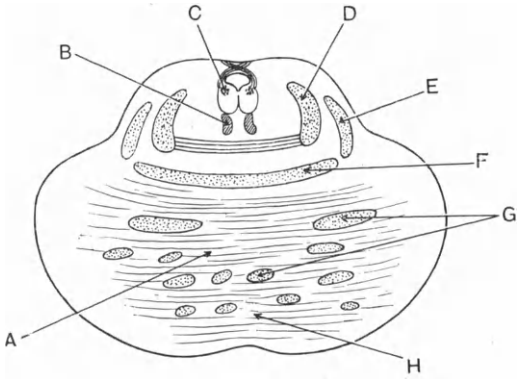

Fig. 20.—Diagram of upper pons. **A**, Nuclei pontis; **B**, Posterior longitudinal fasciculus; **C**, IVth nucleus and nerve; **D**, Superior cerebellar peduncle; **E**, Lateral fillet; **F**, Mesial fillet; **G**, Pyramidal fibres; **H**, Middle cerebellar peduncle.

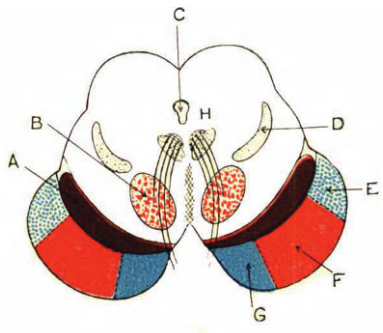

Fig. 21.—Diagram of mesencephalon. **A**, Substantia nigra; **B**, Red nucleus; **C**, Aqueduct of Sylvius; **D**, Mesial fillet; **E**, Temporo-pontic fibres; **F**, Pyramidal fibres; **G**, Fronto-pontic fibres; **H**, IIIrd nucleus and nerve.

Dorsal external arcuate fibres to cerebellum by inferior peduncle of same side; (3) Ventral external arcuate fibres to cerebellum by inferior peduncle of opposite side.

Olivary body, from which fibres pass chiefly to opposite side of cerebellum, a few to same side. Function unknown.

IN PONS.—

Superior olive, similar to, but smaller than, medullary olive. Concerned with co-ordination of eye movements with auditory impressions.

Deiters' nucleus.

Nuclei pontis. Receive fibres from frontal cortex, and from pyramids. Fibres pass to vermis by middle cerebellar peduncle of opposite side. Thus cerebellar cortex of one side is connected with cerebral cortex of opposite side.

IN MID-BRAIN.—

Red nucleus, on ventral side of Sylvian aqueduct.

Substantia nigra, dividing each crus into a dorsal part or tegmentum, and a ventral part or crusta. Function unknown.

Corpora quadrigemina.

Tracts of Brain-stem (*Figs.* 18–21).—

ASCENDING TRACTS.—

1. MESIAL FILLET.—Fibres originate in nucleus gracilis and cuneatus, cross deep in medulla, forming with fibres of opposite side the *sensory decussation*. They are joined by the spino-thalamic tract, forming the mesial fillet, which is joined in the pons by the lateral fillet from nuclei of cochlear division of 8th nerve. Mesial fillet passes up in tegmentum, receiving fibres from sensory nuclei of cranial nerves, to end in anterior corpus quadrigeminum and optic thalamus. From the thalamus, fibres pass to post-Rolandic area of the cortex.

   Lateral fillet ends in posterior corpus quadrigeminum and internal geniculate body.

2. CEREBELLAR PATHS.—*See* p. 180.

DESCENDING TRACTS ORIGINATING IN BRAIN-STEM.—

1. RUBRO-SPINAL.—*See* p. 169.
2. POSTERIOR LONGITUDINAL BUNDLE.—Extends from thalamus through mid-brain, pons, and medulla, and

Tracts of Brain-stem—Descending, *continued.*

becomes continuous with tract of Löwenthal. Fibres are chiefly descending, but a few are ascending. Fibres arise chiefly from nucleus of posterior longitudinal bundle at side of 3rd ventricle, Deiters' nucleus, sensory nucleus of 5th nerve, cells in formatio reticularis of mid-brain, pons, and medulla, and superior olive. Collateral fibres are sent to nuclei of 3rd, 4th, and 6th nerves.

Function.—Mainly to co-ordinate movements of eye muscles by association of nuclei of 3rd, 4th, and 6th nerves.

3. VENTRAL LONGITUDINAL BUNDLE.—Lies on ventral and lateral aspects of posterior longitudinal bundle. Arises in anterior corpus quadrigeminum of opposite side, fibres crossing in Meynert's commissure.

Medullary Centres.—In floor of fourth ventricle are centres of certain reflex actions of vital importance :—

1. RESPIRATORY CENTRE, on either side of mid-line at calamus scriptorius.
2. VASOMOTOR OR VASOCONSTRICTOR CENTRE, just above respiratory centre.
3. CARDIO-INHIBITORY AND CARDIO-ACCELERATOR CENTRE.
4. SWEAT CENTRE.
5. SWALLOWING CENTRE.
6. VOMITING CENTRE.

(For function of these centres, *see* the various systems.)

SECTION OF BRAIN ABOVE MEDULLA.—Animal lives, respiration and blood-pressure remaining normal.

DESTRUCTION OF MEDULLA.—Rapid death from cessation of respiration, or from loss of tone in arteries with rapid fall in blood-pressure.

CHAPTER XIX.

AUTONOMIC NERVOUS SYSTEM.

The part of the nervous system which regulates the viscera, blood-vessels, etc., which are controlled by a self-regulating mechanism, not by the will.

Most of these organs have a double nerve-supply—from the sympathetic and the parasympathetic. The functions of the two are antagonistic. The autonomic system thus comprises :—

1. **True Sympathetic System.**—Arises from 1st dorsal to 4th or 5th lumbar, passing via sympathetic chain.

2. **Parasympathetic System.**—Includes : (*a*) Fibres of 3rd nerve passing to ciliary ganglion ; (*b*) Visceral branches of 7th, 9th, and 10th cranial nerves ; (*c*) Pelvic visceral nerves from 2nd, 3rd, and 4th sacral roots to bladder, colon, rectum, anus, and external genital organs.

1. TRUE SYMPATHETIC SYSTEM.

Structure.—

a. WHITE RAMI COMMUNICANTES. — Present in all thoracic and either 4 or 5 lumbar segments. They arise in lateral horn of spinal cord, and pass out in anterior nerve-roots to enter a ganglion of the sympathetic chain. They are medullated.

b. SYMPATHETIC CHAIN OF GANGLIA.—Lie one on each side of vertebral column. In cervical region, there are 3 pairs of ganglia ; in thoracic region, 11 or 12 pairs ; in lumbar region, 5 pairs; in sacral region, 4 pairs. (In the dog the four upper thoracic ganglia are fused into one, the stellate ganglion.) These ganglia do not originate impulses, nor are they centres for reflexes. A fibre often passes up or down sympathetic cord for some distance before terminating in a synapse with a ganglion cell.

c. GREY RAMI COMMUNICANTES.—Post-ganglionic fibres. Pass from sympathetic ganglia to spinal nerves, and are distributed in these to blood-vessels, sweat glands, hairs

True Sympathetic System—Structure, *continued.*

of part, or to viscera. They may or may not return to the same nerve from which the white ramus communicans arose. Sometimes they pass directly to a peri-arterial plexus.

d. PERIPHERAL GANGLIA.—Such are the semilunar ganglia of the solar plexus, the superior mesenteric, inferior mesenteric or hypogastric, and cardiac ganglia, and the terminal ganglia—e.g., those in the walls of the intestines in Auerbach's and Meissner's plexuses. In some cases white fibres pass through the sympathetic chain to a cell station in one of these ganglia, such fibres being pre-ganglionic and medullated—e.g., splanchnic nerves pass from 6th–12th thoracic segments to the semilunar ganglia. (*Fig.* 22.)

Methods of Studying Sympathetic System.—

1. Electrical stimulation of sympathetic nerves, watching effects.
2. Painting nicotine on ganglia, thus paralysing synapses, while not affecting axons.
3. Section of sympathetic nerves.

   If nerve is stimulated a few days after section, no response occurs, owing to degeneration of the fibres, until the electrodes are moved to post-ganglionic fibres.

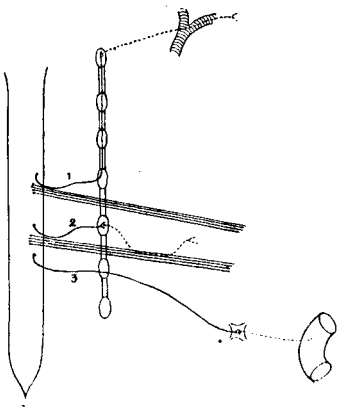

Fig. 22.—Diagram of sympathetic nerves. Shows: (1) Pre-ganglionic fibre issuing from upper thoracic region of spinal cord, running to superior cervical ganglion by way of cervical sympathetic; post-ganglionic fibre distributed by peri-arterial plexus to eye. (2) Pre-ganglionic fibre running by white ramus communicans to sympathetic ganglion; post-ganglionic fibre returns to somatic nerve by grey ramus communicans. (3) Splanchnic nerve: pre-ganglionic fibre runs through sympathetic chain to solar plexus.

Cervical Sympathetic.—No white rami communicantes in cervical region. Fibres for head and neck, emerging from upper four or five thoracic nerves, enter corresponding ganglia, and then run up in cervical cord to one of the three cervical ganglia, usually the superior one, where a synapse is formed. Usually fibres pass through about four ganglia before reaching a synapse. Post-ganglionic fibres either join somatic nerves or run in walls of large arteries to their destination.

EFFECTS OF STIMULATION OF CERVICAL SYMPATHETIC (cf. effects of fright).—

1. Dilatation of pupil, retraction of nictitating membrane, and protrusion of eye (1st and 2nd thoracic roots).
2. Vasoconstriction (2nd, 3rd, and 4th thoracic roots).
3. Increased sweating.
4. Pilomotor effect—i.e., erection of hairs.
5. Cardiac acceleration (2nd, 3rd, and 4th thoracic).
6. A few drops of viscid saliva secreted.

Sympathetic to the Limbs.—

UPPER LIMB.—Fibres arise in 4th to 10th thoracic nerves, having their cell station in stellate ganglion.

LOWER LIMB.—Fibres arise in last two thoracic and upper two or three lumbar nerves, having cell stations in last two lumbar and first sacral ganglia.

FUNCTION.—(1) Vasoconstriction ; (2) Increased secretion of sweat ; (3) Erection of hairs (pilomotor).

Cardiac Fibres.—Arise from 2nd, 3rd, and 4th thoracic nerves, having cell station in stellate and cervical ganglia.

FUNCTION.—To increase rate and strength of heart-beat.

Splanchnic Nerves.—Emerge in lower 5 or 6 thoracic nerves and upper 3 or 4 lumbar nerves, pass through sympathetic chain still as pre-ganglionic fibres, and finally form synapses in semilunar and superior mesenteric ganglia.

FUNCTION.—(1) Vasoconstriction of blood-vessels of viscera ; (2) Inhibition of movement of alimentary canal, but contraction of sphincters.

Pelvic Sympathetic.—Fibres arise in last thoracic and upper four lumbar nerve-roots, and have cell station in inferior mesenteric ganglion.

FUNCTION.—(1) Vasoconstriction ; (2) Motor to circular muscle of bladder, inhibitory to longitudinal muscle of bladder ; (3) Motor and inhibitory of uterus and vagina.

True Sympathetic System, *continued.*

Deep Afferents.—There are a few afferent fibres in the sympathetic system. About one-tenth of splanchnic and hypogastric fibres are afferent, and they transmit sensations which may or may not be painful. Sensation in a viscus is slight, localization vague, and there is inability to detect heat, cold, pain, or touch; but viscera are sensitive to distention or powerful muscular contractions (e.g., colic). The mesentery is very sensitive to dragging or stretching.

PROOFS OF EXISTENCE OF DEEP AFFERENTS IN SYMPATHETIC SYSTEM.—

1. *Referred skin tenderness.* When a viscus is inflamed, there may be tenderness of an area of skin supplied by same nerve—e.g., appendix is supplied by 11th and 12th thoracic nerves, and skin tenderness is in area supplied by these nerves, i.e., just above Poupart's ligament.
2. In severe visceral pain, relief may be afforded by division of the appropriate nerve-roots—e.g., in gastric crises of locomotor ataxia, where severe pain and vomiting occur. The vomiting is not relieved, because the vagus is the nerve concerned with this symptom.

2. PARASYMPATHETIC SYSTEM.

1. **Cranial.**—

a. Through 3rd nerve to cell station in ciliary ganglion, thence in short ciliary nerves to ciliary and sphincter pupillæ muscles of eye.

FUNCTION.—Contraction of pupil.

b. Through 7th and 9th nerves. Cell station is in the sphenopalatine, otic, and submaxillary ganglia. Some fibres enter the 5th nerve and are distributed with it.

FUNCTION.—Vasodilatation of mucous membrane of nose and mouth. Chorda tympani is vasodilator and secreto-motor to submaxillary gland, lesser superficial petrosal and auriculotemporal to parotid gland.

c. Through vagus. Cell station not definite.

FUNCTION.—(i) Motor to œsophagus, stomach, and small intestines; (ii) Motor to bronchial muscle; (iii) Inhibitory to heart (auricle); (iv) Secretory to bronchial, gastric, and pancreatic glands.

2. **Sacral.**—Fibres arise in 2–4 sacral nerve-roots, and pass straight to pelvic plexus, without connecting with sympathetic ganglia. Cell stations are in pelvic plexus or near organs supplied.

   FUNCTION.—(i) Vasodilatation of external genitals (= nervi erigentes), and rectum and anus; (ii) Motor to colon, rectum and anus, and bladder (longitudinal coat).

CHAPTER XX.

SMELL AND TASTE.

SMELL.

End-organs.—In man, situated in area about the size of a postage stamp in each nostril, in mucous membrane of roof of nose over septum and superior turbinal bone. In most mammals it is much larger.

HISTOLOGY.—

Supporting columnar epithelial cells.

Olfactory cells—very slender cells ending peripherally in hair-like processes passing through limiting membrane into nose. Only instance in body of primitive arrangement of epithelial cell taking place of nerve-cell, and giving off fibres (olfactory nerves).

Path for Sensation of Smell.—

OLFACTORY NERVES.—Fibres are non-medullated. They pass up through cribriform plate of ethmoid to olfactory bulb.

OLFACTORY BULB.—Shows *mitral* cells, dendrons of which form synapses with olfactory nerves known as glomeruli.

OLFACTORY TRACTS.—Fibres are medullated. They pass back from mitral cells of olfactory bulb to olfactory area, where tracts unite with base of cerebrum.

Cortical Representation.—Appears to be in hippocampal region, especially its distal portion, the *uncus*.

[EVIDENCE.—

1. These areas are highly developed in animals with keen sense of smell, e.g., dog, atrophied in those who have only rudimentary or no sense of smell.
2. Electrical stimulation leads to reflex sniffing (Ferrier).
3. Destruction of tips of temporal lobes results in loss of taste and smell.]

After head injury, sense of smell may be lost; probably due to rupture of some filaments of olfactory nerve.

Olfactory Stimulus.—

1. Must reach nose as moving vapour.

PROOFS.—(*a*) If breath is held, no odour perceived; (*b*) If nose is completely filled with rose water, scent is not perceived.

2. Sense of smell is very delicate. Only very minute amounts of certain substances are necessary to give rise to sense of smell: e.g., $\frac{1}{4\,000\,000\,000}$ mgrm. of mercaptan in 50 c.c. of air is perceived, whereas 1 mgrm. can hardly be detected chemically.

[**Olfactometer** is used to determine relative delicacy of olfactory sense in human beings. Consists of graduated inner smelling tube and outer cylinder, and between the two is solution of known strength.]

Theory as to Mechanism of Smelling.—Chemical particles in the form of vapour are wafted to olfactory area, dissolved, and stimulate hair processes of olfactory cells. They may reach olfactory area by anterior nares, as in sniffing, or by posterior nares.

According to Müller's law, each odour acts on a particular olfactory cell or cells.

Evidence.—(1) Some people are unable to detect certain odours, e.g., mignonette or cyanides; in them, appropriate olfactory cells are probably absent. (2) Sense of smell for one odour may be fatigued without that for other odours being affected.

Classification of Odours.—No satisfactory classification exists, and it seems impossible to recognize any fundamental odour sensations.]

TASTE.

End-organs.—Taste-buds occur in stratified epithelium of *posterior third only* of tongue, especially in circumvallate papillæ, also on posterior surface of epiglottis, parts of pharynx, and soft palate. They are oval bodies, the central cells of which end in a hair-like process.

Result of Section of Glossopharyngeal Nerve.—Loss of sensation in back of tongue and degeneration of taste-buds. Taste-buds are not essential for taste, since there are none in anterior two-thirds of tongue.

Path for Sensation of Taste.—

1. FROM ANTERIOR TWO-THIRDS OF TONGUE.—Chorda tympani; geniculate ganglion of 7th nerve; pars intermedia of Wrisberg; funiculus solitarius in medulla.
2. FROM POSTERIOR THIRD OF TONGUE.—By glossopharyngeal nerve, having cell station in petrosal ganglion, and from there to funiculus solitarius of medulla.
3. FROM PALATE.—Great superficial petrosal nerve; geniculate ganglion of 7th nerve; funiculus solitarius.

Alternative theory is that all impulses of taste pass through Gasserian ganglion; but removal of Gasserian ganglion does not cause loss of taste in man.

Classification of Tastes.—Five primary true tastes: (1) Sweet; (2) Bitter; (3) Acid or sour; (4) Salt; (5) Metallic. Most sensations known as tastes are really flavours, and are appreciated by sense of smell, being lost during a cold in the head; the five primary tastes are not lost.

Clinical Testing of Taste.—Patient protrudes tongue, and drops of solutions of sugar, salt, quinine, and acetic acid are applied to it in turn with a glass rod. He must decide what the taste is without withdrawing the tongue.

Mechanism of Taste.—Probably each of the five sensations of taste stimulates a separate set of nerve-fibres in tongue.

EVIDENCE.—

a. Sweet is tasted better at front of tongue, bitter at back. Electrical stimulation of fungiform papillæ gives rise to an acid-sweet taste, of back of tongue to a bitter-metallic taste.

b. Certain substances give rise to different sensations according to whether they are placed on front or back of tongue—e.g., magnesium sulphate is salty in front, bitter behind.

c. Chewing the plant *Gymnema silvestre* abolishes taste for sweet and later for bitter, while leaving other tastes unaffected.

[OEHRWALL'S EXPERIMENT.—A number of fungiform papillæ were stimulated, to find out fundamental taste of each. Of 125, 27 gave no reaction; 60 gave taste sensation to all stimuli; 4 to sweet and bitter; 7 to bitter and acid; 12 to sweet and acid; 12 to only acid; 3 to only sweet. None gave only bitter.

Threshold Stimulus.—Determined by finding minimal concentration of a substance which will just give rise to sensation of taste. Delicacy of sense of taste is influenced by temperature, being destroyed by very hot or very cold solutions. Tongue is most sensitive to bitter substances, least to salty ones.

Function.—Taste is the effective stimulus (with smell and sight) for reflex secretion of salivary and gastric glands.]

CHAPTER XXI.

HEARING AND EQUILIBRATION.

EXTERNAL EAR.

Consists of pinna and external auditory meatus.

Function of Pinna.—Slight in man.

1. To collect sound waves and reflect them into meatus.
2. To locate sounds. We locate a sound by turning the head until the sound is equally loud in both ears.

External Auditory Meatus.—About 1 in. long. In its walls are ceruminous glands, secreting an oily fluid which keeps membrana tympani moist and hinders entry of insects or particles of dirt.

DIRECTION.—At first upwards and backwards, then forwards and inwards to end at tympanic membrane.

TYMPANIC MEMBRANE.

A tightly stretched fibro-elastic membrane sloping from above downwards and inwards.

Structure.—(1) Stratified epithelium on outside; (2) Membrana propria, consisting of fibrous and elastic tissue, in the middle; (3) Columnar epithelium on inside. Middle layer is deficient in upper part of the membrane, this area being known as the *membrana flaccida* or *Shrapnell's membrane.*

In the centre of the membrane is a depression, the umbo. Fibres of the membrana propria are arranged partly circularly, and partly in lines radiating from the umbo.

MIDDLE EAR OR TYMPANUM.

An air-containing cavity, the air being replaced from the Eustachian tube as it is absorbed.

Boundaries.—The following features should be noted.

INNER WALL.—Shows :—

a. Fenestra ovalis, a foramen covered in by a very thin layer of hyaline cartilage, lying just above and behind the promontory.

Boundaries of Middle Ear—Inner Wall, *continued.*

b. *Fenestra rotunda*, closed by membrane, lying below and behind the promontory.

POSTERIORLY.—Shows :—

a. *Aditus*, a passage leading from upper part of tympanum to mastoid antrum.

On inner wall of aditus are 2 bulges : (1) For external semicircular canal ; (2) For facial nerve, the aqueductus Fallopii.

b. Bone separating middle ear from mastoid antrum. Jutting upwards and forwards from it is the *pyramid*, containing fibres of stapedius muscle.

ANTERIORLY.—Shows a double canal :—

a. Upper canal contains tensor tympani muscle.

b. Lower canal, the *Eustachian tube*, connects middle ear with nasopharynx. Lined with columnar ciliated epithelium, cilia working towards nasopharynx, tending to prevent ascent of foreign particles from nasopharynx to middle ear.

Functions of Eustachian Tube.—To equalize pressure on the two sides of tympanic membrane. Normally pharyngeal opening is closed, but opens during swallowing. If tube is permanently closed, air in tympanum is absorbed, drum in-drawn, ossicles are locked, and chronic hopeless deafness results.

Contents.—(1) Air ; (2) Ossicles ; (3) Tensor tympani muscle supplied by 5th nerve, and stapedius muscle supplied by 7th.

OSSICLES.—

1. MALLEUS.—

a. Large rounded head, articulating with incus. The tensor tympani is inserted into the neck.

b. Long process or *manubrium*, attached to tympanic membrane.

c. Short process, pressing against upper edge of tympanic membrane.

d. *Processus gracilis*, passing forwards, attached to anterior wall of tympanum by anterior ligament. It is also attached to the walls of the cavity by external, posterior, and superior ligaments.

2. INCUS (anvil-shaped).—

a. *Body*, articulating with head of malleus.

b. *Short process*, attached by a ligament to posterior wall of tympanic cavity.

c. Long process, running down in same plane as handle of malleus, and turning in at tip to articulate with stapes.

3. STAPES (stirrup-shaped).—
   a. Head, articulating with long process of incus.
   b. Neck, serving for insertion of stapedius muscle.
   c. Foot-piece, oval-shaped and attached to margins of fenestra ovalis by a membrane.

FUNCTIONS OF OSSICLES.—
1. To transmit vibrations from the large tympanic membrane to the small fenestra ovalis, thus increasing power.
2. To modify vibrations by diminishing their amplitude and thus increasing their force. Combined effect increases force of vibrations sixty-fold, thus overcoming inertia of labyrinth.

MODE OF ACTION OF OSSICLES.—
They swing as a whole on an axis formed by processus gracilis of malleus and short process of incus. The bones act like a bent lever whose fulcrum is at joint between stapes and incus.

[FUNCTIONS OF STAPEDIUS AND TENSOR TYMPANI MUSCLES.—
1. MÜLLER'S VIEW.—A protective mechanism to membranes by increasing the tension, and thus limiting the amplitude of their vibrations. The muscles may also protect internal ear from very loud noises.
2. MACH'S VIEW.—Concerned in reflex contraction to sounds, adjusting membrane to better reception of sound vibrations. Probably correct.]

INTERNAL EAR.

Structure.—Made up of: (1) *Osseous labyrinth* containing a fluid, perilymph; (2) *Membranous labyrinth*, floating in perilymph, and containing a fluid, endolymph.

OSSEOUS LABYRINTH.—Consists of:—
1. COCHLEA, anteriorly.
2. VESTIBULE, containing membranous bags, the saccule, ductus endolymphaticus, and utricle.
3. SEMICIRCULAR CANALS, posteriorly.

STRUCTURE OF COCHLEA.—
1. Central bony *modiolus*, apex of which points outwards and forwards.
2. Bony tube taking $2\frac{1}{2}$ turns round modiolus in spiral manner.

Structure of Cochlea, *continued.*

3. *Spiral lamina*, a bony spur projecting from modiolus into canal. Just beneath it is the *spiral ganglion*, consisting of bipolar nerve-cells; one fibre ends round sensory cells of the organ of Corti; the other runs in the auditory nerve.

CROSS-SECTION OF TUBE.—Shows :—

1. *Scala vestibuli*, or upper canal, containing perilymph, and ending below in vestibule.
2. *Reissner's membrane.*
3. *Canalis cochleæ*, containing the organ of Corti and endolymph, which enters by canalis reuniens from saccule.
4. *Basilar membrane*, consisting of elastic fibres radiating outwards from lamina spiralis to outer wall of canal. About 24,000 fibres, those at apex being longer than those at base.
5. *Scala tympani*, ending below at foramen rotundum. It and the scala vestibuli communicate at apex of cochlea at the *helicotrema.*

STRUCTURE OF ORGAN OF CORTI.—

1. Two rows of *rods of Corti:* (*a*) Inner, resembling fractured ulna—about 5600; (*b*) Outer, like head and neck of swan—about 3800.
2. *Hair-cells*, one row on inner side of rods of Corti, 3 to 5 rows on outer side, connected with nerves which run to bipolar cells of spiral ganglion.
3. *Supporting cells of Deiters.*
4. *Membrana tectoria*, which lies over and is probably in contact with hairs of hair-cells.

Mechanism of Hearing.—

TRANSMISSION OF SOUNDS.—Vibration in air in external auditory meatus; tympanic membrane and ossicles respond, and vibrations are set up in perilymph. They pass up scala vestibuli, down scala tympani, and affect membranous cochlea.

END-ORGAN OF HEARING.—The organ of Corti, especially the hair-cells. Rods of Corti are absent in birds, so have apparently nothing to do with hearing.

THEORIES OF HEARING.—In historical order: (1) Helmholtz piano theory. (2) Rutherford telephone theory. (3) Waller pressure pattern. (4) Gray's modification of Helmholtz theory; this seems very probable. (5) Keith and Wrightson's modification of Rutherford and Waller theory.

HELMHOLTZ PIANO THEORY.—Each fibre of the basilar membrane vibrates in response to a certain tone as do exposed strings of a piano when particular notes are sung. Longer fibres correspond to lower notes. Vibrating fibre affects corresponding hair-cells, and impulse is carried by cochlear nerve to brain.

GRAY'S MODIFICATION OF HELMHOLTZ THEORY.—If one fibre of the basilar membrane rises, it must draw its neighbouring fibres up also to a greater or lesser extent. Hence, when a note is sounded, several fibres of membrane are set into vibration, but the fibre corresponding to the note vibrates to a maximum, and we are conscious of that note only. Vibrations are transmitted to the hair-cells, crushed against the tectorial membrane, and so a message is sent along the particular nerve-fibre concerned.

[*Evidence supporting Gray-Helmholtz Theory.*—

1. In mammals and birds, where cochlea is flat, there is still a difference in length of fibres of basilar membrane.
2. In boiler makers there is liability to deafness to high notes, and in a few of these cases degeneration of fibres at base of cochlea has been found post mortem.
3. Guinea-pigs were exposed to noise of a siren for some time before death, and cochlea examined, with the following results: siren high-pitched, degeneration at base of cochlea; siren low-pitched, degeneration at apex. The accuracy of these observations is doubtful.
4. Munk destroyed the base of the cochlea in dogs, and found that the animals could hear only low notes. Confirmed by Pawlow.

Criticism.—Difference in length of fibres is not sufficient. *Reply*: Vibration of a cord depends on its tension as well as its length.

RUTHERFORD THEORY.—Basilar membrane vibrates as a whole (like the plate of a telephone) a number of times a second. For each note there are a definite number of vibrations and of nervous impulses which travel up eighth nerve and are analysed by brain.

WALLER'S MODIFICATION OF RUTHERFORD THEORY.—Different pressure patterns are formed on basilar membrane by different notes, and transmitted to brain as such.

Criticism.—Cochlea appears much too complicated for requirements of such simple theories as Rutherford's and those based upon it. Why should there be variations in lengths of the fibres?

KEITH AND WRIGHTSON THEORY.—This presupposes that hairs are firmly attached to tectorial membrane, and that they bend backwards and forwards as basilar membrane moves up and down. In this way, hair-cells, and so nerve-fibres, are stimulated.

DISCORD.—On the Gray theory, with a pure note, only one string has maximum oscillation at same time, figure being a peak. In *discord*, several neighbouring strings vibrate very similarly, resulting figure being a plateau. With sight- and with weight-judging it is

Mechanism of Hearing, *continued.*

easier to make contrasts simultaneously than successively. With musical notes we prefer successive methods to avoid a plateau, i.e., a discord.]

RANGE OF HEARING.—Very variable, especially for high notes. (Galton's whistle is used for emitting very high notes.) Lower limit: about 24 to 30 vibrations per second. Upper limit: about 40,000 vibrations per second. A bat's squeak is about the upper limit of audition, being perceptible to some people, not to others.

INVESTIGATION OF DEAFNESS BY TUNING-FORK TESTS.—

RINNÉ TEST.—

1. Tuning-fork held at external auditory meatus until patient just ceases to hear it, and then transferred to mastoid. Normally patient does not hear sound again.
2. Tuning-fork held on mastoid process, until patient ceases to hear it, then transferred to external auditory meatus. Normally patient hears it again.

Hence, normally, air conduction is better than bone conduction—i.e., Rinné is positive.

In disease of cochlea or 8th nerve, Rinné is positive.

In disease of middle or external ear, Rinné is negative—i.e., bone conduction is better than air conduction.

CENTRAL CONNECTIONS OF HEARING (*Fig.* 23).—The cochlear division of 8th nerve arises in hair-cells of organ of Corti. Passes to bipolar cells of spiral ganglion, which corresponds to a posterior root ganglion. Enters brain-stem at junction of pons and medulla, and ends in two nuclei in pons.

NUCLEI.—

1. *Tuberculum acusticum*, or dorsal nucleus, from which fibres cross floor of 4th ventricle as *striæ acusticæ*, some ending in superior olive, others passing directly to lateral fillet.
2. *Ventral or accessory nucleus*, from which fibres pass to superior olive and trapezoid nucleus of opposite side.

LATERAL FILLET or LATERAL LEMNISCUS.—Consists of fibres from superior olive and trapezoid nuclei, and some direct from dorsal nucleus. Passes through pons and mid-brain to internal geniculate body and posterior corpus quadrigeminum, giving a few fibres to lateral fillet nucleus. Some fibres from auditory nuclei may enter lateral fillet of same side.

AUDITORY RADIATIONS.—Fibres from internal geniculate body and posterior corpus quadrigeminum pass through posterior part of internal capsule to auditory area of cortex—i.e., superior temporal gyrus and island of Reil.

EVIDENCE FOR LOCALIZATION OF HEARING IN CORTEX.—(N.B.—Experiments on monkeys are unsatisfactory.)

1. After removal of both temporal lobes, monkeys will look round at a sound, but this is probably a lower level reflex.
2. Lesions of one temporal lobe in man do not result in deafness, though there may be some impairment of hearing, or the aura of an epileptic fit may be a sound.
3. Stimulation of temporal area in conscious men led to consciousness of a buzzing noise (Cushing). Stimulation of temporal cortex in monkeys leads to pricking up of the ears.
4. Cases are recorded of complete destruction of temporal cortex with persistence of island of Reil, and normal hearing.

VESTIBULE AND SEMICIRCULAR CANALS: EQUILIBRATION.

Semicircular Canals.—Arranged in three planes of space: (1) Horizontal or external; (2) Anterior or superior vertical; (3) Posterior vertical. Plane of anterior canal of one

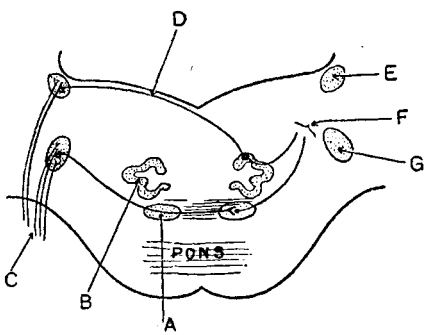

Fig. 23.—Central connections of hearing. A, Nucleus of trapezium; B, Superior olive; C, Cochlear nerve; D, Striæ acusticæ; E, Tuberculum acusticum; F, Lateral fillet; G, Accessory nucleus.

Semicircular Canals, *continued.*

side is parallel with that of posterior one of other side, thus, ⋗⋖. Open into utricle by five openings, anterior and posterior vertical having one opening in common.

AMPULLÆ.—Small swellings at one end of each canal, viz.: anterior end of horizontal and anterior vertical canals; posterior end of posterior vertical canal.

CRISTA ACUSTICA.—A small raised area in each ampulla, covered with columnar cells and a number of nerve-epithelial cells well supplied with endings of the vestibular division of the 8th nerve. The nerve-epithelial cells give off long hairs projecting into interior of canal.

FUNCTIONS OF SEMICIRCULAR CANALS.—To give information about dynamic equilibrium—i.e., to detect movements superimposed from without—and thus to aid in equilibration. They also serve to maintain reflexly the tone of the muscles. Hair-cells are stimulated by pressure-changes in endolymph.

EVIDENCE.—

1. Removal of all canals in pigeons results in wildly inco-ordinated movements, with inability to maintain any normal position, and complete loss of muscular tone. In a few months, power of steady movement returns, but if eyes are blindfolded, symptoms are as bad as ever. In apes and cats removal has not much effect, but cat if dropped no longer falls on its feet, and drowns in water.

   [*Results of Section of both Horizontal Canals.*—Side-to-side movements when head is in horizontal plane.
   Results of Section of Posterior or Superior Vertical Canals.—Movements of head and body in vertical plane, and tendency to turn somersaults.]

2. If a canal is exposed in a pigeon, and air or water blown in, forced movements result and nystagmus (jerking movements of eyes) away from canal.
3. *Infection of labyrinth in man* results in: (*a*) Giddiness—patient may even fall down; (*b*) Nystagmus; (*c*) Nerve deafness.
4. Canals have been removed on both sides in man in a few cases. Loss of sense of rotation results.
5. Certain cases of deaf-mutism do not appear to suffer from sea-sickness, and are found to have destruction of the labyrinth from infancy.

6. *Bárány Tests.*—
   a. Injection of hot or cold water into ear sets up convection currents in endolymph, with nystagmus towards opposite side.
   b. If person is rotated rapidly in one direction a number of times and stopped suddenly, there results: (i) Nystagmus in opposite direction; (ii) Giddiness and sensation of falling in opposite direction. These phenomena continue for 20 to 25 seconds.

Utricle and Saccule.—

MACULÆ ACUSTICÆ.—Two areas, similar to cristæ, in utricle and saccule, but containing calcareous particles called *otoliths*. Macula is situated in floor of utricle, in lateral wall of saccule. Fibres of vestibular branch of 8th nerve end about these structures.

FUNCTIONS.—

1. Form a static organ of equilibration to inform us of position of head at rest or during non-rotatory movements. It may be assumed that, when the head is moved, the otoliths are displaced, and so a stress is put upon the hairs, giving rise to stimuli.
   EVIDENCE.—Some crustaceans have an otolith organ at base of antenna, which is shed when they moult. After moulting, animal places grains of sand in its otolith organ. If iron dust is substituted for sand, and a magnet held over animal, it thinks it is upside down and rolls over.
2. *Participate with ampulla* in causing reflex compensatory changes in position of head.
   EVIDENCE.—If otoliths are removed from certain animals, they show disturbances in equilibrium, especially in compensatory movements exhibited during rotation.

Streeter's Experiment on Tadpoles.—Up to 6th day after fertilization, tadpoles show no power of equilibration, and are unable to swim. After 6th day, auditory vesicles appear, and animal now shows power of equilibration. If both vesicles are removed, animal loses permanently its power of swimming.

Postural Reflexes (Magnus of Utrecht).—Animals with mesencephalon transected show 'righting' reflexes of head and limbs to compensate for being turned upside down or held

Postural Reflexes, *continued.*

in abnormal positions: e.g., bending head to right causes increased tone of right limbs; turning upside down causes extensor tone in all limbs. These reflexes are abolished by destroying labyrinth. A de-labyrinthed rabbit laid on one side will, however, turn its head right way up, but not if the top side of its body is pressed upon: this shows a reflex from pressure on skin.

Tonic reflexes originate from macula in utricle, tone being increased when otolith hangs from macula. Asymmetrical righting reflexes originate from saccule. The centres for postural reflexes are in the brain-stem, from medulla to mesencephalon.

Central Connections of Vestibular Nerve.—

END-ORGANS.—Epithelial cells of cristæ of semicircular canals and maculæ of utricle and saccule. Fibres pass to

SCARPA'S GANGLION, on 8th nerve, outside utricle. Ganglion contains bipolar cells.

THE VESTIBULAR NERVE, issuing from the ganglion, enters brain at junction of pons and medulla, and ends in three nuclei, lying beneath outer angle of 4th ventricle (*Fig.* 24).

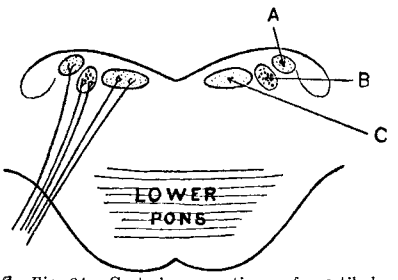

Fig. 24.—Central connections of vestibular nerve. A, Bechterew's nucleus; B, Deiters' nucleus; C, Vestibular nucleus.

NUCLEI.—

1. Deiters' or lateral nucleus (large-celled) } close to resti-
2. Bechterew's or dorsal nucleus } form body.
3. Principal vestibular nucleus (small-celled).

TERMINATION.—From the nuclei, fibres pass:—

1. To cerebellum, chiefly of opposite side, by restiform body.
2. From all three nuclei, in posterior longitudinal fasciculus, to communicate with nuclei of 3rd, 4th, 6th, and other cranial nerves.
3. As vestibulo-spinal tract, which arises in cells of Deiters' nucleus and passes down cord of same side.

Apparently there is no direct track to the cerebrum, the cerebellum forming nerve-centre for semicircular canals and vestibule.

CHAPTER XXII.

SIGHT.

Movements of the Eye.—Executed by four recti and two oblique muscles. All supplied by 3rd nerve, except superior oblique and external rectus, supplied respectively by 4th and 6th.

Superior oblique turns eye down and out.
Inferior oblique turns eye up and out.

Binocular Vision.—Normally eyeballs move together, so that image falls on fovea of both eyes. If the object is a distant one, visual axes are parallel; if a near one, they converge. If mechanism for combined movements fails, images are not formed on corresponding points of each retina, and diplopia (double vision) results.

Results of 3rd-Nerve Paralysis.—Drooping of upper eyelid (ptosis); external squint; fixed dilated pupil; paralysis of accommodation.

Result of 6th-Nerve Paralysis.—Internal squint. In both 3rd- and 6th-nerve paralysis there is double vision, if lesion is recently acquired. In old-standing cases of squint there is often no diplopia, because squinting eye becomes blind.

[**Law of Squint.**—False image is displaced towards side of paralysed muscle. (The false image is fainter than the true one, because it falls on a less sensitive part of the retina of the squinting eye.)]

Structure of Eyeball.—Coats are three in number: (1) *Outer* coat, consisting of sclerotic and cornea; (2) *Middle*, of choroid, ciliary processes, and iris; (3) *Inner*, of retina.

Sclerotic.—A very tough white fibrous tissue.

Cornea.—Continuation of sclerotic anteriorly. Shows 3 layers:

1. Outer layer of stratified epithelium, known as *Bowman's layer*.
2. *Tunica propria*, transparent bundles of modified fibrous tissue, amongst which there are irregular connective-tissue cells, corneal corpuscles. No blood-vessels, cornea being nourished by lymph.
3. *Descemet's membrane*, a single layer of cubical epithelium, on inner surface.

Aqueous Humour.—Watery fluid, containing a trace of salts and albumin. Does not clot. Secreted by ciliary processes, about 70 in number. About 98 per cent passes through pupil and is absorbed at filtration angle (irido-corneal junction) into canal of Schlemm, a circular sinus passing round eye at corneo-scleral junction. About 2 per cent enters vitreous humour. In the disease glaucoma, the filtration angle is blocked, the eye becomes hard and very painful, and sight rapidly deteriorates, resulting in blindness. Secretion of aqueous humour is probably controlled by 3rd nerve.

FUNCTION OF AQUEOUS HUMOUR.—To nourish avascular parts of eye—e.g., posterior part of cornea, lens.

Vitreous Humour.—Transparent jelly-like material containing a few floating particles, which we can sometimes see as *muscæ volitantes.*

Intra-ocular pressure is about 30 mm. Hg in aqueous humour chambers, rather higher in vitreous one.

Loss of aqueous humour is of no importance.

Loss of vitreous is very serious, because it cannot be renewed.

Choroid.—Consists of: (1) Outer pigmented layer, to exclude all light except such as enters through pupil; (2) Inner vascular layer, to nourish retina.

Iris.—Covered in front by flat endothelium. Consists anteriorly of unstriped muscle, circular and radial, with blood-vessels and some elastic tissue. Behind this is double layer of cubical cells containing black pigment—abundant in dark-eyed people, scanty in blue-eyed, absent in albinos. Albinos have pink eyes, and are dazzled in a bright light.

NERVE-SUPPLY OF IRIS.—

Circular muscle is supplied by 3rd nerve, through ciliary ganglion, where there is a cell-station. Stimulation of 3rd nerve contracts pupil; section dilates it.

[Ciliary ganglion is probably diseased in patients with Argyll Robertson pupil (i.e., a pupil that contracts to accommodation but not to light).]

Radial muscle is supplied by sympathetic. Stimulation dilates pupil, section contracts it.

[Fibres arise near 3rd nerve nucleus in mid-brain, pass down through pons, medulla, and cord to end in cilio-spinal centre in upper dorsal region. Thence fibres emerge as white rami communicantes through 1st, 2nd, and 3rd thoracic roots, and run up cervical sympathetic to superior cervical ganglion, where there is a cell-station. New grey fibres pass in nerve plexus on carotid artery to Gasserian ganglion, thence by 5th nerve to eye.]

FUNCTIONS OF IRIS.—

1. To regulate amount of light entering eye.
2. To improve definition of near objects.
3. To cut off periphery of lens, thus avoiding spherical and chromatic aberration.

CAUSES OF CONTRACTION OF PUPIL.—

1. Bright light. The pupil of the opposite eye also becomes contracted—'consensual light reflex'.
2. Accommodation to near object.
3. Stimulation of 3rd nerve.
4. Paralysis of sympathetic.
5. Convergence of eyes.
6. DRUGS.
   a. *Pilocarpine* and *eserine*, by stimulation of 3rd nerve.
   b. *Opium* and *morphia*, by action on brain.

CAUSES OF DILATATION OF PUPIL.—

1. Darkness or dim light, and relaxation of accommodation.
2. Emotions—pain, fear, excitement.
3. Paralysis of 3rd nerve.
4. Stimulation of sympathetic.
5. Later stages of asphyxia.
6. DRUGS.—
   a. *Atropine* and *belladonna*, by paralysis of third nerve.
   b. *Cocaine*, by stimulating sympathetic.
   c. *Adrenalin* dilates pupil of excised eye, but does not have this effect in the body. In intact body, its action is counteracted by some substance derived from pancreas.
7. Abnormal increase of intra-ocular tension—e.g., in glaucoma.

Accommodation.—In normal or emmetropic eye, parallel rays are brought to a focus on the retina. Practically rays from object over a yard away may be taken as parallel. Rays entering eye from less than this distance are focused on retina by accommodation, i.e., alteration in convexity of lens.

FACTORS CONCERNED IN ACCOMMODATION.—(1) Lens; (2) Suspensory ligament; (3) Ciliary muscle and 3rd nerve.

STRUCTURE OF LENS.—Transparent fibres having a serrated edge. Avascular; nourished by lymph. Centre is denser than periphery.

Accommodation, *continued.*

REFRACTION SURFACES.—Refraction of light occurs at: (1) Air-corneal junction—greatest; (2) Corneo-aqueous—negligible; (3) Aqueous-lens—most important because adjustable; (4) Lens-vitreous.

PHAKOSCOPE.—Shows following reflections: (1) A bright upright image at air-corneal junction; (2) A faint upright image from anterior surface of lens; (3) A faint inverted image from posterior surface of lens. These are *Sanson's images.* On accommodation, middle image alters, coming nearer anterior one, other two remaining stationary. Therefore anterior surface of lens moves forwards in accommodadation.

Image on retina is really inverted, but we mentally reverse it.

MECHANISM OF ACCOMMODATION.—Lens is slung in tense elastic capsule connected with ciliary processes and choroid by suspensory ligament or *zonule of Zinn.*

Ciliary muscle consists of two parts: (*a*) Radial, having origin at corneo-sclerotic junction and insertion into choroid and ciliary body; (*b*) Circular, passing round lens.

Normally, with eye at rest, lens is kept flattened by pull of elastic choroid and suspensory ligament on lens capsule. On accommodation, anterior surface of lens becomes more convex.

HELMHOLTZ THEORY OF ACCOMMODATION.—

1. Radial fibres of ciliary muscle contract and pull choroid forwards.
2. Thus suspensory ligament is slackened and tension on lens capsule relaxed.
3. Lens in virtue of its own elasticity becomes more convex.
4. Contraction of circular fibres of ciliary muscle reduces circumference of lens, making anterior surface bulge forwards.

Ciliary muscle is supplied by 3rd nerve. Atropine and homatropine paralyse accommodation by their action on this nerve.

Evidence in Favour of Helmholtz Theory.—(1) Sanson's images; (2) A needle inserted into eye of an animal so as to rest on anterior surface of lens moves forwards during accommodation, as lens bulges.

LIMITS OF ACCOMMODATION.—Far point of vision for normal eye is theoretically infinity. Near point of vision is about $5\frac{1}{2}$ inches in young adults, but varies considerably with age; 10 inches at 45.

DETERMINATION OF NEAR POINT: SCHEINER'S EXPERIMENT.—One eye is closed while the other looks at a pin through two holes, 1 mm. apart, in a piece of cardboard. When pin is held near to eye, it appears double, being focused behind retina, not on it; when further away, single. Near point is distance from eye at which the two images blend into one. If right hole is blocked, left image disappears; by optics, left image should disappear, but mentally we reverse them.

Defects of Accommodation.—

1. MYOPIA (short sight).—Eye is too long for lens, so that parallel light is focused in front of retina. Distant objects cannot be seen, and near point is too close to eye.
   TREATMENT.—Bi-concave lens.
2. HYPERMETROPIA (long sight).—Eye is too short, so that parallel rays are focused behind retina. Near point of vision is too far away, and accommodation is necessary even for distant objects, causing headache and strain.
   TREATMENT.—Bi-convex lens.
3. PRESBYOPIA ('old age' sight).—Begins after 45 years of age. Near point of vision recedes, owing to diminution of elasticity of lens.
   TREATMENT.—Convex glasses for reading.

[**Spherical Aberration.**—Depends on fact that rays passing through circumference of a lens are more refracted than those passing through centre and so are not brought to a focus at same point. Consequently, when centre of an image is in focus, its edges are blurred, and vice versa.
Counteracted by: (1) Centre of lens being denser and so more refractive than periphery: (2) Iris acting like a diaphragm and shutting off rays at periphery.

Chromatic Aberration.—Ray of light passing through a lens is broken up into its component parts, and coloured margins appear round the image—i.e., chromatic aberration occurs. Violet rays, having a short wave length, are most bent, red rays least. Not really noticeable in human eye.]

Astigmatism.—Due to spoon-shaped curvature of cornea, causing inability to focus vertical and horizontal lines at same time.

TREATMENT.—Cylinder lens—i.e., lens spoon-shaped in opposite direction.

Judgement of Size and Distance.—

1. The size of the image on the retina gives a datum. If size is known by experience, distance can be estimated, and vice versa.
2. Comparison of size and distance of unknown with known objects.
3. For near objects, estimation of convergence of internal recti muscles. Hence monocular judgements are very inaccurate.
4. Estimation of amount of contraction of ciliary muscles. This only helps if object is less than 2 yards away.

Judgement of Solidity.—Depends mainly on binocular vision. Slightly different images of an object are given in the two eyes, and fusion of these images results in impression of solidity.

Retina.—Inner coat of eye. Ends suddenly anteriorly at ora serrata.

STRUCTURE OF RETINA.—From without inwards :—

1. Pigment cells—a single layer of polygonal cells. They have an inner pigmented portion consisting of straight processes extending between the rods.
2. Rods and cones.
3. Outer limiting membrane.
4. Outer nuclear layer, consisting of rod granules and cone granules. These are bipolar cells, connected with rods or cones respectively, and with processes of bipolar cells in inner nuclear layer.
5. Outer molecular layer, showing arborization of bipolar cells with corresponding rod and cone fibres. A few stellate cells present.
6. Inner nuclear layer, consisting chiefly of bipolar cells.
7. Inner molecular layer, showing arborization of axons of bipolar cells and dendrons of ganglion cells. Neuroglia cells present.
8. Ganglion cells.
9. Nerve-fibres (chiefly axons of ganglion cells) and blood-vessels.
10. Internal limiting membrane.

There are thus three neurons : (1) Rods and cones and outer nuclear layer — numerous ; (2) Inner nuclear layer—less numerous ; (3) Ganglionic cells—comparatively few—with dendrons in inner molecular layer, and axons constituting the fibres of the optic nerve.

Between nerve elements are connective-tissue elements, the fibres of Müller, ends of which are expanded to form internal and external limiting membranes.

Rods.—Shaped like a bottle, or a cricket bat with a splice showing. They are surrounded externally by pigment, and they, and not the cones, contain a pigment, *rhodopsin* or *visual purple.*

Two Special Regions.—

1. *Macula lutea,* or yellow spot, having at its centre a small depression, the *fovea centralis.* This is the point of best vision. Fovea contains only cones.
2. *Blind spot or optic disc,* a little internal to fovea centralis. Corresponds to entrance of optic nerve.

Optic nerve-fibres are medullated as far as disc, but fibres in retina are non-medullated (as a rule).

When optic nerve is cut, most of degenerating fibres are found between it and brain, differing from cutaneous nerves and nerves of taste, but corresponding to auditory nerve.

We are not conscious of blind spot normally, because brain sketches in this part of the picture to match the rest.

OPHTHALMOSCOPE.—Used for examining retina. Consists essentially of a mirror set at an angle to reflect light into patient's eye, with a perforation in its centre through which observer looks. Two methods of examination :—

1. Direct Method.—Small mirror is used close up to patient's eye. Rays of light passing between the two eyes must be parallel, so as to be focused on observer's retina ; hence patient and observer must both relax their accommodation. Image is upright and magnified.

[2. Indirect Method.—Larger mirror of ophthalmoscope is held about a yard away from patient, and a convex lens interposed close to patient's eye. Image is inverted and not magnified.]

PERIMETER.—Used to determine field of vision, for white and colours. Chief use is to detect blindness in various parts of retina. The visual field is the entire extent of the external world which, when the eye is fixed, forms an image on the retina.

For white, vision extends to 90° on temporal side, only about 65° on nasal side, light rays being cut off by nose.

Retina—Use of Perimeter, *continued.*

The colour field is smaller—least for green, then red, largest for yellow. Thus periphery of retina is colour-blind.

OBJECTIVE EFFECTS OF LIGHT ON RETINA.—

1. Retraction of cones.
2. Extension of retinal pigment between rods and cones.
3. Electrical variations (negative variation, etc.).
4. *Chemical changes.* Ordinary alkaline reaction of retina is changed to acid. Bleaching of visual purple. Visual purple is regenerated by pigment cells. If retina is detached from pigment cells, no regeneration occurs. Can be dissolved out in the dark by a solution of bile salts, forming a solution which can be bleached by light, especially green-yellow part of spectrum.

OPTOGRAM.—If a guinea-pig has its head fixed opposite a window for some time and is then killed, a pattern of the window can be seen bleached out on retina, known as an optogram. This gives a clue to the underlying process in black-and-white vision. A pattern of an object is cast on retina, visual purple in certain rods is bleached, and something liberated which stimulates rods or cones or both, and sends a message up corresponding fibres of optic nerve.

FUNCTIONS OF RETINA.—Main function is to convert physical process of *light* into physiological process of *sight.*

1. FOVEA CENTRALIS.—Used in all skilled work—e.g., reading, recognition of people and objects, and colour vision.
2. REST OF RETINA.—Used in filling in a detailed picture. The two retinæ show corresponding points, accustomed to work together, the two pictures fusing into one. The foveæ are corresponding points, the blind spots are not.
3. PERIPHERY OF RETINA.—Chief function is detection of moving objects.

THE LAYER IN THE RETINA STIMULATED BY IMPULSES GIVING RISE TO VISUAL SENSATION IS THAT OF THE RODS AND CONES, ESPECIALLY THE CONES.—

Proofs :—

1. Fovea centralis, the area with which we see best, shows only cones.

2. At blind spot, rods and cones are absent.
3. *Purkinje's Figures.*—Blood-vessels of one's own retina can be seen by experiment, showing that receiving layer is behind blood-vessels.

Methods of obtaining Purkinje's figures.—

1. In a dark room, with eye fixed on a blank surface, a candle is adjusted so that light enters through sclerotic and not pupil. Tree-like shadows of blood-vessels are seen.
2. In bright sunlight, a white cloud is looked at through a hole in a card and card rotated. The avascular fovea centralis is seen, with vessels radiating from it.

Explanation is that light reaching retina by an unusual route casts a shadow of vessels on a part of retina not accustomed to it. We are not usually conscious of our retinal vessels, because their images always fall on particular rods and cones, and are ignored.

Function of the three neurons in retina is to reduce number of nerve-fibres as compared with number of rods and cones, one nerve-fibre carrying messages for many rods and cones, except in fovea centralis, where there is a nerve-fibre for each cone.

Respective Functions of Rods and Cones.—Generally accepted that rods are used for vision in a dim light, cones for colour vision, clear definition, and vision in a bright light (duplicity theory of v. Kries). Evidence :—

1. In fovea centralis, there are only cones.
2. In dim light, colour vision is lost ; blues persist longest, but red very quickly appears black.

[3. In the disease retinitis pigmentosa, most of rods are destroyed, but fovea centralis is spared, and symptom is night-blindness.

4. In the rare condition, total colour-blindness, cones are defective, and symptoms are : (*a*) Inability to distinguish any colours, everything appearing black, white, or various shades of grey ; (*b*) Dazzling in a bright light ; (*c*) Central scotoma (blindness) which seriously spoils power of recognizing objects. Tobacco poisoning produces a similar condition.

Retina—Functions of Rods and Cones, *continued.*

5. Proportions of rods and cones vary with degrees of daylight and nocturnal vision in different animals. Nocturnal animals—e.g., owls—are well provided with rods and visual purple. In most birds, cones are more numerous than rods, and as their rest commences at sundown, they are not much adapted to dim lights and darkness.
6. In a dim light, colour matches change their value, explanation given being that in a bright light we judge them entirely by cones, but in a dim light by rods as well. Also brightest point in spectrum moves towards blue end (Purkinje phenomenon). In hens, greatest pupil contraction occurs with light towards red end of spectrum, in owls towards blue end.
7. Part of spectrum seen best in a dim light is that which most readily bleaches visual purple.
8. Astronomers, when looking at a faint star, see it best if they look slightly to one side of it, explanation being absence of rods in fovea centralis.
9. *Dark-adapted eye.* The pupil dilates in the dark, so that more light falls on the periphery of the retina. Rods are very sensitive to light, and are rapidly exhausted, so that on passing from a bright to a dim light we can at first see nothing.

Edridge-Green Theory.—Suggests that rods are not visual, but that they secrete visual purple which sensitizes cones.]

Colour Vision.—

1. With a single spot in the retina (except at extreme periphery) we can distinguish the seven primary colours of the spectrum—i.e., violet, indigo, blue, green, yellow, orange, red. (Many people are hexachromic, and unable to distinguish violet from indigo.)
2. Continual staring at one colour results in fatigue, and relative blindness to that colour.
3. Certain colours are complementary to one another—i.e., when mixed they give rise to white—e.g., red and green, or blue and yellow.
4. Given red, yellow, and blue—or, according to others, red, green, and violet—all other colours may be constructed. This is the basis of trichromic theories of colour vision.
5. *Simultaneous Contrast.*—A colour or shade is influenced by its background—e.g., a blue on a dark background appears paler than on a white background. Sherrington's disc can be used to demonstrate simultaneous contrast.
6. *Successive Contrast.*—On staring at a coloured figure until eye is fatigued, and then transferring one's gaze to a uniform background, one sees a negative after-image of same shape but complementary colour—e.g., red object

gives green after-image. A positive after-image is obtained by gazing at a bright light. On transferring the gaze, the bright light is still seen.

7. Colours differ from one another in their degree of saturation, i.e., amount of white light mixed with them.
8. COLOUR-BLINDNESS is probably due to abnormality of cones.
   - *a.* TOTAL COLOUR-BLINDNESS.—Very rare. To such people, the world resembles a photograph in black, grey, and white.
   - *b.* PARTIAL COLOUR-BLINDNESS.—About 2 to 4 per cent of male population, 0·1 per cent of females, are partially colour-blind. Commonest forms are green-blindness and red-blindness. On careful examination it is rare to find a pure red- or green-blind person, most being really red-green-blind. Violet blindness is very rare indeed.

   TESTS FOR COLOUR-BLINDNESS.—
   - *a. Holmgren's Worsted Test.*—Subject is given two skeins of wool, a pale pure green and a vivid red, and told to select from a bundle of skeins all those of same colour, whatever the depth of shade may be.

     Not satisfactory, because: (i) People who are more or less colour-blind can pass the test, given plenty of time, a good light, and their optimum distance from the skein; (ii) It requires a certain amount of intelligence and colour education.
   - *b. Edridge-Green Lamp.*—This is the modern method. With the apparatus a small circle of colour can be shown for a short time. Test can be made more delicate by interposition of fog-glasses.
   - *c. Ishihara's Plates.*—Numerous coloured dots. Normal eye sees one figure outlined by the dots, colour-blind sees another.

   Colour sense in an individual may change in course of years.

THEORIES OF COLOUR VISION.—None explain all the facts.

1. YOUNG-HELMHOLTZ THEORY.—Supposes there are in the cones three chemical substances, say X, Y, Z.

   X is acted on principally by red light.
   Y ,, ,, green light.
   Z ,, ,, violet light.

Theories of Colour Vision, *continued.*

White light stimulates all three. Black is due to absence of stimulus. Yellow stimulates X and Y.

Objection.—Colour-blindness is explained by absence of X in red-blindness, Y in green-blindness. This is fallacious, because if Y substance were absent in green-blindness, patient could not distinguish between white and purple ; but he can do so. The theory, however, can be modified to meet this difficulty.

2. HERING THEORY.—Supposes existence in cones of three chemical substances, say A, B, C, each of which may be acted on in two ways by coloured light—i.e., built up or broken down.

A	is katabolized by	white,	anabolized by	black.
B	,,	red	,,	green.
C	,,	yellow	,,	blue.

In the colour-blind, the B substance is absent.

Explanation of Successive Contrast.—After staring at a red object for some time, B substance is broken down ; on transferring gaze to a neutral ground, B substance builds itself up to its original, with formation of green after-image.

Objections.—(*a*) It seems rather fantastic ; (*b*) It does not explain simultaneous contrast ; (*c*) A yellow can be compounded by mixing red and green, i.e., by stimulation of the B substance. But on fatiguing the eye to such a yellow, it is found also to be fatigued to pure spectral yellow, which stimulates the C substance.

3. EDRIDGE-GREEN THEORY.—Suggests that each of the seven colours acting on single receptor substance in cones induces a nervous impulse of characteristic wave length, so that seven different sorts of nervous impulses travel up optic nerve.

Objection.—Theory is quite contrary to Müller's law, which states that nervous impulses are all alike, and only differ in origin and destination.

Central Connections of Vision.—

PATH (*Fig.* 25).—

OPTIC NERVE AND CHIASMA.—Fibres of optic nerve undergo partial decussation. Those from nasal half of each retina cross in optic chiasma, those from temporal half continue on same side.

OPTIC TRACT.—Consists of: (1) Fibres from temporal half of retina of same side; (2) Fibres from nasal half of retina of opposite side.

NUCLEI.—Fibres of optic tract end in three nuclei:—(1) Anterior corpus quadrigeminum; (2) External geniculate body; (3) Pulvinar of optic thalamus. Fibres from macula pass to external geniculate body. The anterior corpus quadrigeminum is a lower-level centre, and fibres pass from it to nucleus of third nerve and other nuclei, providing a path for visual reflexes, e.g., focusing and light reflex.

CORTEX.—From external geniculate body and pulvinar, fibres run as optic radiations to the two lips of the calcarine fissure on mesial surface of occipital lobe—i.e., the *visuo-sensory cortex*. Fovea centralis is represented at occipital pole on each side.

Characteristics of Visuo-sensory Cortex.—*See* p. 182.

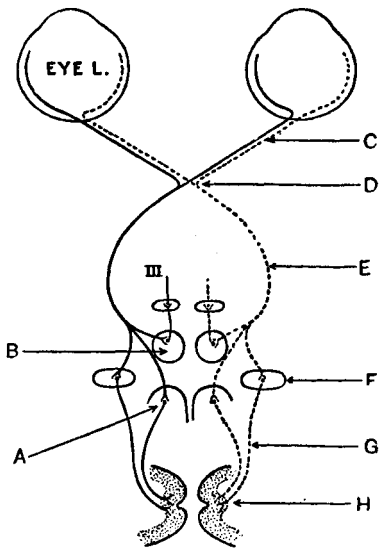

Fig. 25.—Central connections of vision. A, Pulvinar of optic thalamus; B, Anterior corpus quadrigeminum; C, Optic nerve; D, Optic chiasma; E, Optic tract; F, External geniculate body; G, Optic radiations; H, Calcarine fissure.

Central Connections of Vision, *continued.*

RESULTS OF DESTRUCTIVE LESIONS AT DIFFERENT PARTS OF VISUAL PATH.—

1. Optic Nerve.—Total blindness of retina of same side.
2. Optic Chiasma.—Lesion catches the decussating fibres, and consequently causes blindness of nasal half of each retina—i.e., temporal half of each visual field. A pituitary tumour may press on optic chiasma and give rise to this symptom.
3. Optic Tract, Optic Radiation, or Calcarine Fissure. —These three all give rise to homonymous hemianopia—i.e., blindness of same halves of both retinæ. Lesion on left side causes blindness of left half of each retina, and patient cannot see objects to his right-hand.

   A lesion in optic tract can be distinguished from one in optic radiation or calcarine fissure by hemiopic pupil reflex—Wernicke's reaction. In latter case, if light is cast on blind part of retina, pupil contracts, because reflex arc through anterior corpus quadrigeminum is intact. If optic tract is damaged, there is no such pupil reflex.

   Lesion above or below one calcarine fissure results in blindness in corresponding quadrants of both retinæ—e.g., tumour in upper lip of left calcarine fissure causes blindness in upper left quadrant of each eye, and individual will not be able to see downwards and to the right.
4. Visuo-sensory Cortex.—Loss of cortex in this area destroys power of orientation—i.e., finding one's way about in the dark.

VISUO-PSYCHIC AREA.—Situated on outer surface of occipital lobe. Concerned with recognition and interpretation of things seen.

CHAPTER XXIII.

CUTANEOUS, MUSCULAR, AND VISCERAL SENSATION.

Varieties of End-organs in the Skin.—

1. PLEXUS.—Many ordinary cutaneous fibres end by forming a plexus, especially round hair-follicles, and in papillæ of cutis vera.
2. PACINIAN CORPUSCLES.—
   STRUCTURE.—Concentric layers of fine connective tissue, each layer lined by epithelium, and in centre the nerve, which has lost its myelin sheath, and ends in an arborization.
   SITUATION.—Especially in finger-tips, and in cat's mesentery.
3. MEISSNER'S CORPUSCLES.—
   STRUCTURE.—Ovoid bodies, consisting of connective tissue surrounded by elastic fibres and cellular capsule. Medullated nerve winds round corpuscle two or three times, loses myelin sheath, and enters corpuscle.
   SITUATION.—Parts of body not supplied with hairs, e.g., palms of hands and soles of feet.
4. END-BULBS OF KRAUSE.—
   STRUCTURE.—Spheroidal bodies consisting of ovoid cells with medullated nerve.
   SITUATION.—Conjunctiva and external genitals.

Sensory End-organs in Muscle and Tendon.—

1. NEUROMUSCULAR SPINDLES OF RUFFINI.—
   STRUCTURE.—Bundle of fine muscle-fibres surrounded by sheath of connective tissue. Nerve loses its myelin sheath, and axis cylinder coils round several times, ending in branches on surface.
   SITUATION.—Especially in neighbourhood of tendons.
   Neuromuscular spindles must be sensory because: (*a*) If posterior roots are cut, neuromuscular spindles degenerate, motor end-plates do not; if anterior roots are cut, vice versa. (*b*) In disease of anterior-horn

Sensory End-organs in Muscle and Tendon, *continued.*

cells, end-plates degenerate, spindles persist; in disease of posterior-root ganglia, vice versa.

2. ORGANS OF GOLGI.—

STRUCTURE.—Spindle-shaped, having fibrous capsule, and containing terminal arborizations of several medullated nerve-fibres.

SITUATION.—Tendons.

Other Sensory End-organs.—

1. Synovial membrane is richly supplied with nerves.
2. Bone and periosteum, very sensitive.
3. Deep fascia, rather sensitive.

Skin, deep fascia, periosteum, and bone are much more sensitive than fat and muscle.

Varieties of Cutaneous Sensation.—(1) Touch and pressure; (2) Warmth; (3) Cold; (4) Pain.

Distribution of Cutaneous Sensation.—Punctiform distribution, each spot responding to one specific stimulus—i.e., pressure, heat, cold, or pain. Most numerous for pain, then pressure and cold, fewest for heat. Different varieties of spots predominate in different regions—e.g., forehead has chiefly thermal spots, fingers tactile. Cornea has only pain sense.

PROOFS OF PUNCTIFORM DISTRIBUTION OF SENSATION.—

1. On going over skin with a blunt metal point, some spots give sensation of cold, others of mere contact. If point is warmer than skin, at some points it gives sensation of warmth.

   Points may be stimulated by other than their adequate stimuli—e.g., menthol gives rise to a cold sensation. General opinion is that heat and cold spots do not show definite end-organs, while tactile spots lie over hair-follicles or show Meissner's corpuscles.

2. In certain nervous diseases, one variety of sensation is lost while others remain normal—e.g., in syringomyelia (hollowing of the spinal cord), pain and temperature sense are lost, but tactile remains.

DETERMINATION OF TACTILE DISCRIMINATION.—Æsthesiometer (consists of a wooden handle with hairs of different diameters fixed at right angles) or Weber's compass is used, and distance between two points, when they can

be recognized as two, noted. On tongue they are recognized as two when only 1 mm. apart, on fingers at 2 mm., on back of trunk only when 67 mm.

Conduction of Sensations.—Probably each type of sensation has its own nerve-fibres.

Epicritic and Protopathic Sensation: Head and Rivers' Work.—Head and Rivers divided skin sensation into: (1) *Protopathic*, i.e., sensations of pain and extremes of temperature, above 37° C. or below 26° C.; (2) *Epicritic*, i.e., light touch, including localization and tactile discrimination, and small variations of temperature. There is also a deep-pressure sense arising in muscles and tendons.

EVIDENCE.—

RESULTS OF NERVE SECTION, e.g., ULNAR NERVE (*Fig.* 26.)—

1. Epicritic sense lost over little and inner half of ring fingers and corresponding area of hand.

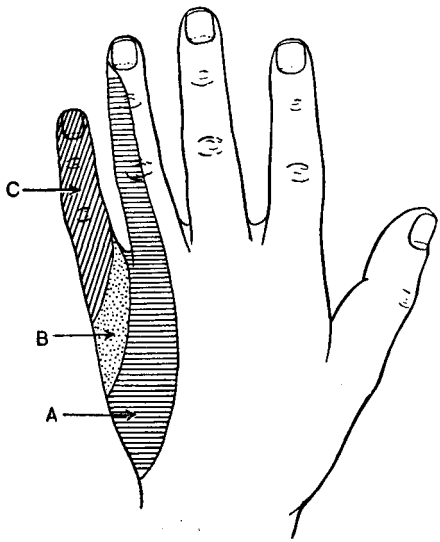

Fig. 26.—Diagram showing loss of epicritic, protopathic, and deep sensation after section of the ulnar nerve. A, Epicritic sense lost; B, Protopathic and epicritic sense lost; C, All sense lost.

Epicritic and Protopathic Sensation, *continued.*

2. Protopathic sense lost over phalanges of little finger.
3. *Deep sense* lost over middle and terminal phalanges of little finger.

Sir Henry Head, after section of his own radial and external cutaneous nerves, found that protopathic sensation returned some time before epicritic. In the case of the radial nerve he found a small area where protopathic sense was lost and epicritic retained.

Theory is that protopathic is a primitive sense to which epicritic has been added. Only protopathic sense is present in glans penis.

[**Order in which Functions of a Nerve Return** (after section and reunion).—

1. Trophic and vasomotor.
2. Deep sensibility.
3. Sensations of roughness and pressure pain.
4. Radiating and badly localized sensations.
5. Sensibility to light touch. At about this time, motor power is returning. Takes 6 to 24 months.
6. Stereognosis (power of recognizing objects by touch)—only late, or not at all.

Trotter observed that, during recovery, any stimulus over the cutaneous area affected gave rise to a definitely painful sensation referred to the most distant part of that area.

Recovery after incomplete division of a nerve is more rapid, being usually under six months for sensation, about a year for motor power. Protopathic and epicritic senses are restored at about the same rate.]

Pain Sense.—Very widely distributed. Pain points show no special end-organs, sensory nerve-endings being stimulated. Cutaneous pains are usually localized accurately, but visceral often very inexactly.

REFERRED PAIN.—Pain arising in a viscus may be felt in the skin. Explanation is that pain is referred to skin area supplied by same spinal segment as viscus.

Muscle and Joint Sense, or Sense of Position.—Copious nerve-endings exist in synovial membrane and ends of bones. About a half to a third of the fibres in the muscular branches of nerves are sensory (Sherrington). Electric current through a joint upsets sense of position more than one through muscles.

Muscle sense is the consciousness of the condition and position of the muscles and the joints moved by them, including the sense of effort (e.g., judging weights) and the spatial relation of the limbs in motion and at rest. Depends on neuromuscular spindles, and organ of Golgi in tendon

Sensations of Hunger and Thirst.—

SENSATION OF HUNGER, as distinct from appetite, arises in the stomach wall. Cannon and Washburn have observed that with an empty stomach hunger pain may be intermittent, and that it is simultaneous with contraction of the stomach musculature. Contractions are increased by vagi, inhibited by splanchnics, or reflexly by mechanical stimulation of mucous membrane of mouth, œsophagus, or stomach.

SENSATION OF THIRST arises at back of pharynx. Commonly due to local dryness, but may be indication of need of body for water. Artificial drying of back of pharynx, or atropine given hypodermically, produces a sensation of thirst.

Sensation in the Alimentary Tract (*see* p. 198).—

1. ŒSOPHAGUS.—Being lined by stratified epithelium, the œsophagus has sensation of heat, cold, and localization.
2. STOMACH.—Absence of tactile and temperature sense. Cutting is not painful unless there is pulling. Dragging is very painful. Dilatation may be very painful. Mucosa may give rise to burning sensation if irritants are applied.
3. BOWEL.—Like stomach. Not nearly so sensitive as the mesentery.
4. PARIETAL PERITONEUM AND MESENTERY.—Very sensitive to cutting, pulling, or irritants, resulting in pain and reflex spasm.

Referred Pain.—Tenderness or pain is often present in area of skin supplied by same nerve as diseased viscus.

CHAPTER XXIV.

REPRODUCTION.

MALE GENITAL ORGANS.

Testis.—

STRUCTURE OF TESTIS.—Fibrous capsule, the *tunica albuginea*; closely packed seminiferous tubules; some connective tissue; interstitial cells of Leydig.

SEMINIFEROUS TUBULES.—Lined by several layers of cells showing active mitosis.

[*Passing from outer layer to centre,* these cells show:—
1. *Spermatogonia,* developed from cubical cells which line seminal tubules.
2. *Spermatocytes,* produced by division of spermatogonia.
3. *Spermatids,* four being formed from each spermatocyte.
4. *Spermatozoa,* each developed from one spermatid.]

SPERMATOZOA.—Consist of:—

a. Head, containing 12 chromosomes in man. During development, chromosomes have been reduced by one-half. Consists chemically of nucleo-protein compound, like nuclei of cells in general. (In fish sperm, protamines are present.)

b. Neck, containing centrosome.

c. Tail.

Fully developed spermatozoa are not present before puberty, but persist well into old age. They pass into epididymis and vas deferens and so to seminal vesicles.

Semen is ejaculated during coitus and at other times. Consists of spermatozoa (may be 60,000,000 to 70,000,000 in each c.c.) and secretions of seminal vesicles, Cowper's glands, and prostate. These secretions probably help to maintain motility of spermatozoa.

INTERSTITIAL CELLS OF LEYDIG.—Probably furnish an internal secretion, which controls development of secondary sexual characters.

EFFECTS OF REMOVAL OF BOTH TESTES.—

1. BEFORE PUBERTY.—*Eunuchism* results. Characteristics: (*a*) Sterility, but not necessarily impotence; (*b*) Generally fat and effeminate appearance; (*c*) Secondary sex characters do not appear—i.e., no beard, moustache, or pubic hair, voice does not break, prostate and external genitals remain underdeveloped; (*d*) Mental and bodily development otherwise normal.

2. IN ADULT LIFE (i.e., after 20 years).—Sterility, and atrophy of prostate; otherwise no effect.

PROOFS THAT INTERNAL SECRETION IS PRODUCED BY CELLS OF LEYDIG:—

1. RESULTS OF TYING BOTH VASA DEFERENTIA.—(*a*) Atrophy of tubules, but cells of Leydig unaffected; (*b*) Sterility; (*c*) Secondary sex characteristics develop normally.

   Ligature of vas is said to cause rejuvenation in feeble aged males (goats, men, etc.) by leading to atrophy of seminiferous tubules, so that more blood goes to interstitial cells (Steinach operation).

2. CONDITION OF UNDESCENDED TESTIS IN MAN.—If bilateral, patients are sterile. If cells of Leydig persist, secondary sex characters develop; if these cells are absent, such characters do not develop, and patients resemble eunuchs.

Penis.—Consists of urethra, and of erectile tissue, which is highly vascular and contains spaces that can be filled with blood from the arteries, contained in a fibrocutaneous sheath.

[These arteries are very peculiar; inside the elastic lamina there is a layer of unstriped muscle which in the flaccid condition makes the lumen of the artery hemispherical; but during active vasodilatation this muscle shrinks aside and assumes shape of a narrow crescent, so that there is an enormous increase of lumen (Kiss of Buda-Pesth).]

The vasodilator fibres for the external genitals are called the nervi erigentes, and are derived from 3rd and 4th sacral roots.

Removal of Prostate and Seminal Vesicles.—Steinach and Walker found that in rats this prevented fertilization of the female, though testes remained apparently normal.

REPRODUCTION IN THE FEMALE.

Structure of Ovary.—Fibrous and unstriped muscular tissue, covered by single layer of cubical epithelium—'germinal epithelium'. Groups of interstitial cells are present similar to cells of Leydig in testis. In the ovary are embedded primordial follicles, Graafian follicles, and corpora lutea. About 70,000 immature follicles exist at birth, of which majority never reach maturity.

1. PRIMORDIAL FOLLICLE.—An unripe ovum. It is a spherical body 0·2 mm. in diameter, having a vesicular nucleus and dark-staining nucleolus, and surrounded by a layer of flattened epithelial cells. It is developed as a downgrowth from the germinal epithelium.
2. GRAAFIAN FOLLICLE.—Formed by proliferation of cells surrounding ovum, and collection of a serous fluid.
   STRUCTURE.—(*a*) Layer of cells lining follicle, *stratum granulosum*; (*b*) *Liquor folliculi* between stratum granulosum and discus proligerus; (*c*) *Discus proligerus*, a mass of cells surrounding ovum; (*d*) *Ovum*.
   When ripe, Graafian follicle is about the size of a pea. It comes to the surface and bursts, shedding its ovum —i.e., 'ovulation'.
3. CORPUS LUTEUM.—After shedding ovum, cavity of follicle becomes filled with blood, and a little later is invaded by cells containing a yellow pigment, lutein. Measures about $\frac{1}{4}$ in. in diameter, is at its maximum in 2 to 3 weeks, and disappears by end of 2nd month. If pregnancy occurs, it continues growing until about end of 6th month, when it is $\frac{3}{4}$ in. in diameter.
   ORIGIN OF LUTEIN CELLS.—Uncertain, but probably from stratum granulosum.

Ovulation.—Usually only one ovum is shed at a time. In animals that have an œstrus, ovulation only occurs at this time. In the human being, probably occurs about once a month, but there is no accurate relation to menstruation, and pregnancy has been known to occur before age of menstruation or after it has ceased. Ovum passes into Fallopian tube, apparently owing to some chemical attraction, probably aided by a current set up by movements of cilia of fimbriæ of tubes.

[EVIDENCE.—
1. In animals with a bicornuate uterus, ova may be liberated from ovary of one side and developed in horn of other side.

2. If ovary is excised on one side and tube on the other, animal may still become pregnant.
3. In human beings where ovary of one side and tube of other have been removed or diseased, in some cases ovum has been found in remaining tube.]

Homotype Mitosis—i.e., normal process of cell division (*Fig.* 27).—

1. Centrosome divides into two parts, connected by a spindle of fine threads, the achromatic spindle.
2. Chromatin forms first a skein, then a rosette.
3. Rosette splits into definite number of V-shaped chromosomes, 24 in number in man, arranged on the achromatic spindle. (Figures vary. Some say 32, or 48.)
4. Each V-shaped chromosome splits longitudinally.
5. Half of each old chromosome now passes into each of the two nuclei, so that each daughter nucleus contains chromatin derived from each chromosome of the parent nucleus. This determines function and characters of the two new cells.
6. By reverse process, each new nucleus is built up, passing through rosette, skein, and resting stages. Centrosome becomes a mere dot.

Maturation of Ovum.—Occurs before or after ovum reaches Fallopian tube.

1. EXTRUSION OF FIRST POLAR BODY.—By heterotype mitosis, there being no longitudinal splitting of chromosomes, so that number is reduced by one-half. Centrosome is extruded.

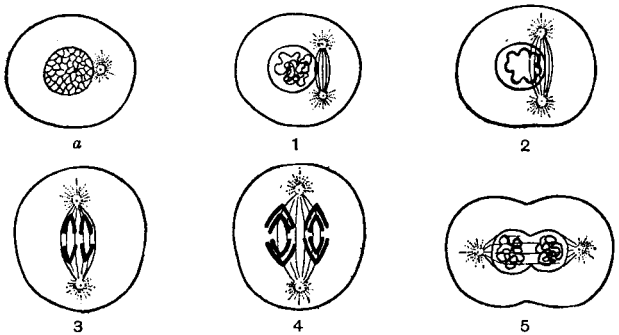

Fig. 27.—Diagram to show homotype mitosis. *a*, Cell before division; 1–5, Steps in the process of mitosis (*see text*).

Maturation of Ovum, *continued.*

PURPOSE OF REDUCING DIVISION.—

a. To get rid of half female chromosomes to make room for male ones.

b. To avert parthenogenesis (i.e., development without fertilization) by extrusion of centrosome. In bees, wasps, etc., where parthenogenesis occurs, first polar body is not extruded.*

2. EXTRUSION OF SECOND POLAR BODY.—By ordinary homotype mitosis (Marshall).

Reason for extrusion of second polar body is unknown.

Fertilization of Ovum.—Usually occurs in Fallopian tube. Spermatozoa have been found alive in tube 14 days after sexual intercourse. When a spermatozoon penetrates ovum, its tail disappears. Head of spermatozoon introduces 12 male chromosomes, while neck contains centrosome. Fertilized cell at once commences to divide and subdivide, so that when it reaches uterus it has attained morula stage. It occasionally happens that the two cells resulting from division of fertilized ovum become separated, and identical twins result. They are always of same sex, and identical in all respects.

ORDINARY TWINS.—Usually due to accident of two ova being fertilized at same time by two spermatozoa. Habit of bearing twins or triplets may descend from mother to daughter, several Graafian follicles being ruptured near same time.

ARTIFICIAL FERTILIZATION.—Introduction of semen into vagina, without coitus, may be followed by pregnancy, in human subject or animals.

PARTHENOGENESIS.—Introduction of male element is not absolutely necessary. In some animals, eggs normally develop at times without fertilization. Some ova, which are normally developed by fertilization with a spermatozoon, can be made to develop by physico-chemical means—e.g., unfertilized eggs of sea-urchins have developed as far as blastula stage by immersion in magnesium chloride. Unfertilized frog's ova can be developed to small tadpole stage by pricking with a fine needle.

[**Causation of Sex.**—Generally speaking, sex is fixed from moment of fertilization, but in some animals (e.g., tadpole) various means of

* There is some variation in the authorities, and in different animals, as to these divisions.

feeding will produce mostly males or mostly females—probably merely a differential mortality. Certain solitary wasps have power of laying male or female eggs at will (Fabre).

THEORY OF X-CHROMOSOME.—In most animals there is an X-chromosome. Always present in ovum, not in every spermatozoon.
With X-chromosome in ovum and in spermatozoon, female results.
" " " " not in " male "

Implantation of Ovum.—When fertilized ovum reaches uterus, it is covered with branching processes, chorionic villi, by means of which it embeds itself in uterine mucosa, which has become thickened and altered to form decidua.

Placenta.—

STRUCTURE.—Chorionic villi from fœtus floating in large spaces in decidua filled with maternal blood. In centre of chorionic villus is a blood-vessel; hence fœtal and maternal bloods are separated from one another by epithelial cells of chorionic villi. There is no communication between fœtal and maternal blood, since in earlier months of pregnancy fœtal blood-corpuscles are nucleated, but not the maternal ones. Chorionic villi show two layers of epithelium, a *syncytium* resting on cubical cells, i.e., *layer of Langhans*.

FUNCTIONS.—

1. NUTRITIVE.—From maternal to fœtal blood pass: (*a*) Amino-acids; (*b*) Carbohydrates; (*c*) Inorganic salts.
   Evidence.—(i) Madder added to food of mother colours fœtal bones; (ii) Sugar has same concentration in the two bloods, indicating diffusion between them.
2. RESPIRATORY.—From maternal to fœtal blood passes oxygen. From fœtal to maternal blood passes carbon dioxide.
3. EXCRETORY.—From fœtal to maternal blood pass urea, ammonia, etc.
   Evidence.—Nitrogenous waste-products have same concentration in the two bloods.
4. GLYCOGENIC FUNCTION.—Excess of sugar is deposited in placenta as glycogen.

Structure of Umbilical Cord.—Two arteries and a vein embedded in a stroma termed Wharton's jelly. *Arteries* contain *impure* blood, *vein pure*.

Menstruation.—Discharge of blood and mucus from uterus, commencing at about 14 years of age (earlier in tropics), and recurring at intervals of about 28 days until about 45 years of age, when menstrual flow permanently ceases (menopause).

Menstruation, *continued.*

CHANGES IN ENDOMETRIUM ASSOCIATED WITH MENSTRUATION.—

STRUCTURE OF ENDOMETRIUM.—

a. Single layer of columnar ciliated epithelium lining uterus.

b. Stroma, and coiling tubular glands.

MENSTRUAL CYCLE.—Divided into 4 phases :—

1. *Premenstrual Phase* (4 to 5 days).—Increased thickness of mucous membrane. Glands enlarged and more tortuous, blood-vessels enlarged, and stroma infiltrated with exudate.
2. *Menstruation* (4 days).—Capillary hæmorrhages and some diapedesis of red blood-corpuscles. Epithelium degenerates and is partly cast off.
3. *Stage of Repair* (7 days).—Mucous membrane returns to normal thickness. Extravasated blood absorbed. Surface epithelium, if denuded, repaired by proliferation.
4. *Quiescent or Resting Stage* (12 days).

[FUNCTION OF MENSTRUATION.—Still doubtful. Probably the enormous demands made on the mother during pregnancy require great preparations of nutriment; if not used, these are expelled by menstruation. Analogous to war-factory whose products are necessarily wasted in peace-time.

Corpus luteum may control premenstrual changes by an internal secretion. If pregnancy occurs, corpus luteum increases in size and uterus continues growing. Otherwise corpus luteum undergoes retrogressive changes and endometrium degenerates, with production of menstrual flow.

Evidence.—

a. Marshall and Jolly find that injection of extract of ovaries taken from an animal at or just before œstrus, into animal not in œstrus, brings on transient condition of œstrus.

b. Allen and Doisy isolated a material from the liquor folliculi of the pig which when injected into spayed rats or mice brought on œstrus.

BLAIR BELL'S EXPLANATION.—Calcium, phosphorus, and other chemicals are regularly stored up for possible pregnancy. If this does not occur, they must be removed.

Evidence.—

a. Considerable amount of calcium in menstrual flow.

b. More calcium in circulating blood before a menstrual period than after it (denied by other workers).]

Effects of Removal of Ovaries.—

1. IN YOUNG ADULT WOMEN.—

a. Sterility.

b. Cessation of menstruation in humans (or of œstrus in animals).

c. Atrophy of uterus, vagina, and breasts.

d. Symptoms of artificial menopause — i.e., flushings, adiposity, and various neuroses. Relieved if a bit of ovary is grafted into abdominal wall.

[In rare cases pregnancy and menstruation have occurred after apparent removal of both ovaries; probably aberrant bit of ovary was left.]

2. IN CHILDREN AND YOUNG ANIMALS.—In young animals, makes little difference except that uterus fails to develop. In children it is never done, therefore results are unknown.

Functions of Ovaries.—

1. Ovulation.
2. Production of one or more internal secretions which :—
   a. Control menstruation. Pressure on an ovary a few days before a menstrual period is expected may accelerate it.
   b. Prevent symptoms of artificial menopause, probably by getting waste products removed. Ovarian extract or ovarian grafting is said to prevent symptoms of menopause.
   c. To some extent control development of other sex organs. Cases of sexual precocity in girls retrogress after removal of an ovary.
3. *Production of Corpus Luteum.*—This provides an internal secretion, and has the following functions :—
   a. Gives rise to the immense overgrowth of the uterus which occurs during pregnancy.
   b. Removal of corpus luteum early in pregnancy in rabbits results in abortion. Not true in women, because both ovaries have been removed at 6 weeks, and pregnancy continued to full time.
   c. Plays some part in development of mammary gland and secretion of milk.

LABOUR.—It is suggested that the ovarian hormone activates the pituitary, which in turn causes uterine contractions; corpus luteum inhibits the ovarian hormone. Labour, therefore, depends on waning of corpus luteum.

LACTATION.

Histology of Breast.—

ALVEOLI.—Lined by cubical or columnar cells which in activity contain fatty granules. It is said that during lactation ends of cells may project into lumen and eventually break off (probably incorrect).

Histology of Breast, *continued.*

DUCTS.—Lined by cubical epithelium. Have unstriped muscle fibres in their wall.

Cause of Lactation.—Development of the breast in pregnancy is probably due to a *hormone* produced by fœtus itself. (A hormone is a chemical messenger carried by blood from one gland to excite activity in another.)

EVIDENCE.—

1. LANE-CLAYPON'S WORK.—Injection of extracts from body of fœtus into virgin rabbit results in genuine development of mammary glands. Similar extracts of ovarian, placental, and uterine tissues have no effect.
2. Case of Siamese twins in which pregnancy and parturition in one was followed by lactation in both. They had a common circulation but separate nervous systems.

   The hormone appears to inhibit mammary *secretion*, since this occurs when hormone is withdrawn by expulsion of fœtus.
3. ACTIVITY OF MAMMARY GLAND IS QUITE INDEPENDENT OF NERVES, because: (*a*) Stimulation of nerves to breast has no effect; (*b*) Pilocarpine and atropine, which act on nerves, have no effect.

It has been suggested that lactation is controlled by a hormone furnished by the corpus luteum.

EVIDENCE.—Pseudo-pregnancy is said to occur in animals, with development of mammary gland, after ovulation without a following conception. But removal of ovaries early in pregnancy in women does not alter lactation.

Maintenance of Lactation.—Due to suction in woman, milking in cow. When these are abandoned, glands undergo retrogressive changes, and secretion ceases in a few days.

Injection of pituitary extract causes increased flow of milk, due to contraction of muscle in wall of ducts, not increased secretion.

HERMAPHRODITISM.

A few cases are on record where both ovary and testis were present in the same (human) subject, or where gonads were male but the general conformation female. In cattle, the genital apparatus may be of male type but the gonads female; apparently this is due to a direct vascular connection in utero between the placentæ of a female and a male twin.

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1673.2 JOHN WRIGHT AND SONS LTD., PRINTERS, BRISTOL.