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Edited by

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Blood—Its Composition in Health and Disease

BY

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THE methods of blood analysis are so perfect and their technique so simple that the quantitative estimation of blood constituents together with a knowledge of physiological composition of blood and of the significance of the actual deviation from the normal is of value in confirming a clinical diagnosis, of still greater value in differential diagnosis, and often of great assistance in prognosis and in controlling the course of treatment.

The change in the concentration of blood urea, uric acid, creatinine and N. P. N. is not diagnostic of any particular condition, as it occurs not only in kidney lesions but in other diseases as well.

Blood consists of formed elements, (red blood cells, leucocytes (W.B.C.) and the platelets) suspended in plasma. The chemical constituents are: (1) constituents that maintain the osmotic pressure; that are responsible for clotting and for transport of O_2 and CO_2; (2) Nutrient and mineral materials enroute to tissue cells; (3) Hormones and vitamins; enzymes and immune bodies (traces); and (4) Waste products on their way to excretory tissues.

Blood Volume.—The average amount of blood in a normal man is about 8·8% of his body weight, *i.e.*, about 4,000—6,000 c.c.—70 to 100 c.c./k. gm. body wt.; of this, plasma is 58% (40-60 c.c.) and the rest constitute the cells. The blood volume varies with age.

It is increased—(1) due to exercise; (2) during pregnancy; (3) splenomegalies; (4) leukemia; (5) polycythæmia and (6) slightly in oedema.

Blood volume is diminished in (1) shock, hæmorrhage and anaphylaxis; (2) rapid severe dehydration as in severe burns, in diarrhœa (cholera), in vomiting due to pyloric stenosis (infantile) and in pernicious vomiting of pregnancy; (3) snake bite; (4) profound toxæmia and (5) in anæmia moderately.

Water content of blood is 77-81% ; of plasma is 90-92% and of the cells 64-65%.

A. ERYTHROCYTES :—The number of R.B.C. in the blood of a healthy male is 4·5-5·5 millions per c.mm. They are *diminished* in number in the various types of anæmias ; and *increased* in erythræmia or Osler Vaquez disease and in erythrocytosis, which is secondary to (1) concentration of blood due to dehydration as in cholera etc. ; (2) chronic anoxia due to residence at high altitudes, heart failure and congenital heart diseases ; lung diseases such as emphysema, fibrosis and pneumonia ; and (3) chronic poisoning by CO_2, arsenic and phosphorus. There is increased number of R.B.C. in new-born infants till 2 weeks of birth.

B. LEUCOCYTES :—In healthy individuals the W. B. C. vary from 7,000—10,000 per c.mm. The count is minimum when the person is at rest.

Leucocytosis occurs physiologically (1) in new-born infants ; (2) during later months of pregnancy ; and (3) after exercise ; and pathologically in (*a*) acute infections ; (*b*) acute intoxications and poisoning ; (*c*) hæmorrhage ; (*d*) leukemias ; and (*e*) in malignant diseases.

Leucopenia occurs in (1) certain infections such as enteric, undulant fever, influenza, measles, kala azar, dengue and sandfly fever ; (2) agranulocytosis due to the depressed function of the leucopoietic tissues ; (3) in cases of poisoning with arsenicals, benzol and mustard gas ; and (4) in certain types of anæmia.

C. PLATELETS :—The average number is from 250,000 to 400,000 per c.mm. of blood and has wide variations in health.

The platelets are reduced in number (below 40,000) in the various types of purpura hæmorrhagica and thrombocytopenia due to inorganic and organic poisons, aplastic anæmia, cachexias and chronic splenomegalies.

D. CHEMICAL CONSTITUENTS :—

Bicarbonate Contents of blood *i.e.*, Alkali Reserve.—Bicarbonate is one of the buffer substances that keep up the H ion concentration *i.e.*, the reaction of blood constant. This bicarbonate content of blood *i.e.*, "alkali reserve" shows CO_2 combining power of blood. It is 55-75 cc. CO_2 per 100 c.c. blood. Estimation of the alkali-reserve is of great value from a prognostic point of view in cases of diabetic coma, in which it is reduced to below 30 c.c. CO_2. Its content is 164 mgm./100 cc. plasma and 112 mgm./100 cc. of cells. *Alkalaemia* is due to excess of the bicarbonate content of blood and occurs (1) during ether anæsthesia ; (2) due to forced breathing (at high altitudes and in cardiac failure) ; (3) ingestion of large doses of alkalies ; (4) gastric dilatation due to pyloric spasm, obstruction due to atony ; (5) infantile vomiting (loss of Hcl), alkalosis due to repeated vomiting or severe diarrhoea ; and (6) high obstruction of the small gut. *Acidaemia* (Increased H ion concentration)—Depletion of alkali reserve *i.e.*, *excess of* H_2CO_3 *in blood* as in (1) morphine poisoning ; (2) during sleep when alveolar CO_2 rises ; (3) in heart failure ; (4) in emphysema or *low bicarbonate content of blood* as in (1) anæsthetics and poisons like CO_2 ; (2) in increased pulmonary ventilation ; (3) in starvation, severe exercise ; (4) diarrhœa and infantile vomiting ; (5) toxæmic vomiting of pregnancy and eclampsia. This lowered alkali reserve is not the cause but the result of eclampsia ; (6) epilepsy ; (7) in treatment of

pyelitis ; (8) diabetes due to accumulation of fatty acids. If less than 20 cc. CO_2, diabetic coma sets in. But the alkali reserve is normal in hypoglycæmia due to hyperinsulinism ; (9) Ch. nephritis, when due to renal failure there is lowered acid excretion and accumulation of acid phosphates ; and (10) uræmia.

Blood urea and N.P.N.—Their estimation forms one of the best guides both regarding diagnosis as well as prognosis, and yields information about renal impairment, though Van Slyke's urea clearance test is more delicate. However, there is no quantitative relationship between the amount of nitrogen retention and the extent of renal damage. Their estimation enables us to foresee a probable uræmia, gives us an indication as to when to evacuate the uterus in toxæmias and also the way for a safe prostatectomy. Figures above 50-60 mgm. are contra-indications for prostatectomy in one stage ; one week after suprapubic cystotomy blood urea becomes almost normal and then the prostate can be removed. Blood urea level is of greater importance not in fully developed uræmia but in incipient uræmia.

Normal blood urea is 20·40 mgm. ; it is 20 in young and 40 or over in older people. It is safe to conclude that 50 mgm. urea or 20 mgm. urea nitrogen is the upper limit and any value beyond this is definitely pathological. Normal blood N.P.N. is 25-35 mgms. Blood urea and N.P.N. usually rise and fall together and have the same significance. These two are within normal limits in pure congestive failure without renal involvement, in early stages of nephrosis and in subacute parenchymatous nephritis ; they are normal in preeclamptic toxæmia and so pregnancy need not be terminated in this condition.

High blood urea and N.P.N. in (1) high protein diet ; (2) hypercalcæmia ; (3) high intestinal obstruction (due to absorption of nucleo-proteins from the gut) ; (4) pneumonia and other infections ; (5) renal diseases :—glomerulo nephritis (first and third stage), acute nephrosis, nephrotic nephritis, polycystic kidney, final stages of arterio sclerotic kidney ; (6) *Uraemia.*—The values are only slightly higher than normal in acute and latent uræmia but much higher in chronic uræmia ; (7) there is marked retention in all cases where there is obstruction to the urinary flow (enlarged prostate etc.) ; (8) they are not markedly increased in toxæmias of pregnancy but the values are certainly higher than the low values of normal pregnancy. There is increase in nephritic toxæmia of pregnancy (pregnancy in chronic nephritis) and if it is above 50 mgm. pregnancy must be terminated ; (9) blood urea and N.P.N. are high before the onset of eclampsia and during eclampsia ; and (10) higher figures than normal are seen in acute abdominal lesions, peptic ulcer, severe gastro-enteritis and prolonged vomiting leading to dehydration, advanced diabetes and coma.

Blood Creatinine.—The estimation of blood creatinine gives reliable information about the degree of renal damage. The normal value for blood creatine is (3-7) 10 mgm./100 cc. and for blood creatinine is 1-2 mgms. Values above 2 mgm. indicate definite pathological condition of the kidneys, 3-5 mgm. indicates considerable renal damage ; if it exceeds 5 mgm. the patient dies invariably in a few months.

Blood creatinine is normal in the second stage of glomerulo nephritis but high in the first and third stages, in cases of prostatic obstruction,

in malignant nephrosclerosis. In renal uræmia it is greatly raised even to 30 mgm.

Amino Acid Nitrogen is increased from 5-8 mgm. in leukemia, acute yellow atrophy of liver and severe nephritis.

Blood Uric Acid.—Normal human blood contains between 2 and 3·5 mgm. of uric acid/100 ccm. There is increase in (1) gout especially during the acute exacerbations ; (2) in nephritis, uric acid is the first nitrogenous constituent to be retained ; then urea and finally creatinine (*Stair case phenomenon*). High figures occur in uræmia ; (3) in severe cases of pernicious vomiting of pregnancy and eclampsia ; (4) in fevers (Pneumonia), leukemia, wasting diseases and rapidly degenerating sarcomata all associated with much nuclear destruction ; and (5) congestive heart failure.

Blood fat and Cholesterol.—Fat exists in blood as : (1) neutral fat ; (2) cholesteride and free cholesterol ; (3) lecithin (·12-14 mgm,/100 c.c. blood). Cholesterol of blood is in combination with unsaturated fatty acids mostly and its normal value is 130-190 mgm. and is equally distributed between plasma and the cells. Blood cholesterol is normal in acute (first stage) and chronic interstitial (third stage) of nephritis, in kidney of essential hypertension, in malignant nephrosclerosis and in "pregnancy kidney." Estimation of blood cholesterol is useful in detecting nephrosis and nephrotic nephritis. Rise in blood cholesterol value is of bad prognosis in diabetic patients.

Hypocholesterolaemia occurs in—(1) all forms of primary and secondary anæmias (pernicious, splenic) ; (2) acute stage of all febrile infections ; (3) in many chronic infections ; (4) acholeuric jaundice; and (5) renal uræmia rarely.

Hypercholesterolaemia : High values—(1) due to ingestion of food rich in cholesterol (eggs, cream, butter and liver etc.) for prolonged periods ; (2) rises after recovery from acute infectious diseases ; (3) in pregnancy it increases from 3rd month till shortly before term with corresponding decrease in cholesterol esters. Blood is normal soon after puerperium ; (4) jaundice of chronic obstructive types ; gall stones ; (5) early malignant disease ; (6) splenomegalies, Gaucher's ; Niemann-Pick's etc. ; (7) arterio sclerosis ; (8) anæmia ; (9) some cases of gout ; (10) in severe diabetes, the most abnormal degree of lipæmia occurs ; blood is milky. In normal people following a normal meal, blood fat increases and this lasts several hours ; in the diabetic this alimentary lipæmia is increased many times and lasts for much longer time ; and (11) blood cholesterol is increased in cases of severe renal impairment such as nephrosis, second stage of glomerulo nephritis, chronic nephritis due to hypertension and arterio-sclerosis.

Plasma Proteins.—Plasma contains albumin, globulin (pseudo and eu), fibrinogen and prothrombin. These maintain the osmotic pressure, viscosity and H ion concentration of blood. Total plasma proteins 6·7-8·2 mgms./100 gms. of plasma of which albumin is 4·6-6·7, globulin 1·2-2·3, fibrinogen 0·3-0·6.

Plasma protein values are normal in acute diffuse glomerulo nephritis., third stage of G. nephritis, uræmia, hypertensive arterio-sclerotic kidney.

Total Proteins low in—(1) infancy due to the low albumin content ; (2) in prolonged starvation and nutritional œdema due to low protein intake ; in tuberculosis and gastro-intestinal disorders that lead to malnutrition ; (3) in certain infections and toxaemic states ; (4) plasma albumin and globulin low in the first six months of pregnancy ; (5) congestive heart failure ; and (6) nephrotic nephritis, second stage of Bright's disease, nephrosis (amyloid, lipoid). In these they are reduced to 3·5-4% due to marked albumin diminution to even 1% so that A—G ratio becomes inverted to 1 : 3.

Oedema occurs when total proteins fall below 5% especially albumin below 2·5%. There is *increase of plasma globulin* in cases of nephrosis, malignancy, infections, anaphylaxis and in muscular activity.

Fibrinogen is markedly reduced in conditions associated with injury to or insufficiency of the liver as in phosphorus or chloroform poisoning or cirrhosis because liver is the principal site of formation of fibrinogen. It is low in typhoid too.

Increased fibrinogen content occurs in the first six months of pregnancy, in septicæmia and pneumonia.

Blood Sugar.—The estimation of blood sugar has enabled us to distinguish between alimentary, renal glycosuria, potential diabetes, treated diabetes. Normally it is entirely active form of glucose but trace of pentose is also present. Glucose is present in the cells as well. Blood sugar varies at different times of the day but the limits usually lie between 80-110 mgm./100 cc. venous blood. But these results obtained by FOLIN and WU method are a bit high by 20 mgms., due to presence of creatinine and glutathione. Thus the "true values" for Glucose are 60-90 mgm. This is for venous blood ; but capillary and arterial blood give identical sugar values. While arterial and venous blood sugar values during fasting are only slightly different but differ greatly after food.

Glucose tolerance test :—Fasting blood sugar in a normal person is 80-100 mgm. 100 c.c. ; half an hour after 50 grams glucose meal it rises to 130-160 mgms. and falls steadily during the next 2 hours. But in a diabetic, the resting sugar value is higher (about 120) and the maximum reaches much above the renal threshold of 180 mgm. and begins to fall only after two hours, becoming normal only after 4-6 hours. Age, exercise, excitement and nausea affect the G.T.T. curve.

Hyperglycaemia—occurs during smoking, as nicotine stimulates the output of adrenaline ; (2) in general anæsthesia ; (3) due to excitement or apprehension ; (4) even slight ingestion of glucose increases it ; (5) breathing high concentration of CO_2, asphyxia and morphinism—which depress the respiratory centre ; (6) experimental puncture diabetes or hæmorrhage into IV ventricle ; (7) injection of Adrenaline raises blood sugar by stimulating the conversion of glycogen in the liver ; hyperglycæmia of emotional origin is due to adrenal secretion ; (8) injection of Pituitrin causes a transient rise as also certain pituitary lesions ; (9) Thyroxine produces hyperglycæmia as in Grave's disease by indirectly depleting liver glycogen rapidly ; and (10) there is increased value in *diabetes mellitus*. In diabetic coma the fasting blood sugar value is very high (300-400 mgm.). In diabetes, the difference between arterial and venous blood sugar content disappears and reappears if Insulin is injected.

Hypoglycaemia occurs—(1) during lactation; (2) due to exercise (in Marathon runner) causing muscle glycogen to be used up; (3) *insulin shock* due to overdosage of insulin. The symptoms, especially convulsions, come on only when sugar falls below 50 mgm.; (4) hyper-insulinism due to tumour (adenoma or carcinoma) of islets or their hypersecretion; (5) liver deficiency diseases such as cancer, acute yellow atrophy, phosphorus and chloroform poisoning, alcohol addiction; (6) recurrent vomiting of children due probably to fatty degeneration of liver; (7) Von Gierke's disease; (8) adrenal cortical deficiency; and (9) just before eclampsia.

Blood Ketones.—100 c.c. blood contains 1·3-2·6 mgm. expressed as acetone, in children it is 16·3 mgm. and in diabetic coma 40-100 mgm.

Blood Calcium and Phosphorus.—Serum calcium content is fairly constant, being 9-11 mgm.%. R.B.C. are devoid of calcium: (*a*) 2 mgm. is in active ionised form; (*b*) half the content is loosely combined with proteins in organic combination, is unionised and non-diffusible; and (*c*) the remainder is active and diffusible. The amount of serum calcium depends on (1) amount absorbed from the gut; (2) parathyroid secretion; (3) vitamin D; (4) concentration of plasma protein; (5) varies inversely with inorganic phosphates; (6) reaction of blood. The serum of infants and of woman during pregnancy or lactation contain more than 11·5 mgm.

Blood calcium rises if parathormone is injected; in arthritis deformans, in otosclerosis and in hyperparathyroidism (generalised osteitis fibrosa cystica) due to oversecretion of parathormone due to tumour of the glands. Serum calcium falls to normal, when the glands are removed.

Blood calcium is low in (1) Rickets due to lack of vitamin D which promotes absorption of calcium and phosphorous from gut; (2) osteomalacia due to deficiency of vitamin D and calcium in the diet in adults; (3) different types of tetany (spasmophilia); (*a*) parathyroid tetany due to extirpation of the glands; (*b*) alkalæmia; (*c*) rickets; (*d*) hyperpnoea. Tetany occurs when calcium falls below 7·5; (4) parathyroid deficiency or extirpation; (5) skin conditions (acne, folliculitis, eczema); (6) in terminal stages of azotæmic nephritis it falls to 6 mgm. even; also in uræmia especially convulsive types. Thus a reduced calcium and increased phosphorus content occurs in uræmia and indicates grave prognosis; and (7) in sprue cœliac disease and renal rickets.

Blood phosphorus (inorganic) content of children is 5-6 mgm. but it is 3-4·5 mgm. in adults. But there is a larger amount of organic phosphorus (lecithine) in R.B.C.—85 mgm./100 c.c. Blood phosphate is always normal in osteomalacia and in some cases of rickets. It is *high* in cases of healing fractures and not in ununited fractures; (2) in parathyroid tetany; and (3) considerably in azotæmic nephritis and in uræmia even to 15 mgm.

Blood phosphate decreased in severe rickets and hyperparathyroidism.

Blood Sodium and Potassium.—Blood plasma contains 330-340 mgm. of Sodium; and 16-22 mgm. of Potassium. R. B. C. contain 420 mgm. of Potassium/100 c.cm.

Plasma Potassium rises to 30 mgm. in the crisis of Addison's Disease, in tetany, acute infections (pneumonia) and uræmia.

Plasma Sodium content is maintained at fairly constant level by adrenal cortical hormone and when there is deficiency of this hormone as in Addison's Disease, the Sodium/Potassium ratio in plasma is changed, the value of Sodium content falling down while plasma Potassium rises.

Sodium is increased in *tetany*.

Plasma Chlorides vary from 350-380 mgm./100 cc. and chloride content of the cells is 130-160 mgm. Slight changes occur during digestion.

Blood chlorides low in (1) alkalosis; (2) renal uræmia due to vomiting; (3) eclampsia; (4) acute intestinal obstruction; (5) crisis of Addison's Disease; (6) during the heat cramps of miners; (7) diabetes; and (8) fevers (pneumonia, etc.).

The chlorides are increased in nephritis but the increase is slight and of little significance and also in cardiac conditions, prostatic obstruction and in eclampsia.

Blood Magnesium.—In adults plasma contains 2·4 to 3·0 mgm. and whole blood about 4·5 mgm. as the R.B.C. also contain magnesium. There is slight decrease in cases of epilepsy.

Blood bromine:—Normal is 0·8—1 mgm. per 100 c.c. and it is diminished in manic depressive psychosis.

Iodine is present in blood to the extent of between one in ten millions and two in ten millions. The value is 8-15 mgm/100 c.c. normally and it is high in hyperthyroidism and low in cretinism.

Plasma Bilirubin:—Normal serum contains ·1-·5 mgm./100 c.c. and in infants 0·6-0·9 mgm. There is only slight bilirubinæmia in catarrhal jaundice; high in biliary obstruction and hemolytic jaundice. If patients have more than 2 mgm. they have jaundice. The value is *low* in secondary anæmia.

Lactic Acid.—5-20 mgm% at rest and it is raised to 100 mgm. in heart failure. It is increased in exercise and eclampsia.

References:

1. Price—Text Book of Medicine.
2. Cameron—Bio Chemistry of Medicine.
3. Cameron—Text Book of Bio Chemistry.
4. Beaumont and Dodds—Recent Advances in Medicine.
5. Greene—Pathology.
6. Samson Wright—Applied Physiology.

Blood and its Diseasses

BY

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Blood, a vital element of the human system, taking its origin from the mesodermic layer of the embryo, slowly and gradually develops and plays an important part to keep the human structure in perfect order.

This viscid fluid maintains the circulation, supplies nutrition and preserves the natural defence of the whole body.

Composition.—Blood consists of red-blood corpuscles (chromocytes or erythrocytes), white blood-corpuscles (leucocytes), blood-platelets (thrombocytes) and liquid plasma. The blood plasma is of greatest importance both in health and disease. It has been principally studied in connection with opsonins, agglutinins, precipitins, antitoxins and lysins and is known to carry in solution many other bodies of vital significance. The shed plasma consists of oxygen, nutrient proteins, carbohydrates, fats, cholesterol and salts as well as a multiplicity of other less-understood substances necessary to normal nutrition, such as hormones, vitamins and waste products,

Life history of blood cells.—One theory is that all the blood cells are derived from lymphoidocytes, the reds branching off in one direction and the whites in another but the commonly accepted view is that the reds originate from the megaloblasts and the whites from the myleloblasts of the marrow.

R.B.C.—In adult, R.B.Cs. are formed from the endothelial cells of the bone marrow capillaries. The endothelial cells, with the help of an unknown agent, are converted into megaloblasts. The P. A. factor produced by the interaction of extrinsic and intrinsic factors of Castle promotes the change from megaloblasts to normoblasts and then to erythrocytes.

The red cells in the healthy normal blood are non-nucleated except in embryonic life and immediately after birth. In man the number is 50,00,500 per cm. The sizes of these cells vary in health and disease. This change is known as anisocytosis.

In certain diseases reds undergo pathological changes. They vary in size, shape and structure.

The pathological red cells are :—(1) Microcytes, (2) Megalocytes, (3) Gigantocytes, (4) Poikilocytes, (5) Normoblasts, (6) Megaloblasts, (7) Gigantoblasts, (8) Microblasts.

Of these the last four are nucleated. The nucleated cells are found in intra-uterine life and few days after birth. They are also found in pernicious anæmia and in severe types of anæmias.

W.B.C.—The white cells evolve from the myeloblasts. The different types of white cells originate as follows :—

Neutrophile—myelocyte becomes the neutrophile.
Eosinophile—myelocyte becomes the eosinophile.
Basophile—myelocyte becomes the basophile.

The large mononuclear cells appear to be genetically allied to the

myelocyte group. The lymphocytes have probably double origin, some coming from marrow and others from lymphoblasts of the lymphoid tissue.

The number of these white cells varies from 6,000 to 10,000 per c.m. The following are the different types of W.B.Cs. found in normal blood :—

Polymorphonuclear—60 to 65%.—Multiple nucleus joined by fine strands of chromatin, cytoplasm is finely granular, the granules being closely packed. It is both amœboid and phagocytic.

Eosinophils—2 to 3%—Cells with multipartite nucleus with large and coarse granules. The nucleus is similar to that of neutrophiles but not so much twisted. It often consists of two lobes joined by a band. It is actively amœboid. It is increased in all helminthic diseases.

Mast cells—·5%.—The nucleus is usually bi or tri lobular. The cytoplasm contains large granules.

Large hyaline (large mononeuclear) 3 to 5%.—The nucleus in kidney shaped or notched with clear cytoplasm. It is amœboid and phagocytic.

Large lymphocytes—5 to 10 %—with round nucleus with clean and nongranular cytoplasm.

Small lymphocytes—20 to 25%—nucleus round, almost fills the cell leaving a rim of clear cytoplasm.

Blood Platelets :—These are discoid bodies concerned in preserving capillary tone and in blood coagulation. They number from 200,000 to to 3,000,000 per cmm. They are especially abundant in the vegetation of acute endocarditis. They are much reduced in number in certain diseases, specially idiopathic purpura, and increased after hæmorrhage and in some of the severer forms of anæmia.

Haemoglobin :—The colouring matter of R.B.C. It is about $2\frac{1}{2}$ grs. (total amount) in normal healthy blood. The severity of anæmias is better estimated by the quantity of hæmoglobin contained in each individual corpuscle than by the number of reds. The amount of Hb in each individual red is the colour index. It is the ratio of the hæmoglobin percentage to the corpuscle percentage.

Chemical substances :—The most important chemical substances present in the blood are urea, sugar, bilirubin. The normal blood contains ·02 to ·05% of urea ; ·09 to 0·12% of glucose, if blood taken after fasting for some hours ; ·15% of glucose, if blood taken after a meal containing carbohydrate. The bilirubin exists in serum in a different state when its presence is due to excessive breakdown of red corpuscles from that when its presence is due to obstruction.

Changes in blood in diseases.—(1) Anisocytosis ; (2) poikilocytosis ; (3) polychromatophilia ; (4) leucocytosis ; (5) leucopenia, and (6) change in hæmoglobin. The changes in R.B.C. and hæmoglobin have already been mentioned. I shall describe below the W.B.C. changes.

Leucocytosis :—The leucocytosis helps the resistance power of the body against bacterial invasion by increasing the number of phagocytes by chemotaxis process. The leucocytosis may be physiological and pathological. The physiological leucocytosis may occur from 3 to 4 hours after each meal but it soon passes off. It may occur after administration of certain drugs, in pregnancy and childhood. The pathological leucocytosis

is the increase of leucocytes lasting sufficiently long till the leucocytes reach over 10,000 per cmm. This leucocytosis may be general or of a particular type. The main change in general leucocytosis is an increase in polymorphonuclear cells. It occurs in all general infections (except enteric without complications, measles, malaria, mumps, influenza, miliary, tuberculosis and leprosy). The particular of single type of leucocytosis are: —(1) Neutrophilecytosis ; (2) lymphocytosis ; (3) largemonocytosis ; (4) eosinophilecytosis and (5) basophilecytosis.

Leucopenia :—The fall in the total leucocytes below 5,000 per cm. is leucopenia. It occurs in pernicious anæmia, in very severe anæmias, in kala-azar, in enteric fevers, in measles, in typhus, in pneumonia, and in malignant diseases of œsophagus. It has also been observed after administration of certain drugs *e.g.*, Quinine large doses, Atropin etc.

Blood, an agent for diagnosis :—Blood is an important agent for diagnosis of diseases : The following are the most important blood tests and methods adopted for the diagnosis of diseases :—

Serum tests :—

(1) Aldehyde test } for kala-azar.
(2) Chopra's test }
(3) Wasserman Reaction } for syphilis.
(4) Khan's test }
(5) Widal test for enteric.
(6) Erethrocyte sedimentation rate test and nuclear count for T. B. lung.
(7) Blood culture for septic diseases.
(8) Chemical examination of blood for bilirubin, urea and sugar.
(9) Estimation of fragility of R.B.C.
(10) Estimation of coagulability of blood.
(11) Examination of blood for parasites.
(12) Examination of blood for total R.B.C. and W.B.C.
(13) Examination of blood for different W.B.C.
(14) Estimation of hæmoglobin.

I hope it would not be out of place if I point out here how blood helps in diagnosing different diseases from the blood pictures given below. Only important diseases are mentioned here :—

Cholera :—R.B.C. 7 to 8 millions per c.m. ; W.B.C. 15,000 to 2,000 per c.m. Definite decrease in the percentage of lymphocytes and increase in the percentage of large mono.

Malaria :—In malaria the general blood picture is one of a rapidly progressing anæmia, R.B.C. in extreme cases falling to 50% or less and Hb. so low as 25%. Just before the attack leucopenia is noticed, at the height of attack moderate leucocytosis, later on leucopenia with relative increase in mononuclear upto as much as 20%.

Pernicious anaemia :—The blood is thin and pale. Total quantity of blood is unaltered. The specific gravity is lower. The number of R.B.C. is often low and less than 1,000,000 per c.m, ; the shapes and sizes of cells are varied, increase of cells above the normal size is very characteristic, the staining reactions abnormal ; there are always present nucleated red

cells both normoblasts and megaloblasts. The colour index is high. The W.B.C. is diminished. Common figure is from 2,000 to 4,000 per c.m. The blood platelets are few in number. There is a decrease in polymorphonuclear cells.

Kala-azar :—The general blood picture is one of a rapidly progressive anæmia. R.B.C. in extreme cases fall to about 50% of the normal. The Hb. is proportionately diminished to the R. B. C. Marked leucopenia. W.B.C. 2,000 per c.m. or under. Large mono cells are increased but not to such an extent as in malaria ; 8 to 12% is a fair average.

Typhoid fever :—There is leucopenia with relative preponderance of the lymphocytes. The eosinophiles may be found absent sometimes.

T. B. lung :—The differential count according to HOUGHTON. The monocyte represents tubercle formation, the neutrophil represents tubercle undergoing abscess formation, and the lymphocyte represents the healing process of the tuberculous lesion. A relative lymphocytosis appears to indicate a good potential resistance to the disease though there are some exceptions to this rule.

Small-pox :—There is an increase in total number of leucocytes 15,000 to 20,000 per cmm. The increase being largely of poly and mono-nuclear cells and to a lesser extent of eosinophils. Marked secondary anæmia develops rapidly during the progress of disease. In severe cases normoblasts have been found in large numbers, which is a very unfavour-able sign.

Biliary cirrhosis (infantile) :—W. B. C. 10,000 to 20,000 per cm. R.B.C. 3 to 4 millions per c.m. R.B.C's. are very fragile. Hb. 60 to 70%. poly 22 to 42%, lympho small and large 44 to 60 %, mononuclear, 7%, zosino 2%, mast cells 1%.

Blood, a therapeutic agent.—Now-a-days blood is extensively used for the treatment of diseases. In the present war blood is an important factor in the treatment of hæmorrhages and shock.

Blood transfusion.—Whole blood or citrated blood is an ideal for trans-fusion where all the elements of blood are required to fulfil the loss sustained by acute hæmorrhage. This may be either used fresh or preserved.

Plasma or serum transfusion :—It is better than whole blood in shock without hæmorrhage. Plasma is an ideal therapeutic agent to combat shock. Plasma can be separated, filtered and used at once or stored in a refrigerator for future use or dried by various processes and later on redissolved and used. Transfusion of plasma is not usually attended with any reaction.

Haemoglobin - Ringer.—Used to give some organic iron to the system. This is washed R.B.C. hæmolysed and filtered with Ringer solution.

R.B.C. suspended in Isotonic Saline.—Used as a substitute for blood transfusion.

Diseases of blood —The following are the diseases of blood in short. It is not possible to discuss all these diseases in detail here. I only mention the diseases with their definitions.

Anaemia.—Classification —I. Due to deficiency. II. Due to inter-ference with blood formation. III. Due to hæmolytic processes.

GROUP I.—High colour index anæmia and low colour index anaemia. Both are the results of a deficiency of one or other of the factors essential for blood formation. A reversion to megaloblastic blood formation occurs and a hyper chromic macrocytic anaemia results when an insufficient supply of the specific anti-anaemic factor found in liver is available to the bone marrow. This insufficiency may arise from different causes, that is inadequate food intake, defective gastric secretion or imperfect absorption from alimentary tract. It is not surprising that a similar blood picture may occur in widely different diseases *e.g.*, Addisonian pernicious anaemia. Similarly hypochromic microcytic anaemia occurs when an iron-deficient diet is eaten over prolonged intervals; when iron absorption is defective, or when increased demands are present as in pregnancy menorrhagia etc.

GROUP II.—Includes toxic causes.

GROUP III.—Includes two forms of acholuric jaundice familial and acquired, as well as the anaemias secondary to intravascular haemolysis such as in malaria or in haemolytic poisons, *e.g.*, snake venom, etc.

Chlorosis.—A disease, peculiar to young women, characterised by an anæmia due essentially to a diminution in the amount of hæmoglobin.

Pernicious Anaemia.—A severe progressive anaemia of unknown aetiology characterised by destruction of R.B.C., a high colour index and a leucopenia.

Leukaemia.—A disease characterised by increase of one or more of the leucocytic elements of the blood.

Purpura.—It is a spontaneous extravasation of blood in and beneath the skin and mucous membrane, of uncertain aetiology, more particularly to denote a disease in which extravasations are the chief symptoms.

Haemophilia.—It is a hereditary disease of males characterised by a tendency to uncontrollable bleeding, either spontaneous or arising from wounds, which in normal persons hardly bleed at all.

Policythaemia.—A condition characterised by the presence of more than 5,000,000 R.B.C. in the c.mm. of blood.

Chloroma.—A sarcomatous growth of marrow-like tissue with a green tint invading the bones, specially the skull accompanied by changes in the blood resembling leukaemia.

Anaemia pseudo-leukaemica infantum.—A disease of infants characterised by great enlargement of the spleen, a high degree of anaemia and the constant presence of myelocytes.

Other haemorrhagic diseases.—(1) Haemorrhage due to congenital syphilis, (2) melœna neonatorum, (3) epidemic haemoglobinuria, (4) Buhl's disease, and (5) haemorrhage into the suprarenal capsules.

In conclusion, I express my heartfelt gratitude to those authors whom I have freely quoted to complete this article.

References :

1. Manson's Tropical Diseases,
2. Osler's Practice of Medicine.
3. Price's Practice of Medicine.
4. Hutchison & Rainy's Clinical Method
5. Harry Campbell's Aids to Pathology.
6. Medical Annual 1934.
7. 'Antiseptic' Vol. 37 No. 7.
8. 'Antiseptic' Vol. 36 No. 9.
9. 'Antiseptic' Vol. 39 No. 11.
10. 'Antiseptic' Vol. 34 No. 5.
11. 'Antiseptic' Vol. 34 No. 7.
12. 'Antiseptic' Vol. 34 No. 9.

normal rabbit's marrow in comparison to one white cell to 1000 red cells in the peripheral blood of the rabbit. In men, SCHILLING found 44% myeloid to 36% erythroid cells in the marrow. A study of the different myeloid and erythroid cells in the marrow gives a very interesting finding. The least mature cells of the two series, *i.e.*, the myeloblast of the myeloid series and the early erythroblasts of the erythroid series are present only in very small numbers. The most mature phase, on the other hand, *i.e.*, the myelocytes of the myeloid series make up about 85% while the corresponding cell, the normoblast of the erythroid series makes up about 70%. These marrow cells supply the leucocytes and erythrocytes to the peripheral blood.

It has been observed that considerably less erythroid marrow is required to maintain the normal level of 5 million red cells per c.mm. in peripheral blood than is necessary for the myeloid marrow to maintain the normal level of 5000–8000 leucocytes per c.mm. of blood. The reason is believed to be that the red cells are long-lived and performtheir function within the vessels, while the leucocytes are much short-lived and that they are constantly being transported to distant parts for extravascular functional activity where they are mostly destroyed and so require constant replacement. The bone marrow thus comes to be the chief site of origin of the blood cells. If the blood cells, which form the vital constituent of mammalian existence, *i.e.*, the erythrocytes, the granulocytes and the blood platelates, are taken into consideration, bone marrow forms the only source of these cells in extra-uterine life. The clasmatocytes, the monocytes and the lymphocytes also arise in the bone marrow but the lymphnodes, spleen, liver and diffuse connective tissue from the normal sites of their development. The liver, stomach and endocrine glands (particularly the pituitary, thyroid and the adrenals) play an indirect role in hæmatopoiesis, particularly erythropoiesis.

A diagram *(vide page 563)* showing the origin and relation of blood cells is presented here. The origin of the blood cells takes place from the undifferentiated mesenchymal cell, the reticulo-endothelial cells (R.E. cell). The R.E. cell is shown as two cells, the connective tissue reticulum (R) which divides by mitosis and serves as the stem cell for the four commonly recognised forms of white blood cells, the granulocytes, the monocytes, lymphocytes and the blood platelets. These form the myeloid series. The endothelium (E) on the other hand, lines the intersinusoidal sinuses and produces erythro-poiesis in which the hæmoglobin—containing oxygen-carrying erythrocyte is the final stage. This is the erythroid series.

Both the myeloid and the erythroid series are divided into 5 zones separated by circular lines according to the formation of the different types of cells. Thus the zone I represents the primitive reticulo-endothelial cell R and E. The zone II represents the stage of proliferation in which the blast cells, myeloblasts (MB) of the myeloid series and megaloblast (MG) of the erythroid series show multiplication by mitosis. The zone III represents the stage of granulation in the myeloid series forming the myelocyte (MC) and stage of hæmoglobinization in the erythroid series forming the late erythroblast. The early erythroblast is not shown as it behaves like megaloblast as it multiplies by mitosis and does not contain hæmoglobin. The late erythroblast, on the other hand, does not multiply by mitosis and contain hæmoglobin. The zone IV represents the stage of ma[redacted]tion. Thus in the myeloid series from myelocyte (MC) appears

neutrophilic, eosinophilic and basophilic myelocytes. From the myeloblasts originate the megakaryocytes, the monoblasts, the lymphoblasts. In the erythroid series, the erythroblast (EB) matures into normoblast (NB) and the reticulocyte (RC). These are all the cells of the bone marrow and are the precursors of the cells circulating in the peripheral blood. Thus reticulocytes (RC) form erythrocytes (EC), megakaryocytes form blood platelets (PL), myelocytes (MC) form neutrophiles (NP), eosinophiles (EP), basophiles (BP), monoblasts and lymphoblasts form monocytes (MC) and lymphocytes (LC) respectively.

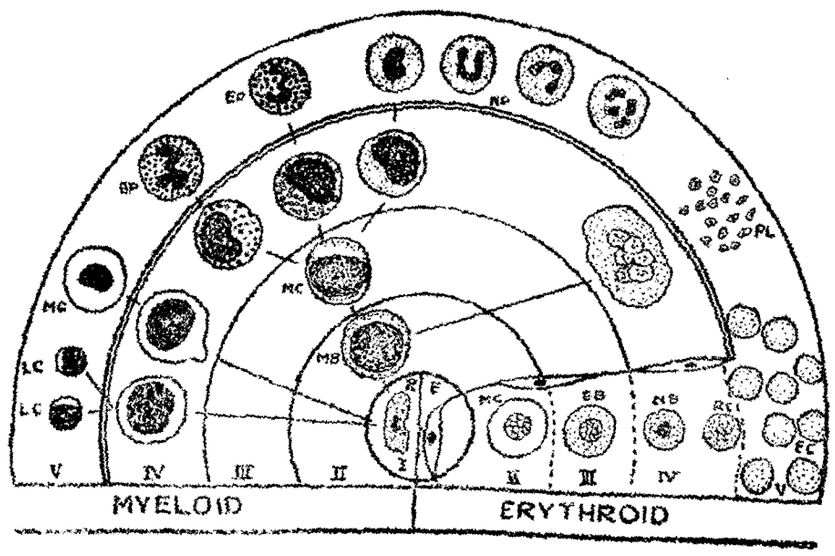

Figure showing the role of bone marrow in Haemopoiesis:

I. Reticuloendothelium—the mother cells.
II. Stage of proliferation.
III. Stage of granulation (Myeloid) and hæmoglobization (Erythroid).
IV. Stage of maturation.
V. Stage in peripheral circulation. *(Description in text, vide page 562.)*

This function of the normal bone marrow regarding the origin and relation of blood cells is repurcussed in every instance of disorders of blood. Thus the cytological organisation of the bone marrow in the different zones of its activity as shown in the diagram form the basis of the proper understanding of the problem of diseases which manifest themselves in the change of the blood picture, all depending on the change of functions of the marrow with respect to the origin, maturation, delivery and other changes of the cells of the marrow.

Role of bone marrow in abnormal erythropoiesis.—An attempt is now made to correlate the pathology affecting the different zones of the marrow activity as shown in the diagram, and the common disorders of the blood.

1. *Pathological conditions affecting the stage of proliferation.*—

A. HYPOFUNCTION: Etiology:—Mainly toxin *e.g.*, X-rays and [redacted], nephritis, syphilis, chronic infections and chemical poisons *e.g.*, *etc.*

Pathology :—Inability of the marrow to proliferate and utilize the hæmatinics.

Diseased condition :—Toxic or aplastic anæmia.

Blood changes :—Normochromic or hypochromic, normocytic or microcytic anæmia.

B. HYPER FUNCTION: Polycythæmia vera:—Uncontrolled marrow hyperplasia of the erythrogenic tissue and also uncontrolled production and delivery of the circulating erythrocytes.

2. *Pathological conditions affecting the stage of maturation.*—

A. IN THE MEGALOBLASTIC STAGE: Etiology :—Deficiency of hæmopoietic principle or the erythrocyte maturation factor (E.M.F.)

Diseased conditions :—Pernicious anæmia, tropical nutritional anæmia, pernicious anæmia of pregnancy, sprue, cirrhosis, or yellow atrophy of liver (failure to store hæmopoietic principle).

Blood changes :—Hyperchromic macrocytic anæmia with megaloblastic hyperplasia in the bone marrow.

Pernicious (macrocytic) anæmia:—Arrest of maturation of R B.C. at the megaloblastic level due to the absence of the extrinsic factor in the diet. Absence of significant changes in the granulocytes in the blood indicates relative increase in erythroid elements in the marrow than the myeloid. This shows that each of the cell typed in the marrow is susceptible of individual stimulation or inhibition.

Bone marrow becomes hyperplastic in order to compensate for the deficiency in maturing the cells. The lack of E.M.F. leads to a release of cells into circulation which are abnormal in shape and size and due to the lack of the same factor red cells are destroyed in excessive number in the marrow, thus more iron is set free and more bile pigment is formed than normal.

B. IN THE ERYTHROBLASTIC STAGE: Etiology :—Deficiency of iron, copper, vitamin C, thyroxine etc.

Diseased conditions :—Chlorosis, nutritional anæmia of infancy, anæmias of pregnancy, scurvy, myxœdema, thyrotoxicosis etc.

Blood changes :—Hypochromic microcytic anæmia.

Bone marrow becomes more active than normal, but due to deficiency of iron the red cells contain less hæmoglobin than normal.

3. *Pathological conditions affecting the stage after delivery in the blood circulation*—

A. HÆMORRHAGE: Etiology :—Injury to the blood vessels or abnormality of blood, ankylostomiasis.

Diseased conditions :—Hæmorrhages, acute or chronic, hæmophilia, purpura etc.

Blood changes :—Hypochromic, normocytic or microcytic anæmia.

Hæmorrhage or blood destruction leads to increased delivery of new mature erythrocytes with secondary increase of platelets and granulocytes. In chronic long continued hæmorrhage smaller less uniform cells are produced by the marrow and if there is low intake of iron, the amount of hæmoglobin per red cell is sharply reduced.

Hypochromic microcytic anæmia due to hæmorrhage with severe granulopenia :—This indicates that both the myeloid and erythroid marrow have been involved simultaneously. In these cases administration of liver and iron often leads to increased erythropoiesis, the granulopenia remaining the same. A course of nucleotide injections often lead to granulocytic recovery. This shows that both the myeloid and erythroid marrow respond to separate stimuli, thus affecting the two cellular types separately.

Bone marrow becomes hyperplastic in order to compensate the loss of red cells and also of hæmoglobin. The cells delivered into the circulator thus becomes smaller in size and often contain less hæmoglobin. Due to loss of blood through haemorrhage less haemoglobin is liberated as there is less destruction of R.B.C. in the circulation, so less iron is set free and hence less bile pigment formed. The erythrocytes show evidence of normal regeneration, *e.g.*, variable degrees of anisocytosis, polychromatophilia, hypochromasia and reticulocytosis.

B. HAEMOLYSIS:—Etiology and diseased conditions:—Infective (malaria, blackwater fever, Weil's Disease), toxic (lead and other chemicals), intrinsic (acholuric jaundice, sickle-cell anaemia).

Blood changes.—Hypochromic monocytic anaemia.

In malaria, the bone marrow is normoblastic but more red cells are destroyed in the circulation than normal, so more bile pigment is formed than normal.

Role of Bone marrow in abnormal leucopoiesis.—

1. *Pathological conditions affecting the stage of proliferation.*—

A. HYPERPROLIFERATION: Etiology :—Leukaemia (leucosis) and new growths of the leucopoietic system.

Leukaemia leads to anaplastic reversion of the bone marrow to the most primitive of the myeloid cells with inability of the cells to devolop specific granulations. This hyperplasia may also restrict erythropoiesis with production of anaemia.

Diseased conditions are mainly the hyperproliferation as—

(1) Myeloblastoma which may be classified as (*a*) myeloblastic leukaemia, (*b*) neutrophilocytic, basophilocytic or eosinophilocytic leukaemia, and (*c*) myelosarcoma.

(2) Lymphoblastoma which may be classified as (*a*) lymphoblastic leukaemia, (*b*) lymphocytic leukaemia, (*c*) lymphosarcoma, (*d*) lymphogranuloma (Hodgkin's Disease).

(3) Monoblastoma.—(*a*) monocytic leukæmia, (*b*) monosarcoma.

(4) Megakaryoblastoma.—(*a*) Megakaryoblastic leukaemia, (*b*) megakaryocytic leukaemia.

(5) Plasmacytoma.—*(a)* plasma cell leukaemia, *(b)* plasma cell myeloma, *(c)* multiple myeloma.

Blood changes,—Appearance of huge number of the different types of cells in peripheral blood and also in the bone marrow, spleen, liver, lymphatic glands, etc.

B. HYPOPROLIFERATION: Etiology :—Toxins, *e.g.* X-rays, radium, arsenicals of Salvarsan group, drugs of Sulphonamides group, inanition, etc,

Diseased conditions and blood changes.—Aplastic condition of the leucopoietic tissue resulting in great diminution of granulocytes, *i.e.*, leucopenia and granulopenia. Immature granulocytes may appear in blood with occasional lymphocytosis.

1. *Hypoplasia of myeloid marrow by poisoning* :—Certain poisons, *e.g.*, Benzol, Arsenicals, Radium and X-rays, and certain infections produce depletion of the marrow particularly of the cells of the myeloid series in the zone of proliferation producing hypoplasia which may also produce thrombopenia leading to purpuric manifestations. X-rays have selective destructive effect on the lymphogenic tissue, *e.g.*, in enlarged lymph glands and spleen. It also affects the bone marrow affecting first the granulocytes and platelets and latter the red blood cells. During regeneration, erythroblastic reaction starts early. It is said that X-rays stimulate mitotic activity in the myeloblasts while they exert a destructive influence on the more mature myelocytes, thus explaining the usefulness of X-ray therapy in chronic myelogenous leukaemia than in the more acute stage of the disease.

2. *Pathological conditions affecting the stage of maturation* : Etiology:—Infections mainly.

Diseased conditions and blood changes:—Pyogenic infections lead to increase of neutrophiles, helminthic infestations increase eosinophiles, protozoal infections monocytes, and typhoid and similar affections lymphocytes.

3. *Pathological conditions affecting the stage of delivery into the circulation* :—

Etiology:—Foreign protein (*e.g.*, unclean derivatives) injections producing increased redistribution.

Blood changes:—Improvement of leucopenia by mobilisation of the reserve for emergency demand. There exists always a reserve of mature cells already delivered by the marrow into the circulation but not serving any function, being entangled into inactive regions of the circulation or in splenic sinuses. These are normally requisitioned when demand occurs or may be mobilized by administration of Adrenalin, increased vasomotor contraction, etc.

The role of bone-marrow in hæmopoiesis may be summarised in a tabular form as follows:

Factors affecting erythropoiesis.

Stage	Proliferation	Maturation			Delivered blood cell
Marrow cell	Endothelium	Megaloblast	Erythroblast	Normoblast / Reticulocyte	Erythrocyte
Etiology	Toxin	E. M. F. (Erythrocytes maturation factor)		Fe, Cu, Vit. C.	Hæmolysis (Blackwater fever), hæmolytic jaundice, hæmorrhages, purpura
Diseased condition	Aplastic anæmia	Macrocytic anæmia		Macrocytic hypochromic anæmia	Hypochromic anæmia with evidence of blood regeneration

Factors affecting granulopoiesis.

Stage	Proliferation	Maturation		Delivered blood cell
Marrow cells	Reticular cells	Myeloblast	Myelocyte	Granulocyte
Etiology	Toxin X-ray inanition	Infection		Foreign protein, *e.g.*, nucleic acid by increasing redistribution.
Diseased condition	Agranulocytosis	Granulocytosis, neutrophilia in septic infection, Eosinophilia in helminthic, Monocytosis—protozoal, Lymphocytosis—typhoid, etc.		Granulocytosis Lymphocytosis Monocytosis

The Spleen and Diseases of the Blood

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Some anatomical points.—The spleen, being developed in the mesogastrium behind the stomach, is intimately connected with the posterior border of the primitive stomach, which rotates to the left and becomes the left border, or greater curvature. Part of the mesogastrium becomes the gastro-splenic omentum, a peritoneal fold of varying size which attaches the spleen to the stomach, and contains the splenic vessels. The splenic vein, a large and very fragile vessel, runs in this fold across the back of the abdomen to join the portal vein. The blood from the spleen thus goes to the liver together with that from the alimentary system as a whole. But as far as is known the spleen has no alimentary function. Its chief work is the destruction of red blood corpuscles that are worn-out, and the formation of lymphocytes. If it is removed, the lymphatic glands all over the body become enlarged, apparently in order to take over function from the spleen. Otherwise removal of the spleen seems to have no effect on the working of the body. In some diseases in which there is an excess of destruction of the red blood cells, removal of the spleen produces a complete cure. In this article, injuries, abscesses, and cysts of the spleen will not be considered, but a general sketch will be given of the chief diseases in which splenectomy is indicated, and other blood diseases associated with the spleen.

Malposition of the spleen.—As already mentioned, the spleen may be abnormally mobile, and may give rise to symptoms due to its dragging on the pedicle which is a highly sensitive part of the peritoneum. These symptoms consist in vague pains in the left abdomen, with no relation to food, but relieved by lying down. The spleen will be palpated in the abdomen, in various positions, and can be detected by its notch. It will be seen to be movable around a centre which represents the position of its pedicle. If the spleen is in the abdomen, the dulness in the left chest in the normal position of the spleen will be absent. If the symptoms are

distressing to the patient, the spleen may be fixed in its proper position by operation. A horizontal incision is made from inside the abdomen through the peritoneum only, in the neighbourhood of the twelfth rib, and the peritoneum is stripped downwards from the incision to make a pocket of the right size and shape to hold the spleen. The spleen is placed in this and gently fixed there with a few stitches.

Tumours of the spleen.—The commonest tumour of the spleen is sarcoma. This is usually first detected by the presence of ascites which, on being tapped, yields a blood-stained fluid. The spleen will usually be palpable as a rounded, rather movable tumour in the left side of the abdomen. Mononuclear, round cells may be found in the ascitic fluid. The treatment of sarcoma or other tumour of the spleen is splenectomy.

Other enlargements of the spleen.—There are many diseases in which enlargement of the spleen occurs, but only in some of them it is advisable to remove the organ, and in at least one of them it is imperative to do so as being the only hope, and that a very certain one, of cure.

Malarial enlargement of the spleen:—This is by far the commonest cause of splenic enlargement in the tropics. The spleen is firm in consistency, and its edge is easily palpable. It is very liable to injury, and if damaged by a blow the mortality is over 50 per cent. Liability to damage is the chief indication for splenectomy in cases of malarial spleen. Young people stand the operation very well, but older men do not, and are apt to have very friable splenic veins, so that in them splenectomy is usually contra-indicated.

Anti-malarial treatment, with Iron and Quinine and Arsenic should always be given a chance to reduce the size of the spleen. If this does not occur, splenectomy may be indicated, but its risks should be pointed out to the patient, and the operation is best reserved for those who are under 35 years of age. It must of course be determined that such enlarged spleens are due to malaria, and not to kala-azar. The mortality of splenectomy for malarial spleen if not complicated by adhesions, is less than 5 per cent. in young people. Personally I have never lost a case in young patients.

Pseudo-Leukæmia of infants.—This is an enlargement of the spleen in young children due to a secondary anæmia. The spleen is a blood-forming organ in fœtal life, and in young children it is capable of taking on this function again if called upon to do so by anæmia. The red blood cells in this condition number about 1 to 2 millions per c.mm., the white corpuscles being 20,000 to 80,000. The colour index is low, 0·5 to 0·7. Most of the white cells are lymphocytes. Spleen and liver are both enlarged considerably. The treatment of this condition is medical, Iron, Arsenic, and fresh air being combined with a diet rich in vitamins.

Gaucher's splenomegaly.—The spleen in this rare disease slowly enlarges until it is of immense size. It may be noticed in the first year of life or even as late as the thirtieth. It is familial, involving several members of one generation, but not being transmitted to the next generation. There is a moderate anæmia, with leucopenia. The treatment is splenectomy, which should be done before the spleen becomes too large in size. Histologically the spleen will be found to have numerous large hyaline cells, each with some 20 small nuclei, the so-called Gaucher cells.

Splenic anæmia.—The spleen in this disease becomes gradually enlarged, giving rise to no symptoms, until in a few years a secondary anæmia is produced, and hæmorrhages in the gastro-intestinal tract take place. Death usually occurs about ten years from the onset of the disease. In the later stages of the disease cirrhosis of the liver occurs, and ascites is a grave sign, as it occurs near the end of the illness, and signifies that it is then too late to do any useful treatment. In the second stage of the disease, before the liver enlarges, the blood count shows a red cell count of 2 to 3 millions, and a leucopenia, the white cells being about 4,000 to the cubic millimetre. The blood platelets may be normal or low, colour index is low, and there is poikilocytosis. The only cure for this disease is splenectomy, and it should be done before the liver is badly affected. The spleen will be found to have adhesions to the surrounding organs, especially the diaphragm. The mortality of the operation is about ten per cent. and the prognosis in those cases who have a low platelet count (below 2,00,000) is good. Others sometimes get thrombosis of the mesenteric or portal veins sometime after the operation. When the liver has become enlarged, a condition known as Banti's disease, operation will fail to save the patient's life.

Acholuric or hæmolytic jaundice.—In this disease there is hæmolysis of the red cells, which gives rise to jaundice as a prominent symptom, but without any bile in the urine. The spleen is usually enlarged, but not always. There are two types of the disease, congenital and acquired. In the congenital type, there are often no symptoms except the yellowness of the eyes and finger-nails, and slowly enlarging spleen. Occasional crises occur with pain very like a biliary colic. Splenectomy cures the condition, which is a primary splenic disease, in which the destruction of the red corpuscles takes place in the spleen.

The acquired form of the disease occurs usually in adult life and is more rapid in its course. The attacks of pain are more frequent than in the other type, and last for a longer time. Splenectomy is often but not invariably curative in this type of the condition, but is indicated, for no other cure is known. The blood count is simply that of a mild secondary anæmia, but in addition to this, there is a greatly increased fragility of the red corpuscles. They rapidly undergo hæmolysis in a hypotonic salt solution. Owing to the replacement of the destroyed red cells by immature ones from the bone-marrow, the red cells show reticulocytosis, as many as three quarters of them being reticulated. The leucocyte count is normal.

Leukæmia.—In spleno-medullary leukæmia, the spleen may be immensely enlarged. There is a slowly increasing leucocytosis, the white cells rising to 500,000 or even more. There is secondary anæmia. The disease usually lasts some 5 or 6 years, but may be more rapid. It is invariably fatal, but cases may be kept alive and fairly healthy by exposures to the X-rays at intervals. The spleen and the long bones are radiated daily for five minutes or so for a period of ten days, this treatment being repeated every six months or so. Splenectomy is sometimes of benefit, but only after radiation has been given. It bears a considerable risk in this condition. The present writer has kept cases of this type, if leukæmia alive for ten years, by means of repeated X-ray treatments, usually given every six months.

Purpura hæmorrhagica.—There are two forms of this disease—

1. *Acute form*:—The patient has a sudden attack of severe

bleeding, under the skin, from the nose and mouth, and from the anus. There is blood in the urine, vomit, and fæces. The blood shows a low platelet count. In 1937 the writer had a male patient aged 12 who had a severe gastric hæmorrhage twice every year. Splenectomy completely cured the condition.

2. *Chronic or relapsing form*:—The bleeding is not so severe, and occurs at intervals of some months, a succession of milder attacks extending over a few weeks being followed by a period of complete remission of symptoms.

The treatment of both these conditions is splenectomy. It has a higher mortality (20 per cent. or so) than in some other conditions, but is the only cure of the condition. All cases with a very low platelet count (below 50,000) should have splenectomy performed. The spleen is not enlarged, but its abnormal working seems to be the real cause of the disease.

The operation of splenectomy.—Except for the suture of wounds in the spleen, and the method of fixing a movable spleen already described, splenectomy is the only operation likely to have to be performed on the spleen. The best incision is a long vertical one, splitting the left rectus in its inner third, and extending from the top of the rectus muscle as far down as may be desired.

The elaborate incisions described in many text-books are not superior to this simple one, and have the great disadvantage that they involve the cutting of many nerves to the abdominal wall. The spleen is first examined gently to see if there are any adhesions around it. If there are, the operation will be more difficult, and in the presence of very dense adhesions it may be impossible.

First, the adhesions will have to be separated all round. This is best done gently with the fingers. A few may require clamping and tying as they may contain vessels. The gastrosplenic omentum is then divided in its lower part, between clamps. The outer part of the lieno-renal ligament is then divided. The spleen can then be drawn out of the wound, or at least moved about to render its pedicle accessible. In tying the pedicle, the splenic artery must be clamped first. This will allow some of the blood to drain into the splenic vein and save some loss of blood to the patient. The remainder of the pedicle, containing the splenic veins, must then be clamped with a double set of clamps, and the veins dealt with very carefully and tied firmly with the thickest possible silk. Thin silk or catgut may cut right through the vein; thick gut may slip off; thick silk or linen thread, therefore, should always be used on the splenic pedicle. The spleen is removed with clamps on the vessels, and at once transferred to the upper end of a jug of suitable size, sterile, and containing 100 c.c. of 4% Sodium Citrate solution. The clamps are then taken off, and the blood from the spleen is allowed to drain into the jug. It is then available in case of hæmorrhage or collapse, and a large spleen can in this way be made to provide a pint or two of blood. Great care must be taken in observing a splenectomy patient for a few days after the operation, and especially during the time of reaction from a spinal anæsthetic. Prompt diagnosis of bleeding from a slipped ligature will enable re-operation to save life, neglect of bleeding until the patient is markedly distressed from loss of blood will render re-operation so risky as to be almost certainly fatal. Rise in the pulse rate should be noted at once, and air hunger must not be awaited—it is a grave sign.

Anæmias in the Tropics

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IT is no exaggeration to say that every second man you meet on the street is a victim of anæmia. The sallow pale appearance, emaciated tissues, swollen body and general debility is much too a common picture to miss. Apart from socio-political reasons, tropical climate exercises a certain amount of strain on the hæmopoietic system. Ill-nutrition due to poverty, multiple pregnancies (without proper spacing of births) due to widespread ignorance, and lack of suitable amenities and recreative activities obtainable to an average man produce very many ill effects on the general physique. Deficiencies of essential food factors due to divergent tastes in food and individual whims further lead to improverished condition of the blood. Tropical fevers of which malaria is the greatest scourge, and other diseases like kala-azar, hookworm disease and dysentery always leave the man bed-ridden and run-down for quite a long time after such diseases have been cured. The task of treating such a state of affairs can be undertaken successfully only by the State; but a proper understanding of all the relevant factors may help in individual efforts. In this article we propose to describe the various types of anæmias with particular reference to tropical (macrocytic and secondary) anæmias.

The term anæmia is applied to the condition in which there is a reduction of red blood cells and hæmoglobin, or of the amount of the blood as a whole. The classification of anaemias has proved to be very unsatisfactory, which is apparent from the fact that too many are in vogue. Here below is a description of the different types of anæmias (and their treatment) on Davidson's classification, which is more scientifically based on the aetiology, keeping the physiology of blood formation in mind:—*(a)* Nutritional deficiency anaemia—macrocytic and microcytic; *(b)* post-haemorrhagic; *(c)* haemolytic; and *(d)* microcytic hypochromic anaemias (secondary).

I. Normally the stomach secretes an enzyme called the 'intrinsic factor' which interacts with extrinsic factor in food to form the 'anti-anaemic' factor—which is normally stored in liver and is responsible for normal blood formation. If this normal process is disturbed due to any deficiency causing a gap in this link, abnormal condition results, for example—

1. In Addisonian pernicious anaemia, there is a deficiency of intrinsic factor due to a constitutional defect in gastric secretion (gastric atrophy with failure of secretion of intrinsic factor and of hydrochloric acid even after injection of Histamine) leading to megaloblastic blood formation with the typical blood picture of primary hyperchromic macrocytic anaemia. Such a condition is fortunately rare and 'tropics' cannot particularly be blamed for it. What we aim at in the treatment of this malady is 'substitution therapy,' and as the defect is a permanent one, it may have to be continued for life. Raw liver or parenteral liver extract with Ventriculin (or dessicated pig's stomach extract) should be administered and maintenance dose has to be continued for long with reticulocyte response as the guide. Sometimes proteolysed liver succeeds when all other usual preparations have failed. Blood transfusion may also be found useful.

2. Anaemias of pregnancy :—During pregnancy there is often a lowering of gastric function, and increased demands of the mother and fœtus for the anti-anaemic principal, which may lead to magalocytic anaemia. But more commonly there is iron and other deficiency due to disturbed gastric function, vomiting and consequent loss of extrinsic food factor and haematinic principle, resulting into mycrocytic hypochromic anaemia. Apart from administration of liver extract, iron and vitamin B, properly balanced diet must be given. It is also suggested that parenteral (intra-muscular administration of 5% Cholestrol in olive oil in weekly doses of 2 c.c. may be tried with success.

3. Secondary macrocytic hyperchromic anaemia may develop due to (*a*) loss of intrinsic factor consequent on acquired causes, *e.g.*, chronic gastritis, gastrectomy, cancer stomach and persistent vomiting due to any cause; or (*b*) due to deficiency of extrinsic (food) factor. The latter is the '*tropical macrocytic anaemia*' on which much useful work has been done at the Calcutta School of Tropical Medicine by NAPIER and others. It differs from Addison's pernicious anaemia in :—*(a)* The gastric secretion free Hcl. is usually normal. *(b)* Plasma bilirubin is not increased (except in concurrent chronic malaria. *(c)* Central nervous lesions never develop. *(d)* Purified liver extracts are often ineffective as compared to crude extracts. *(e)* Autolysed yeast products (containing all factors and Nicotinic acid) like Marmite and vitamin B complex products are very effective, while we have practically no response from such oral administration in Addison's disease.

It has not been ascertained fully as to what particular deficiency gives rise to this condition. It may possibily be deficiency of animal protein and vitamin B complex in diet, as a result of which there arises gastric and hepatic dys-function (non-hæmolytic type of anaemia). It is very often associated with the co-existence of malarial infection which produces haemolytic effect due to over-action of the reticulo-endothelial system which is hypertrophied as a result of chronic irritation (haemolytic type). Another cause is failure of absorption of the specific anti-anaemic factor due to intestinal impermeability, or small intestinal hurry. Diarrhœas like sprue and dysentery, multiple anastomosis and cancer of stomach cause failure of absorption and produce multiple deficiencies of calcium, iron, vitamins and proteins. More often this defective absorption and assimilation, or reduced intake of vital factors in food lead to *tropical microcytic hypochromic anaemia*—as in simple achlorhydria (not histamine-fast), starvation pregnancy and insufficient or defective dietary. The treatment consists of completing the particular deficiency and stimulation of the haemopoietic system. Apart from liver, iron and vitamins, Calcium should be administered to act as tissue tonic. Acid fruits and curds should not be allowed in diet, because it produces the imbalance of sodium and calcium irons in the blood. Exhibition of vitamin D sometimes gives still better results when administered with Nicotinic acid and Riboflavine. So does vitamin C which not only helps metabolism but provides the structural material for the red blood cell-formation.

4. Megaloblastic blood formation may result from either a failure of storage or of final synthesis of the anti-anæmic factor in the liver due to advanced hepatic disease (making liver incapable of final elaboration of the A.A. factor) or due to depressed activity of the bone-marrow which has been injured by toxic products arising as a result of liver failure. The diagonistic feature of this condition is the low plasma protein (in the absence of any kidney disease).

5. Achrestic anæmia may result from a failure of the bone-marrow to utilise or mobilise the specific A.A. factor which is normally available from the stored depots in the liver and kidney. Such cases have normal gastric secretion, develop hyperchromic macrocytic anæmia and fail to respond to active liver preparations, Iron, Marmite, Adrenalin, Thyroid extract, anterior Pituitary extract and splenectomy. Repeated blood transfusions only produce a temporary improvement.

Sometimes when the bone-marrow is exhausted or injured, aplastic anæmia results. Patchy aplastic condition reveals absence of formative tissue, congestion and hæmorrhages histologically; and other parts of the bones may show hyperplastic erythroblastic reaction in an attempt to compensation. Such a granulocytic anæmia commonly develops these days from sulphanilamide poisoning, X-ray exposures and benzol poisoning. These cases improve with great difficulty with any recognised lines of treatment. X-ray exposures only help in some aplastic conditions, while Nicotinic Acid and Nucleotide are useful in Sulphanilamide poisoning.

II. **Microcytic hypochromic anæmias (Secondary).**—1. *Post-haemorrhagic*—resulting from hæmetemesis, melæna, menorrhagia, etc. The treatment consists of proper attention to the cause of such bleeding and later on administration of the hæmatinic princples.

2. *Haemolytic*:—When acute haemolysis takes place due to malaria, black-water fever, kala-azar, haemolytic streptococcal septicaemia, snake-venom and other poisons, the typical microcytic anaemia naturally results. Sometimes haemolysis is associated with excessive activity of the reticulo-endothelial system, and obscure affections of liver and spleen—resulting in profound dyscrasias of the haemopoietic system. Hodgkin's disease, Banti's splenomegaly, congenital acholuric jaundice, myeloid and lymphatic leukaemias, spirochaetosis are all such obscure conditions. Tuberculosis and other chronic infections also produce a severe type of anaemia. Hookworm disease (ankylostomiasis) also gives rise to anaemia which can only successfully be treated by preliminary de-worming and then usual administration of haematinics.

3. Defective diet with deficiency of iron, copper, calcium, thyroid and vitamins, or failure of absorption of blood-forming elements produce hypochromic anaemia. The description of such a condition has been fully given above and the treatment has also been made out.

4. Chronic poisoning with lead, mercury, arsenic and sulphanilamides produce secondary anaemia. Administration of such drugs must be discontinued before an attempt to treat anaemia is undertaken. It has been noticed that chronic habit of tobacco-chewing also results in anaemia, and that no treatment succeeds until and unless this pernicious habit is eschewed.

From the above description it is clear that anaemia is a very common condition and that it is very debilitating. The treatment must be rationally based on the cause which must be clearly ascertained before any therapy is instituted. Much confusion about the aetiology and treatment of anaemia has been dispelled by numerous researches carried out at various centres and by competent authorities, but much work has yet to be done to master this intricate problem, particularly in the field of dietetics and the role of vitamins.

Anæmia of Pregnancy

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THOUGH the association of anæmia either of a serious or mild type with pregnant women has been recognised by some medical men some fifty years back, it is not until recently that the attention it deserves has been devoted to this subject, and even now the value of a routine blood count and hæmoglobin estimation during pregnancy in saving the pregnant women who are ill-fitted to stand the ordeal of labour, is little recognised or appreciated.

The subject of this article being anæmia of pregnancy and not anæmia in pregnancy, we have to omit from the theme of this article such of those anaemias as are due to well-recognised causes as ankylostome and other parasites, anaemias due to conspicuous haemorrhage, as haemorrhoids, neoplasms, menorrhagia, etc., and anaemias due to other diseases as sprue, tuberculosis, syphilis etc.

Anaemia of pregnancy can be classified as :—

(1) *Hydraemia* or the so-called physiological anaemia of pregnancy.

(2) *Deficiency anaemia* :—(*a*) Iron deficiency : Macrocytic, hypochromic anaemia. (*b*) Macrocytic anaemia due to (i) deficiency of extrinsic factor; (ii) deficiency of the intrinsic factor.

(3) *Erythronoclastic or haemolytic anaemia* :—(*a*) Plastic ; (*b*) hypoplastic ; (*c*) aplastic.

(4) *Post-haemorrhagic anaemia* : Due to ante-partum haemorrhage.

Hydræmia.—Studies of gravid women clearly show that there is an increase in the total volume of blood, the increase being more in the plasma volume than in the red cell and haemaglobin volume. Hence though the actual amount of circulating R.B.C's and Hb are increased, the blood is more dilute and hence a blood count shows a condition of anaemia. This anaemia caused by the physiological increase in the blood volume is termed the physiological anaemia of pregnancy or better still, hydraemia.

Blood picture :—Total increase of R.B.C. and Hb. is about 20% ; total increase of plasma volume is about 25%. The colour index remains at about unity. The Hb percentage is about 80%. There is diminution of serum protein. The viscosity of the blood is low.

This hydraemia becomes less towards the end of pregnancy and disappears completely during the puerperium.

Theory of Causation of Physiological Anæmia of Pregnancy.—Whether this type of anaemia is due to blood dilution or due to a transference of iron from the mother to the fœtus is a controversial question. The demand for iron during the period of gestation comes from (1) the fœtus, uterus and placenta ; (2) the increase in maternal tissues other than the uterus, placenta and the fœtus ; and (3) the blood loss during parturition. The iron content of the fœtus depends on the body weight, the hæmoglobin level and its blood volume and the average is found by many workers to be about 400 mg. The iron content of the placenta is about 100 mg. The iron content of the uterus is about 50 mg.

Since there is an average increase in weight of a pregnant woman of about 20 lbs., the iron requirement for her is about 500 mg. It has been found by RICHTER, MAYER and BENNET that the average iron loss in parturition is about 175 mg. Against the above is the off-set due to stoppage of iron loss due to menstruation which may be approximately 100 mg. per each period. Hence some conclude that the iron transit to the fœtus is not a causative factor and this anaemic condition can be explained by the physiological phenomenon of hydraemia. But it is impossible accurately to estimate the intake and out-put of iron during pregnancy and parturition and when accurately estimated it is found that the additional drain of iron from the mother is certainly the cause of this condition. Latest researches also support this theory.

Microcytic hypochromic anæmia is the anaemia in a pregnant woman brought on by the deficiency of iron.

AETIOLOGY :—As we have seen before, the mother requires iron to build up the uterine muscle for the vascular uterine bed and the fœtus. The maternal reserves are dependent on intake and absorption of iron, and when the diet is deficient in iron, or when there is diminished absorption of iron from the alimentary tract due to a temporary hypochlorhydria, anaemia results. *Age* :—Common between 20 and 30 years. *Race* :—No race is exempt. *Relation to parity* :—The incidence is greater in the primipara but repeated pregnancies do produce this type of anaemia in later pregnancies. *Economic incidence* :—More percentage is found in the poorer class patients.

SIGNS AND SYMPTOMS :—*Blood picture* :—The red count is diminished. The reduction of Hb is greater. The colour index is less than unity. The R.B.C. are pale in colour, smaller than normal, the cell diameter being reduced and the pigment distributed around the periphery resulting in ring staining. The bilirubin content of the blood serum is normal. The globulin content of the blood is increased while the albumin content is diminished. The ester cholesterol content of the blood is very much diminished while the free cholesterol is diminished slightly.

Gastric symptoms :—Digestive disturbances are present as a rule. This may vary from a mild form of dyspepsia to Plummer-Vinson syndrome characterised by achlorhydria, glossitis, dysphagia and koilonychia.

Cardio-vascular symptoms :—There is breathlessness on the slightest exertion. Excessive fatiguability and loss of sense of well-being is invariably present, the woman tending to lie down lazily rather than take active interest in the surroundings and house-hold work. In severe cases, there is dyspnœa and œdema of the dependent parts. There is an atonic condition of the heart. Sudden death due to heart failure, though rare, may occur.

Urinary symptoms :—Albumin in the urine is absent in the majority of the patients. The urinary output is diminished, sometimes as low as 10 to 20 ozs. per diem. No casts are present. There is no increase in the urobilinogen content of the urine.

Oedema :—There is swelling of the extremities and face. The facial markings are obliterated. The œdema pits on pressure and fills easily. In a great majority of cases it is usual to find a condition of general anasarca.

Temperature.—There is an irregular and intermittent temperature before confinement in a majority of cases.

Other symptoms.—Miscarriage and premature labour are more common. The labour tends to be difficult and prolonged. Maternal and infantile mortality are high. Liability to puerperal sepsis is very common.

PROGNOSIS :—Is favourable only if diagnosed and treated early.

TREATMENT:—*Diet:*—A full mixed diet must be administered. Iron-containing article of diet as red meat, green vegetables, must be given in plenty. When achlorhydria is present, oils and fats must be omitted. Carbohydrates must be given in moderation. Fruit juices as those of sweet lemon or oranges, tomatoes, grape fruits must be given daily.

Drugs.—Iron is the drug of choice. It must be given in massive doses to produce any effeet. Of all the iron preparations the ferrous salts and the scale preparations are the most efficacious. Ferrous Carbonate, (Blaud's Pill or Bi-palatinoids) must be given in doses of 15 grs. thrice daily, after food. Ferrous Chloride made up into capsules 6 grs. three times a day is very good since all the available iron is converted into ferrous chloride in the stomach. Ferrous Sulphate (FERSOLATE) and ' Poly-Hæmin ' 2 tablets three times a day, half an hour after food, is very useful. When the patient is unable to take the capsules or the tablets.

Ferri et Ammoni Citras	...	℥ ii.
Aqua Chlor.	...	ad ℥ iii.

Ounce I t.d.s. is a very useful prescription.

When improvement is not taking place or is not striking, these doses can be safely increased without any fear of constipation, as iron preparations, contrary to popular opinion, never constipate. Haemoglobin preparations though popularly prescribed, for every pregnant women, are not of much value in these cases. Injections of iron are not of any use, unless given in such large doses that are certainly toxic. It is better to avoid such injections in the treatment of this anaemia. Though the addition of small doses of Copper, Manganese, Bile or Chlorophil are supposed to increase the efficacy of the action of iron, they are not absolutely necessary. Liver extracts either orally or by injection are useless. Also stomach extracts find no place in the rationale of treatment. Many patent medicines containing liver, iron and other metallic salts fail to do good since they do not contain sufficient amount of iron that is required for the treatment of this condition.

SYMPTOMATIC TREATMENT :—When achlorhydria is present, Acid Hydrochlor dil must be given in 15 minim doses diluted with about 5 ozs. of water during meals thrice daily. Constipation must be relieved by daily prescribing Liquid Paraffin ½ oz. at bed-time. Drastic purgatives must be avoided. The passage of bougies to relieve the dysphagia due to Plumber-Vinson syndrome must be mentioned only to be avoided. When there is an associated thyroid deficiency. Thyroid must be given in small doses, 1 gr. daily being sufficient. Blood transfusion is rarely necessary except when the anaemia is very severe or when an operation is going to be performed.

Macrocytic anæmia.—*Aetiology* :—The red blood cells are developed from the endothelial cells lining the capillaries of the red-bone marrow. Megaloblasts are formed by the endothelial cells and these megaloblasts mature to normocytes by the action of the intrinsic factor formed in the stomach by the action of the gastric enzyme on foods and by the action of the extrinsic factor which is allied to vitamin B_{12}, and is absorbed from the intestines, stored in the liver and supplied to the bone marrow. Hence

macrocytic anaemia can be produced by (1) deficiency in the extrinsic factor. The work of LUCY WILLS has clearly established that this disease is due to the absence of the vitamin B complex in the diet of Indian woman ; (2) deficiency in the intrinsic factor ; and (3) deficiency in the absorption and utilisation of the ' liver factor ' produced by the inter-action of the above two factors. In certain cases of macrocytic anaemia the production and storage of the ' anti-anaemic factor ' has been found to be satisfactory whereas the bone-marrow fails to respond. *Age:*—20 to 40 years. *Parity:*—More common in multipara. Especially common in those who have suffered from a microcytic anaemia of pregnancy in former pregnancies.

SIGNS AND SYMPTOMS.—1. *Blood Picture* :—The red cell count is very much diminished. A count of 2 millions is not common. The Hb is reduced but not to such a great extent as the cells. The colour index is greater than unity. The size of the R.B.C. is increased. Anisocytosis and poikilocytosis are present. Immature cells as normoblasts and megaloblasts are present. The shape of the cells is altered. They may be shrunken or crenated.

2. *Gastric symptoms.*—Achlorhydria is present.

3. *Urinary symptoms.*—Urinary output is diminished. In severe cases albumin is present.

4. *Cardio-vascular symptoms* :—Spleen is usually enlarged. Palpitation is a source of worry. Some cases show a slight dilatation of the heart. Haemic murmur is always present in the pulmonary area.

Other symptoms:—Syncopial attacks are frequent. Retinal haemorrhages may be present. The skin is pale. There is general anasarca. The skin over the extremities and abdomen is shining and the face is swollen beyond recognition. Premature labour is common as also sudden death. There is fever which is irregular.

DIFFERENTIAL DIAGNOSIS.—(1) Dyspnœa is present and there is soreness of the tongue from true Addisonian anaemia : Addison's anaemia occurs in the late years of life when menopause is present and spinal-chord involvement is invariably present, and the condition persists even after delivery, and (2) from microcytic anaemia : where the colour index is below 1 and macrocytes are absent. Response to iron differentiates it.

PROGNOSIS :—Is good if treated effectively early, but maternal and fœtal mortality is more in those types of cases than in those of purely microcytic anaemia.

TREATMENT :—1. *Severe cases* :—Cases in which the blood pressure is low, pulse is rapid, the heart dilated, anasarca present, and dyspnœa is also present at rest, immediate transfusion of one pint of blood from a suitable donor is absolutely necessary. 5 c.c. of Hepatex P.A.F. intravenously must be administered. Later, intra-muscular injections of 5 c.c. of Liver Extract must be continued daily for 4 days. Later still, injections, every alternate day, will suffice.

Iron must also be administered for a month to prevent the iron shortage occurring as a result of the rapid production of the R.B.Cs.

Diet :—Barley water, milk, glucose and orange juice must be administered for the first week. Then, protein and carbohydrates are added to the diet. Ultimately, a full mixed diet must be given.

SYMPTOMATIC TREATMENT—Acid Hydrochlor dil. min. 15 three times a day along with food must be administered. If the general anasarca does

not disappear or is causing respiratory embarrassment, any mercurial diuretic as Mersalyl or Neptal 2. c.c. intramuscularly given is useful. A Saline diuretic mixture containing Ammonium Chloride gr. 40, Pot. Citras gr. 40, Pot. Acetas gr. 40, Spt. Aetheris Nitrosi dr. 1½, Liquor Ammon. Acetatis dr. 2, Aqua Chlor. add oz. 4. Dose: oz. 1 every 6 hours is also useful. Vitamin B preparations must be given. Above all, rest in bed is essential and, in very severe cases, Caesarian section must be done after blood transfusion. .

2. *Moderate cases*:—Cases where there is lassitude, palpitation, dyspnœa on exertion, and dyspepsia and slight œdema, Liver extract 5 c.c. must be given intramuscularly for four days, daily; then, weekly injections of 5 c.c. must be continued.

Diet:—A balanced diet is indicated. Barley water and glucose are useful adjuncts to the diet. Vitamin B preparations are useful.

Drugs:—Iron and Hydrochloric Acid dil. must be administered as for the above. When the patient refuses to have the injections, half a pound of cooked liver must be given daily. But, since taking the liver orally is not palatable and eaten with relish, preparations in the market containing extracts of 500 grammes of liver can be usefully mixed with the diet and eaten. Hog's Stomach Extracts are also valuable. Preparations like Ventriculin and Pepsac are quite handy. The patient must remain in bed.

This type of macrocytic anaemia disappears after labour, resulting in a spontaneous cure. In this connection, it is well to remember that whole liver extracts act better than preparations containing only the 'anti-anaemic factor.'

Hæmolytic anæmia.—The onset is usually during the last three months of pregnancy.

SYMPTOMS:—The patient rapidly becomes pale, dyspnœa is present. The skin and mucous membrane are pale and the conjunctiva is icteric. The spleen and liver are enlarged. The urine contains urobilinogen in excess. The Vandenberg reaction is positive, indirect.

Blood picture:—The R. B. Cs. and the Hb. are reduced. Colour index is about unity only. The R.B.Cs. are not enlarged. Anisocytosis and poikilocytosis are present. Nucleated R.B.Cs. are present if the bone-marrow remains undamaged, resulting in a *plastic* form of anaemia. If the bone-marrow is damaged slightly, it is *hypo-plastic* form of anaemia, and if the damage is entire, without any sign of regeneration in the bone-marrow, it is *aplastic* anaemia.

Obstetric shock is a common phenomenon and maternal mortality is high.

DIFFERENTIAL DIAGNOSIS:—From the pernicious anaemia of pregnancy is by the absence of macrocytes in the blood picture and the presence of leucocytosis.

TREATMENT:—Blood transfusion is the only chance; 300 to 500 c.c. of blood must be intravenously given and repeated, if necessary. The administration of Calcium, Liver Extracts and Iron are next to useless as also injections of Adrenalin and Oestrogenic Hormones. *Post haemorrhagic anaemia* is due to the loss of blood and is only of microcytic type. Here efforts must be made to treat the cause first and then the anaemia.

Ante-natal work in India is still in its infancy, and a thorough examination of the blood of all pregnant women is not possible except in well-equipped institutions and the proverbial shyness of the expectant mother in India to resort to such institutions is well-known. Hence, it lays a heavy duty on the general practitioner to diagnose these cases early, so that efficient treatment on right lines can be instituted and much suffering and many lives can be saved. In this connection, it must be mentioned that the combined treatment with Liver Extract and Iron in the pious hope that one or the other must be the deficient factor responsible for the anaemia must be strongly deprecated, because the Doctor cannot know which of the preparations he has to continue for maintaining the improvement till recovery is complete and also unnecessary use of the needle can be avoided if no parenteral medication is called for.

CASE REPORTS: 1.—A Gosha lady, aged 25 years, 3rd para, was seen in the early stage of pregnancy.

Condition:—Slight œdema of the ankles; dyspnœa on slightest exertion; palpitation; scanty urination. Blood examination showed it to be a case of hypochromic microcytic anaemia.

Treatment adopted:—Ferri et Ammon Citras drs. 2; Aqua Chlor. add oz. 3. oz. 1 t. d. s. was given till the date of delivery. Patient tolerated the dosage well.

Labour:—Due to obstetric disproportion, craniotomy had to be performed and the child extracted.

Result:—Patient made an uneventful recovery and continues healthy uptodate.

Case 2.—An elderly primi-para, Hindu, aged 28, was healthy till she conceived. Oedema of the legs began to appear about the 4th month of pregnancy. Urine contained no albumin. Blood examination showed it to be a case of microcytic anaemia.

Treatment:—Iron as given for the above case, was prescribed.

Labour:—Was normal. Iron was continued for 3 more months after labour. During subsequent pregnancy which occurred after 20 months of the first, no anaemia was present and labour was normal.

Case 3.—A Gosha lady, aged 30, 4th para, was seen in the early stage of pregnancy. She had suffered from anaemia of pregnancy in previous labours, with swelling of the legs and face, disappearing completely after normal labour.

Condition:—General anasarca. Face contours gone, shining abdomen and leg. Severe dyspnoea even when resting in bed. Palpitation.—Heart dilated. Pulsating jugulars present. Urine very scanty, about 10 ozs. a day.

Blood examination:—Macrocytic, hyperchromic anaemia.

Teatment given:—Liver Extract 5 c.c. intramuscularly daily was given for 4 days. Then, twice a week. Neptal 2 c.c. intramuscularly, along with diuretics, was administered to reduce the œdema. Iron was also given for a month. Labour started in the 8th month of pregnancy. 3 hours after the onset of pains, the patient suddenly collapsed and died.

This is a case of microcytic anaemia, in previous pregnancies, paving the way for the macrocytic type due to repeated pregnancies.

References:

1. B. M. J. 1936.
2. Text-book of Medicine by Price.

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Treatment of Anæmias

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A THOROUGH-GOING clinical examination of every case is necessary to find out the cause of and treat a case of anaemia. In every instance total red blood cell count, haemoglobin percentage, and examination of the blood smear are necessary. If the R.B.C. count is below 1.5 million and haemoglobin below 10% then that is a case of anaemia which should be treated with complete rest in bed. (For the purpose of this article haemoglobin 100% is equivalent to 16 grams of haemoglobin for 100 c.c. of blood. Zeiss haemoglobinometer is calibrated to this scale). If the R. B.C. count is below 1 million per c.m.m. then blood transfusion is indicated in those cases.

When blood smear examination shows a red cell which is bigger than normal in size and fully haemoglobinised, the patient is said to suffer from macrocytic, hyperchromic anaemia. Bone-marrow in these cases shows a megaloblastic reaction. In this condition, if the volume index is done then the same is found to be more than 1·1. The figure may be as high as 2. This is a condition which has got to be investigated to find out the nature of the gastric secretion. If there be no hydrochloric acid secretion normally and no response of the same even after an injection of Histamine, then it is a case of pernicious anaemia, when purified liver extract as Anahaemin (B. D. H.) will give very good results. For the gastric symtoms that is occasionally present Acid Hydrochlor dil with Pepsin gives very good relief.

When the blood smear examination shows red cells which are bigger than normal in size and vauolated, then the case is one which requires liver extract and iron in some form. This kind of blood picture is met with in tropical macrocytic anæmia, sprue and disorders of the intestine. In these cases fractional test meal invariably contains acid, and in the few cases in which the acid is absent, on Histamine injection free hydrochloric acid is secreted. Volume index is never so high as in pernicious anæmia. Bone-marrow in these cases shows a megaloblastic reaction as in pernicious. In tropical macrocytic anæmia free acid is present in gastric secretion. Liver as crude extracts gives very good results, but can be replaced by Marmite (autolysed Yeast). ½ oz. of Marmite made as soup and given thrice a day is a very good substitute. Marmite soup can be made palatable by serving it hot with a little salt and pepper powder. Served in this form marmite has no disagreeable smell or taste. Marmite can also be given with bread and rice cakes.

When the blood smear shows normocytic cells fully hæmoglobinised, it indicates that the hæmopoietic principles are there as also iron but for some reason or other productions of the red cells is totally inhibited. These cases are likely to be either true aplastic anæmia or there is toxic depression of the bone marrow. Bone marrow biopsy shows uniform suppression of all stages of the red cell series and there is no megaloblastic reaction as in the previous series. In these cases if the depressing factor cannot be eradicated then repeated blood transfusion should be given with the object of giving rest to the bone marrow ; and final recovery of the same after a time.

When the blood smear shows vacuolated cells which are small then the case is one which requires iron medication. Volume index is always less than one. In these cases anæmia is always secondary to some cause as ankylostome or malarial infection. For every one case of macrocytic anæmia there are more than a dozen of microcytic anæmia cases seen. In these cases, to arrive at the cause of the primary condition, in addition to examination of the blood smear for parasites and differential count, the faeces and urine must be examined for parasitic infection. The most common cause of parasitic infestation of the alimentary canal in these parts is ankylostome infection. Treatment for ankylostome anaemia used to be iron in some form as Ferri-et-Ammonium-Citras 90 to 120 grains a day or Ferrous Sulph grains 10 a day. Build up the R.B.C. count to 2·5 million and haemoglobin to 40%, and then to give Oleum Chinnapodium 1 c.c. and Carbon-Tetrachloride 2 c.c. in liquid Paraffin 1 oz. ½oz. at 6 A.M. second ½oz. at 7 A.M. and 2 hours later followed with a Saline purgative. In 1939 HARE and DUTTA reported the beneficial effect of Tetrachlorethylene on a series of cases. Soon after this was tried by Lt. Col. G. R. MCROBERT in the Madras General Hospital. The writer has used the drug on a series of 80 cases in the years 1941 and 1942. An analysis of these 80 cases is shown below.

Analaysis of 80 cases of Ankylostomiasis treated with Tetrachlorethylene.

No. OF CASES.	R.B.C. COUNT.	No. OF CASES.	HÆMOGLOBIN PERCENTAGE.
8	less than 1 million.	20	less than 15%
34	,, 2 ,,	25	,, 30%
25	,, 3 ,,	23	,, 50%
10	,, 4 ,,	7	,, 70%
3	,, 5 ,,	2	,, 80%
		3	,, 100%

In not one of these cases was any preliminary treatment done. The routine adopted by the writer on finding the ankylostome ova was to put the patient on Terachlorethylene 4-c.c. in 2 oz of concentrated Sodasulph solution first thing in the morning and repeat the same treatment at the end of a week. In between the specific treatment the patient was put on iron mixture. Even when the patient was markedly anaemic no unpleasant symptoms were observed. The advantage with this line of treatment is the Antehelminthic and the Saline being in one dose, saves a great deal of nursing trouble. With the old line of treatment the nurse had to give Antehelminthics twice and two or three hours later a Saline mixture. In a general ward with serious cases demanding constant attention it is nothing unusual for the nurses to give the Antehelminthics and fail to give the Saline or give only one dose of the antehelminthic. Apart from the nursing point of view the cost of the drug is very low. The only unpleasant effect of the drug is that the patient may feel drowsy for two or three hours after administration of the drug. This drowsiness, however, has never lasted for more than six hours. The pulse was not affected and general condition remained good. The drug is also pleasant to take. It settles to the bottom as clear oily drops in the Saline and so has to be shaken well and administered. In one case where a patient was given Oleum Chinnapodium 1 c.c. and Carbon-Tetrachloride 4 c.c., Ankylostome ova was seen even after giving the drug twice. Tetrachlorethylene

4 c.c. in 2 oz of concentrated Sodasulph solution was given. The motion was strained and contained over 100 ankylostome worms.

In the mixed infections as ankylostomiasis and ascariasis, 1 c.c. of oil of Chinnapodium can be added to 4 c.c. of Tetrachlorethylene and given. The result is not so very satisfactory in the writer's opinion as to give Tetrachlorethylene and Santonin separately. In cases of ankylostome anaemia, Iron mixture alone restores the blood to the normal condition. But what happens is that the initial rise of the haemoglobin and R.B.C. count is rapid and reaches 50 to 55% and thereafter if specific treatment is not given the further response to treatment is poor. If, on the other hand, specific treatment is given then the response continues to be satisfactory, but even then when the R.B.C. count reaches 3·5 millions and the haemoglobin 60% further response is slow. Gastric analysis has been done on a series of cases and it was found that out of 77 cases of ankylostome anaemias, 27 cases were achlorhydric and of these 27 cases 11 cases were followed up. Of these 11 cases, 4 cases responded to Histamine and 7 were Histamine fast. As the anaemia improved one case started secreting free acid and three responded to Histamine and three continued to be histamine fast. At the same time another observation was also made, namely the presence or absence of free acid did not in any way interfere with the response of the anaemia to the treatment.

The writer has worked out the average haemoglobin response of these patients as 2%per day with 10 grains of Ferrous Sulphate a day; and 1% a day with 90 grains of Ferri et-Ammon-Citras a day. The advantages of Ferrous Sulphate mixture are (1) the mineral content is small, (2) can be given in pill form, or mixture form and (3) is cheap. The absorption of iron in Ferrous Sulphate is 14% which is very high. Practically the highest excepting the Ferrous Chloride. The drug is also available freely and being marketed by a number of firms under different trade names as Fersolate (Glaxo) or Ribothiron (Sharp and Dome) plastules (John Wyeth), or Polyhaemin. The chief disadvantage with the drug is that it is likely to upset the digestive system in a number of cases, producing intestinal colic in some patients and in a small number severe diarrhœa. With Ferriet-Ammonium-Citras, utilisation percentage is 1·5 to 3%. There is no intestinal disturbance. The response of haemoglobin is only 1% a day. It is also pleasanter to take.

In cases of microcytic anaemias with enlargement of spleen in the absence of ankylostome ova, chronic malarial infection should be suspected, though parasites cannot be demonstrated in the blood smear. The writer has come across malarial parasites in the blood smear even when the patient was afebrile. The common forms met with are the crescents of the malignant tertian parasite and the growing forms of the benign tertian parasite. In these cases Quinine in any form 5 grains 3 times a day is indicated along with Iron mixture.

Microcytic anaemia is met with in some cases of haemorrhoids and duodenal ulcer cases. In one case of duodenal ulcer motion examination showed occult blood and the patient gave a typical history of duodenal ulcer. The patient was markedly anaemic and did not improve with Iron mixture, but when put to bed and put on alkalies and sedatives the ulcer symptoms cleared up and with that the blood condition also improved. This condition should be kept in mind particularly in this presidency

where there are so many cases of duodenal ulcers and when a microcytic anaemia fails to respond to iron mixture. It is rather an exception for a severely anaemic patient to complain of ulcer symptoms though the writer has seen two such cases. Probably this is due to the fact that the gastric acidity is markedly lowered by severe degrees of anaemia. Out of a series of 100 cases investigated only 4 had hyperchlorhydria.

Cases of myxœdema or thyroid deficiency also show microcytic blood picture. In these cases the clinical appearance is like that of an advanced case of ankylostomiasis. The anæmia is not so marked as in some cases of ankylostomiasis. In all the four cases of myxœdema that the writer treated the blood picture was microcytic and hypochromic and R.B.C. count was over two millions per c.m.m. Treatment in these cases with thyroid extract is by itself sufficient to improve the blood condition as well as the general condition.

In cases of scurvy also a fair degree of anæmia is met with. These cases are very rarely seen as frank cases of scurvy are seldom met with. Treatment is to give vitamin C in sufficient doses to compensate for the deficiency. These cases can be spotted by examining the urine for the excretion of the vitamin C. Generally in these patients after the arrest of the hæmorrhage, the anæmia improves markedly even without the administration of any iron.

In all microcytic anæmias, if the patients do not respond to iron, traces of copper may improve the condition. If still the response be very poor or nil it is good to look for any septic foci or a constitutional disorder like chronic nephritis which may be depressing the bone marrow.

Summary.—1. Blood should be investigated thoroughly in all cases of anaemia.

2. Macrocytic anaemias are relatively rare and incidence of pernicious anaemia in Madras is very low, hence most of the macrocytic anaemias met with in Madras respond to crude or total liver extracts rather than to purified liver extracts as Anahaemin. Tropical macrocytic anaemia responds to Marmite by mouth.

3. Common microcytic anaemias are due to chronic malaria and ankylostomiasis. An analysis of 18 cases of ankylostomiasis treated with tetrachlorethylene is reported. Many of them were given specific treatment at a stage of anaemia when the other antihelminthics could not be given. This means the stay in the hospital is considerably lessened. Other microcytic anaemias are due to thyroid deficiency and vitamin C dificiency. These are relatively rare. The rarer anaemias are not dealt with.

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References:

1. K. A. Hare and F.C. Dutta—Ind. Med. Gaz., April 1939.
2. Lt. Col. G. R. McRobert, D. Govindha Reddi, and R. Subramaniam—Ind. Med. Gaz., June 1940.
3. Whitby and Britton — Disorders of Blood. 4th Edition.
4. Piney—Recent Advances in Hæmotology.

Pernicious Anæmia

BY

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PERNICIOUS anaemia is the most important of the nutritional-deficiency anaemias. It is a disease characterised by megalocytic anaemia, achylia gastrica, symptoms of degeneration of spinal cord and which is often interrupted by remissions.

Aetiotogy :— The cause of this disease is the absence of "intrinsic factor" which is normally present in gastric juice and is probably a rennin-like ferment. The "extrinsic factor" is proteins that we take with our food. It is from the interaction of the extrinsic and intrinsic factors that haemopoietic or ante-anaemic principle, also known as pernicious anaemia (P.A.) factor, is formed. MEULENGRACHT believes that in the pig intrinsic factor is secreted by the pyloric glands and by Brunner's glands in the duodenum. The pernicious anaemia factor thus produced is carried to the liver and other organs. It is stored in the liver and to a lesser degree in the kidney and spleen. When this is absent pernicious anaemia develops owing to failure of conversion of megaloblasts into normoblasts and erythroblasts in the bone marrow. When these megaloblasts are liberated into the blood stream they are destroyed by the reticulo-endothelial system. The iron is deposited in the spleen, liver and kidneys. The excess of bilirubin in the blood is partly due to the haemolysis of megaloblasts and partly to the failure of the bone marrow to utilise it in the production of red cells.

In most cases of pernicious anaemia gastric juice shows no free HCl, pepsin, or rennin after intramuscular injection of 0·1% Histamine. If gastric juice obtained from a case of pernicious anaemia is incubated with beef, the haemopoietic principle is not produced. STURGIS and ISAAC have shown that the haemopoietic principle is present in dried hog's stomach. WILKISON demonstrated that the mucous membrane and muscular layer of the hog's stomach yields a light powder when dessicated at 40 Cin vacuo. This stomach extract is potent in the treatment of pernicious anaemia. The extrinsic factor is possibly closely allied to vitamin B. Marmite, a yeast extract rich in vitamin B complex, is in some cases efficacious in the treatment of pernicious anaemia, but probably in those cases in which there is a small quantity of intrinsic factor present in the gastric juice.

PREDISPOSING FACTORS:—Cases of pernicious anaemia have been recorded in all civilised countries. It affects both sexes equally from 35-65 years of age. It is rarely found before 30 years of age. A familial incidence is noted in some cases. Damage to gastric mucosa by disease or operations leads in many cases to this disease.

SYMPTOMS :—The patients usually complain of the following : (1) progressive weakness of insiduous onset ; (2) there is increasing indisposition to exertion with uncomfortable feeling of faintness and breathlessness ; (3) there may be palpitation and at times anginal pains due to anoxaemia of the heart muscle ; (4) there is soreness of the tongue due to atrophic glossitis, loss of appetite and in some vomiting or diarrhoea ; (5) numbness or tingling in legs and hands ; and (6) failing vision due to optic atrophy may alsobe present.

Clinical examination : - *General.*—The patient is generally an adult, body is well covered, broad face, short deep chest, wide subcostal angle. The colour of the skin is lemon yellow, it may be pigmented (Addison), with patches of leucoderma at places. There may be much subcutaneous fat. Temperature is normal, or slight irregular fever may be present. Pulse is soft and compressible.

Alimentary system :—Tongue is raw, flabby, denuded of epithelium, ulcers may be present. There may be tenderness in the epigastrium. Spleen is generally enlarged and liver may be palpable. Jaundice and ascites is present in a few cases.

Cardio-vascular system :—Heart sounds are feeble and haemic murmurs may be audible in many cases. In some cases swelling of the feet or ankles may be found.

Urinary system :—Urinary symptoms are very rare, but a few patients may complain of difficulty in micturition particularly in the beginning of the act. There may be signs of cystitis, urethritis and pyelitis. Examination of urine shows increase in urobilin, traces of albumen may be found in some cases.

Nervous system.—Nervous symptoms are due to sub-acute combined degeneration and may be from slight ataxy to paralysis of all limbs. They appear due to involvement of posterior and lateral columns of the spinal cord. Symptoms due to posterior column may be : anaesthesia, parasthesia, numbness and tingling, due to lateral column may be flaccid or spastic paralysis. Vibration, muscle and joint sense are the first to go. Patient may get fits of unconsciousness like epilepsy.

PATHOLOGY :—Extensive investigations have been done on the pathology of this disease. The skin and superficial fat has often a characteristic lemon-yellow tint, whereas the muscles retain their normal deep red colour. The long bones are filled often completely with a gelatinous red marrow, replacing the usual yellow marrow and sometimes causing enlargement of the medullary cavity. On section, the marrow shows evidence of marked and active regeneration of red cells, with a large preponderance of megaloblasts ; many myelocytes are also seen. The liver may be enlarged and show extensive fatty degeneration, it may be of rusty colour due to the deposition of iron pigments in its cells. By staining with an acidified solution of Potassium Ferrocyanide these pigments become blue (the Prussian blue reaction), and are then seen to be situated chiefly in the liver cells at the periphery of the lobule and also in the Kupffer cells of the sinusoids. Later the continued overloading of the liver cells with pigment leads to atrophy of the cells with replacement fibrosis, a type of cirrhosis described by QUINOKE. Similarly free iron may be demonstrated in the tubular epithelium of the kidneys. Chemical analysis has shown that the liver contains an excess of total iron, amounting in some cases to four times of the normal, and upto fifty times in the case of the kidneys. The iron is also present in an abnormal form.

In the early stages the spleen is slightly enlarged, red and firm ; some hyperplasia of its endothelial cells may also be seen, accompanied by increased phagocytosis of red cells. A strongly positive reaction for iron is present. As the disease progresses fibrosis replaces the hyperplasia, and finally there may be atrophic sclerosis of the organ, with but few signs of red cell destruction.

Small haemorrhages into the skin or under the serous or mucous membrane are fairly common. Retina may show the presence of flame-

salt and pepper. Place the pulp in between buttered pieces of bread and serve.

2. *Liver injections* :—It is more pleasant and often cheaper to give liver in the form of I.M. or I.V. injections, in doses equivalent to ½ lb. of fresh liver. When gastro-enteritis is present which prevents absorption, it is much more convenient to give highly concentrated extracts by intramuscular injection. Some of the liver extract preparations available in the market are : Campolon (Bayer), Hepatax (Evans), Hepastab (Boots), Examen (Glaxo), Siotrat (Albert David), Liver Extract (Lily, Parke Davis), Erythegen (Carnick), Liverax (Bengal-Immunity), Neoliveron (Union) and T.C.F. whole liver extract. In severe cases with red cells below one million per c.m.m., the patient is put to bed and 5-10 c.c. of one of these preparations is given intravenously, very slowly diluted with 20 c.c. of warm Normal Saline solution. An initial blood transfusion is now seldom required. The next day 4-6 c.c. are injected intramuscularly and this dose is repeated daily until a reticulocyte crisis occurs. This is to be expected between the fourth and tenth days. The peak of reticulocyte rise varies inversely with the original degree of anæmia. Thus with an initial cell count of 0·5 million, the reticulocytes may touch 55%, with one million red cells a reticulocyte figure of 35% may be expected, with 2 million red cells 14% reticulocytes and with three million red cells 4% reticulocytes. The number of reticulocytes then falls rapidly by a crisis as the mature red cells start to increase in the blood. Subsequently 2-4 c.c. of the liver extracts are injected intramuscularly every week, until blood count is normal and there are no symptoms. Then a maintenance dose of 2 c.c. is required every two, three, four, or even six weeks. If blood count does not rise over 3 or 3·5 million, or mean corpuscular hæmoglobin concentration is 30%, iron should be given as Ferrum et Ammon Citras in doses of 30-45 grs. t. i. d. Iron is especially valuable in all cases in which nervous symptoms are present. The great advantage of treating patients with liver injections lies in the fact that the patient must report every three or four weeks for injection, then a blood count can be done to ensure that the haemoglobin is maintained at over 90% and the red cells over 4 millions. Failure to do this will involve the patient in the risk of developing potero-lateral sclerosis and become a cripple.

A more concentrated liver preparation, Anahaemin, is put up in ampoules containing 100 m.g. in 1 c.c. In severe cases 0·5 c.c. should be injected daily for a week, the reticulocyte crisis being expected between the fourth and the seventh day, or a single injection of 4 c.c. may be given I. M. At the end of a week if response has been obtained 2 c.c. should be injected I. M. and repeated every two weeks until blood count is normal.

3. *Stomach preparations* :—Some authorities prefer to treat this type of anaemia by dessicated preparations of hog's stomach given orally. Thus Extomak (Banger), Pepsac (Boots) and Ventriculin (P. D. & Co.) are available, the dose being 10 gr. t. i. d. The powder must be given cold on food or in drinks. The maintenance dose is usually 28 grams daily.

When the extrinsic factor is also lacking this can be supplied by Marmite in doses of ½ oz t. d. s., at first, and 1 drachm t. d. s. as maintenance dose. Dilute Hydrochloric Acid ms. 30-60, well diluted taken with meals improves the appetite and sometimes stops the diarrhoea which may be a feature of the disease. Arsenic and intestinal antiseptics should be avoided. When the patient has recovered from acute stage, septic foci should be removed.

Chlorosis

BY

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THE subject with which I am coming to the readers of this special issue of the "*Antiseptic*" is Chlorosis. It is a primary anaemia almost confined to girls at puberty, characterised by pallor and symptoms of secondary anaemia with the absence of wasting.

The disease is most common among the ill-fed, over-worked girls of towns, who are confined all day long in closed rooms, where sun is scarcely seen. Age of onset of the disease is 14 to 20 years, *i.e.*. during and shortly after puberty. Among the special factors, which lead to its occurrence, may be mentioned :—*(a)* Sexual development ; *(b)* Constipation ; and *(c)* Poor air, over-work and food deficient in iron. Duration of the disease is prolonged. If untreated it will drag on for many years. Recurrences, which are common, may extend into the third decade.

Symptoms.—A girl suffering from *chlorosis* looks developed as the subcutaneous fat is increased. Complexion is peculiar.. It is neither the blanched aspect of haemorrhage nor a muddy pallor of grave anaemia but a curious yellow greenish tinge, which has given the disease the *green sickness*. Occasionally the skin shows areas of pigmentation, particularly about the joints. The colour may be deceptive, as the cheeks may have a reddish tint particularly on exertion *(Chlorosis rubra)*.

Eye balls have blue tinge, eyes are bright and sharp-sighted. The subject complains of shortness of breath, giddiness, faintness and palpitation. They are easily tired. Swelling of the feet, disturbed menstruation, constipation, head-ache, emotional and easily nervous are among the symptoms. Pulse is rapid, easily accelerated, full and short. Haemic bruits are common on pulmonary area. Constant pulsation at the veins in the neck with continuous murmur at right jugular vein *(Bruit De Diable)*. Heart may be dilated.

Gastro-intestinal system.—Appetite variable and capricious. They are fond of vinegar and acid. There is awful constipation, which is an important adjuvant of the disease. Dyspepsia, flatulence and hyperacidity may be present in some cases. Blood—red blood corpuscles—6 millions, haemoglobin 40 to 50 per cent., colour index 0·5 or even less. In severe cases poikilocytosis, a few normoblasts and no megaloblast. Leucocytes may be normal or slightly increased. The total volume of the blood is markedly increased. Absolute reduction of haemoglobin is not very great, while plasma is abnormal in amount.

Pathogenesis.—Vœco's theory—There is hypoplasia of the circulation of the generative system. Modern researchers do not support this theory.

Bunze's theory—Intestinal fermentation—H_2S formed from excessive fermentation fixes the iron from food as insoluble sulphide, thus causing iron starvation.

Third theory. - Some abnormality in abdominal organs as gastroptosis lead to its occurrence.

Diagnosis.—The blood should always be examined to differentiate it from pulmonary and glandular tuberculosis, gastric ulcer, nephritis,

exophthalmic goitre and neurasthenia. Symptoms special to it as plumbness, puberty and pallor (*i.e.*, P_3) combined with symptoms of secondary anaemia without wasting should be marked.

Treatment.—1. Rest in bed in recumbent posture.

2. Iron is specific for chlorosis. It increases in R.B.Cs. even above normal, the increase in haemoglobin is slower and maximum percentage may not be reached for a long time. There is no better form to push iron than Blaud's pill. During the first week gr. xv of the same during a day, in the second week gr. x a day, and gr. xv in the third week. Iron is to be given for at least three months and, if necessary, subsequently it should be resumed in smaller doses as recurrences are so common. Other forms of Iron as *(a)* Ferri Sulph. gr. ii t.d., reduced Iron gr. iv t.d., Tr. Ferru Phosphatis gr. x t.d. or the following mixture may be preferred :

Ferri Sulph	...	Gr. ii
Mag. Sulph.	...	℥ i
Acid Sulph dil	...	♏ x
Tr. Zinger	...	♏ x
Infusion Gentian Co	...	℥ i

Mist one sig, to be taken t. d. s.

3. Regulation of the bowels :—Free evacuation of bowels should be specially noted daily. Morning saline is perhaps the best.

4. Diet :—Moderate mixed diet. When there is dyspepsia it should be checked by proper medicines and milk diet prescribed. In milder cases light diet, then give fish, and afterwards add meat to the diet.

5. Care of teeth :—Teeth should be cleaned two times after principal foods regularly and the face should be washed with moderately warm saline water,

6. Treatment during convalescence :—Fresh air, regular habit, moderate exercise, regulation of bowels. Advise ordinary mixed diet with meat. Medicinal—Iron—Arsenic and Strychnine should be given in the form of Easton's Syrup 3 i t.d.s.

Banti's Disease—Splenic Anæmia

BY

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IN the kaleidoscopic picture of the field of Haematology, Banti's Disease—though not very picturesque in its blood film—is still very interesting in its clinical data and sometimes rather knotty in its diagnosis. While a typical case of Banti's with its initial splenomogaly, later heptomegaly and final ascites is easy to diagnose the "A—typical" cases of splenic anaemia set one uneasy as regards diagnosis and prognosis. It is such "elastic" cases of Banti's as also the recent accumulation of information regarding treatment that has been the inspiring factor for choosing to discuss on what one might ordinarily style as a 'remote' malady of mankind.

Definition and Course.—Splenic anaemia is essentially a condition of signs, *viz.* more a syndrome than a disease ; a chronic condition characterised by the enlargement of the spleen and hypochromic haemolytic anaemia with a slow leucopenia and relative lymphocytosis. In about two or three years there is a hepetomegaly with obvious cirrohotic changes and slight jaundice. In another two or three years the liver tends to shrink and then haemorrhage from the oesophagus and stomach—haemetemesis, from the intestines-malena, from the kidney—haematuria, from the nose—epistaxis and under the skin—purpura. Severe haemorrhages are followed by peritoneal filling ascites. At no stage in the disease are lymphatic glands enlarged. While the foregoing indicates the usual landmarks in the course of this disease, it must be remembered that there is no water-tight compartment and that there are many atypical forms.

Etiology and Pathology.—Here for the sake of brevity we shall refresh ourselves mainly with those features which throw light on the treatment of the disease, most common in third and fourth decades of life but which is found to occur at all ages outside infancy.

Spleen :—Increased size due to dilatation of blood sinuses, and increase in the fibrous tissue round the central artery of the malpighian capsule ; perisplenitis is common. Thus the histological picture is one that is found in long-standing "passive congestion." In this connection it must be stressed that this histological picture of passive congestion in the spleen is identical with that found in the spleen in cases of "primary cirrhosis of the liver." It is in view of this fact we conclude *ipso-facto* the splenic changes in Banti's desease are secondary to portal obstruction which *per se* is against the school that advocates splenectomy as a therapeutic measure in this disease.

Liver :—Even in very early cases there is invariably some degree of cirrhosis of the liver *viz.*, "periportal cirrhosis". The œsophagial veins show marked dilatation

Differential Diagnosis.—Briefly the other allied conditions to be considered are : (1) Acute and chronic diseases which produce splenic enlargement, *viz.*, infective endocarditis, malaria, syphilis and schistosomiasis, when the patient has lived outside India ; (2) Leukaemias and pernicious anaemia. Acholuric jaundice from which it is differentiated by the increased fragility of the R.B.C. (in Banti's fragility normal). (3) Tumours

of the left hypochondrium which stimulate an enlarged spleen. Carcinoma of colon or stomach or a peptic ulcer can be excluded by a radiogram. The differential diagnosis between hepatic cirrhosis and Banti's, though not easy, yet it is usual to state that in Banti's, the spleen is usually enlarged before the enlargement of the liver. Further the enlargement of the spleen in cirrrhosis is not as big as in splenic anaemia.

While a strightforward case of Banti's is diagnosed without an "if" or a "but," there are cases which tax one's clinical acumen to the utmost and yet keeps one guessing. In this connection we would cite in detail one of our recent cases.

Patient, H., male 57, has done lot of travelling over the continent, Great Britain and Ireland. Was in Burma service for over 25 years travelling both in forests and towns of the whole of the province of Burma.

Previous history :—Healthy and strong except for chronic malaria and incompletely treated amoebic dysentery of 9 years duration and diabetes of 7 years' recognition. Within the past three years patient has had six bouts of severe haematemesis at intervals of about 3 to 6 months. Each attack of haematemesis would last about two to four days, the quantity of blood being half to over a pint at a time, repeated thus three to five times during each attack. During the first 5 attacks patient developed marked ascites with severe secondary anaemia. Measurement of abdomen over the umbilicus being 38". During the sixth attack the peritoneal filling was partial. (Present measurement of chest and abdomen being 37 and 34 inches respectively). The ascites during the second attack was so distressing that the abdomen had to be tapped thrice to relieve dyspnœa. Three months back patient had a sensation of internal-gastric haemorrhage, *viz.*, giddiness and heaviness in the abdomen. There was malena lasting three to four days after that.

The clinical findings in the case are spleen palpable four fingers below the costal margin, hard not tender; liver two fingers below the costal margin, hard no tenderness; caecum thickened and tender; transverse and decending colons markedly thickened. The following are the laboratory findings three months after the patient got over his last attack of haematemesis and severe ascites and was out of bed moving within the house: Total R.B.C. 3·35 millions. W.B.C. 4,247 per c.mm. Haemoglobin 62%. Fragility lysis of R. B. C. 0·4% + 0·35%++ 0·30%+++ Vandenburg indirect positive.

Differential Counts :—Poly 79%, lymphocytes 13%, monocytes 2·1%, eosinophils 4·3%, basophils 1·6%, B. P. 136/88. W. R. negative. Fractional test meal showed slight achlorhydria. Barium enema—head of meal normal. Lung fields in radiogram nil abnormal. Skiagram of teeth showed root infection of one or two teeth.

GLUCOSE TOLERANCE TEST.		BLOOD SUGAR.	URINE SUGAR.
Fasting ...	...	254·8	++
½ hour after 50	gms. of Glucose.	294·2	+++
1 hour ,,	...	367·0	++++
1½ hours ,,	...	400·0	++++
2 hours ,,	...	400·0	++++

The case thus affords very interesting data for discussion. Whether it is one of primary cirrhosis caused by a gastro-enteritis, with the toxins of amoebic dysentery and malaria, running a chronic course in spite of such severe attacks of haematemesis, or is one of those "benign atypical" cases of splenic anaemia, without much of a leucopenia, or a relative lymphocytosis and a small sized spleen, responding well to symptomatic treatment even in the third stage of the disease *i.e.*, ascites and giving a fresh lease of life, we leave it open.

Treatment—1. Splenectomy.—Till recently there were many adherents to this, but of late there is a wide school of thought developing which holds that splenectomy is definitely not indicated since, as we discussed before, the pathological changes wrought in the spleen are entirely due to primary changes in the liver and that owing to the fact that cirrhosis may progress in the liver and hæmatemesis recur or what is more even start for the first time subsequent to splenectomy. It is on this score DAVIDSON exonerates the spleen. He does not also believe that the spleen has any toxic or inhibiting action on the regeneration of R.B.C. His indication for splenectomy is only on anatomical and mechanical basis, running a risk of 5 to 10% mortality in early and 30% in late cases of splenic anaemia. BEAUMONT opines that in more than 50% of splenectomised cases there is recurrence of haemetemesis. Ligature of the splenic artery is sometimes resorted to by those who believe in splenectomy, when after opening the abdomen it is realised that splenectomy is highly dangerous. While the operative risk of ligation of splenic artery is less, very severe reactions are said to result. DAVIDSON on authentic observation holds that the little benefit that may accrue from splenectomy is due to the establishment of collateral circulation in the post-operative adhesions, and if this is what is desired by the advocates of splenectomy it might be better achieved by the less serious operation of Talma-Morrison's. Lastly, it is suggessed that if splenectomy is decided upon, it should be undertaken only when the haemoglobin has gone up to 70 or 80% by iron therapy and by blood transfusion, if necessary.

Symptomatic treatment.—Of late massive doses of iron has been found to be beneficial, like Ferri et Am. Citras gr. 30 t.d.s. or Ferrous tablets of Glaxo, or Colliron of Evans. Iron therapy fails only when hepatic failure is approaching. BEAUMONT suggests combining this with X-ray treatment to the spleen.

Blood transfusion.—Blood by grip transfusion is indicated when there is shock secondary to severe haemorrhage.

As a rounding off to what has been already mentioned, we might add vitamin C which prevents to some extent capillary haemorrhage and vitamin B with Insulin and Glucose to "patch up" a cirrhotic liver and a diet rich in blood-forming ingredients like liver kidney, avoiding highly seasoned and coarse dishes like pips and skin of vegetables which may irritate the dilated veins of œsophages and stomach.

Deficiency Anæmias and Substitutional Therapy

BY

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I PROPOSE to deal, in this paper, with a group of anaemias, which are the direct result of a deficiency of one or more factors necessary for the formation or regeneration of blood and the substitution of which bring about a cure of the respective anaemias. So, an important group of anaemias, due to destruction of blood, either as a result of haemorrhage, sudden and copious, or small and long continued, or to haemolysis, will not be considered. So also those secondary to so many diverse diseases, as a result of depression of the erythropoietic tissues by infection, toxaemia or cachexia and those due to destruction or aplasia of the bone marrow, will not be described, though these anaemias are more or less influenced by the administration of the two important nutritional factors, iron, and anti-anaemic principle of the liver.

I will just recapitulate the physiology of blood formation and the nutritional substances necessary in the different stages of the same. The foremost precursor, the great grandfather of the R B.Cs. is the big endothelial cells, lining the intersinusoidal capillaries of the bone-marrow. These cells divide and redivide by a process of mitosis, and are now called megaloblasts. These are large cells, much larger than R.B.Cs., and have got big reticular nucleii. Their cytoplasm is basophilic taking on the blue colour of the Leishman stain. These again divide and redivide and become normoblasts, which are smaller in size than the megaloblasts. They contain pyknotic, deeply staining nucleii and their cytoplasm is not so basophilic, since they contain more haemoglobin than their immediate precursor, megaloblasts. After some time these normoblasts throw out their nucleii by a process of extrusion or solution and ultimately become erythrocytes. For some time, immediately after the disappearance of the nucleii, the normoblasts retain some of their original basophil cytoplasm and the erythrocytes appear slightly blue in ordinarily Leishman-stained specimens and are called diffuse basophils. When these cells are treated with brilliant Cresyl blue, their basophil cytoplasm is precipitated into a reticulum of fine strands and so are known as reticulocytes. Thus it will be seen that diffuse basophils and reticulocytes are one and the same cells revealed by LEISHMAN and CRESYL blue stains respectively. The presence of reticulocytes is an index of the speed and intensity of the blood regeneration, and hence of much importance in diagnosis and checking the results of treatment.

It has been found out that at each stage of the maturation of the R.B.Cs., some substance or substances are required for the completion of the process. Thus, for conversion of primitive marrow cells into megaloblasts, the substances necessary are not found out. From megaloblasts into normoblasts, a factor called the anti-anaemic factor, otherwise called P.P. factor (pernicious anaemia preventive factor) is essential. This is produced as follows: The thermolabile enzyme produced by the stomach (intrinsic factor of Castle) acts on the protein in the diet and produces a haemopoietic hormone, which, in turn, acts on the "extrinsic factor" of Castle, believed to be vitamin B, and the resultant anti-anaemic principle is stored up in the liver. For the maturation of normoblasts into erythrocytes, iron, copper, manganese, vitamin C and thyroxin are necessary. Thus

it is seen that if any of these substances are not available in required amounts, the maturation of R.B.Cs. stops short at that level in which these substances are necessary for their further maturation. Thus, if P.P. factor is not available, maturation of megaloblasts into normoblasts cannot take place and they are thrown into the circulation. So also, if other substances, chiefly iron, are not available, normoblasts cannot become erythrocytes; they multiply and encroach upon the shafts of long bones. In all these conditions, mature R.B.Cs. are not thrown into circulation in proper amounts, megaloblasts or normoblasts are thrown into the circulation as the case may be and anaemia appears.

Now, as to how deficiency of one or more of the factors are brought about. Deficiency of iron may occur as in any other deficiency by (1) deficient supply, (2) increased loss, and (3) increased demand. It is a well-known fact that in India, the economic conditions are such that the majority of the people are not able to consume, even in barely minimum amounts, the chief iron-containing food-stuffs as red meat, milk, yolk of eggs, and green vegetables, and no wonder that hypochromic microcytic anaemia is rife in India; and those few individuals who are getting the bare minimal amount of iron, break down and become severely anaemic, when there is an increased demand for that commodity as in pregnancy and lactation, or increased loss as in infections, haemorrhagic conditions etc. Infants, no doubt, come into the world with a sufficient amount of iron reserve to last them for a period of nine months, when iron containing food can safely be given. If they should come down with much less reserve of iron, as not infrequently they do, when they are premature, or when their mothers themselves were suffering from severe anaemia during pregnancy, their small reserve lasts them at the most for a couple of months and then they breakdown and anaemia results. Even if they are fortunate enough to have normal reserve, prolonged lactation, feeding on the bottle for a long time, and the numerous infections to which the infants are subject to, all conspire together and exhaust the normal store and bring about anaemia. The infections, in particular, deplete the iron reserve rapidly, not only by using more iron to fight the infection, but also by having a depressive action on the haemopoietic tissues, and by interfering with the ingestion of iron due to restricted feeding, which these infections entail.

Even an adequate intake of iron may fail to keep the blood at normal level, if the patient is achlorhydric or even hypochlorhydric. Iron is better absorbed from the intestines when its contents are acid in reaction than when they are alkaline. In rare cases of normal gastric secretion, there is deficient absorption from the intestines due to intestinal dyspepsia. This hypochlorhydria is important, as it is almost always found in all cases of microcytic hypochromic anaemia, whose incidence is very common in women. Of course in all these cases, aggravating factors, as pregnancy, lactation, infections, and flow loss as in menorrhagia etc., may be found.

A deficiency of the anti-anaemic factor of Castle may be brought about by: (1) deficiency of the extrinsic factor, giving rise to tropical nutritional anaemia; (2) deficiency of the intrinsic factor due to achylia as in pernicious anaemia and in cancer of the stomach, and post operative resection of large parts of stomach; (3) deficiency of absorption of the anti-anaemic factor as in sprue, cœliac disease, idiopathic steatorrhœa, stenosis, resection or ulceration of small intestines, and infestation of the

intestines with Bothricephalus latus parasites; and (4) ineffective storage of the P.P. factor and utilisation of the same by the bone marrow.

Individuals differ greatly and widely in their ability to withstand anaemising agencies. In this respect women are more vulnerable than men, and all the anaemias with the exception of those due to malignant disease are more common in women. This vulnerability might be a peculiar feature to women, but the occurrence of pregnancy and lactation add not a little to the frequency of anaemia in them. It has been estimated that in most women, during their child-bearing age, there is a relative iron deficiency with temporary exacerbations of the same during pregnancies.

Children also differ greatly from adults in their response to anaemising tendencies. A condition producing mild secondary anaemia in an adult with slight leucocytosis and perhaps a few normoblasts will induce in a child profound anaemia with enlargement of liver and spleen, œdema, and appearance of nucleated R.B.Cs. even megaloblasts and immature white cells. So anaemia in a child is a more serious and urgent disease, jeopardising the chances of recovery even in trivial infections and haemorrhages, which would have been inocuous if the child were not anaemic. But fortunately they recover soon, and completely too, if proper treatment is instituted at the correct time and anaemias of aplastic nature, which are generally fatal in adults, can almost always be repaired in a child.

I do not propose to go into the signs and symptoms of anaemias but to stress the fact that signs and symptoms might be out of proportion to the severity of the anaemia and by the time the conjunctivae and mucous membrane become conspicuously pale, profound haematological changes have happened in the blood. In slight cases, nothing abnormal, either subjective or objective, can be found. Even in moderately severe cases, the signs and symptoms might be very few, and only after prolonged and careful questioning the patient might tell you that she is feeling weak and run down, breathless on exertion and perhaps slight œdema. It is remarkable in children, that they play about as if nothing is amiss, with as low a percentage of haemoglobin as 30%. So a diagnosis of anaemia must be made by the estimation of haemoglobin and thorough blood examination, not only for the determination of the presence of anaemia but also for the purposes of determining whether they belong to hyperchromic macrositic anaemia due to the deficiency of anti-anaemic factor, or to hypochromic microcytic anaemia, due to deficiency of iron, copper etc. This diagnosis is important, for by the replacement of the correct deficient principle, the anaemia can be completely and rapidly brought under control. Huge amount of money is being wasted by the indiscriminate use of liver extracts in all anaemias-for a condition, more commonly met with, which can be rapidly cured by the administration of a few pice worth of iron a day, is being treated inefficiently with costly liver extracts.

Treatment.—Hypochromic microcytic anaemia. When a definite deficiency of iron is found, it is useless to try to increase the level of iron by administering iron-containing food. It is costly, even if tolerated by the patient who is most probably suffering from diarrhœa. Recent investigations have shown conclusively the futility of the administration of small quantities of iron and need for massive doses of the same. Different preparations of iron differ greatly in activity. The injections of Iron are

not only very painful, but the iron content in them is infinitesimal. Even if they happen to be potent enough they give rise to toxic symptoms. So the doctor and not the patient is benefitted by these injections! Metallic iron is insoluble and is inactive. The number of organic preparations of iron in the form of haemoglobin are a legion and are even now being prescribed in all anaemias. They might do some good in conditions of general debility and weakness, but in definite cases of anaemia they are worse than useless. Ferrous salts, scale preparations and Ferric salts are all effective; but the Ferrous is the most potent and Ferric least potent of these. These things when given in the following doses, Ferrous Sulphate nine grains per day, Blaud's pills 45 grs. daily, Ferri et Am. Citras 90 grs. daily and Ferrous Chloride 7½ grains daily, are all effective and induce 1% or more of rise of haemoglobin level in a day. It will be found that Ferrous Sulphate and Ferri et Ammonia Citras answer all the purposes of the general practitioner. Ferrous Sulphate is superior to scale preparations in that 20% of the former as compared with 2.5 % of the latter are utilised for haemoglobin formation and so is more economical; (2) Ferrous Sulphate tablets are very handy, can be carried about and need not be renewed very frequently as a mixture containing the scale preparation; (3) no blackening of the teeth or tongue occurs as in fluid preparations; and (4) but most important in this country is cheapness, a few pice worth of Ferrous Sulphate a day is enough. Ferri et Ammonia Citras is supposed to be least upsetting to the digestion and is very useful in children in whom the advantage of a fiuid preparation is obvious. In children, a dose proportionate to the age should be given. Generally, in infants and children, 3 grains of Ferri et Ammonia Citras for every 2 lb. of body weight per day, answers the purpose well; and this quantity of iron is equally divided by the number of feeds and then administered in the last few ounces of every feed.

When once the administration of iron is begun, there is no rise in the percentage of haemoglobin for the first four or five days, and then it begins to rise. This may be very quick at first *e.g.*, from 30 to 50% within a few days and it takes more time to rise from 50 to 80% and several weeks and full doses of iron may be necessary to reach this level. Infections, no doubt, retard the rapid rise of hæmoglobin. With such massive doses, diarrhœa is more common than constipation. Unfortunately it so happens cases requiring massive doses of iron have diarrhœa as part of the picture, preventing the administration of such doses. In such cases, it is necessary to accustom the patient to iron and to begin with smaller doses and gradually increasing to requisite level and to combine it, if necessary, with Dover's powder, Tr. Camph. Co. or Liquor Bismuth, etc. Effective patent preparations of iron are on the market and one can make wide variety of selections to suit the needs and purse of the patient: (1) Glaxo's Fersolate tablets containing 3 grains of Ferrous Sulphate with some copper and manganese in each tablet; (2) Plastules Haemotinic Co-Plain (John Wyeth & Brothers) containing 5 grains of fluid Ferrous Sulphate with vitamin B, in capsules; (3) Elexir Ferrone (Upjohn) with 30 grains of Ferri et Ammonia Citras in one tea-spoonful; and (4) Syrup of Citrated Ferrous Chloride (B. D. H.), etc.

Hyperchromic macrocytic anæmia.—When this variety of anaemia is diagnosed, treatment with liver should be instituted. In cases of megalocytic anaemias due to absence of extrinsic factor, as in tropical nutritional

anaemia of pregnancy, and due to defective absorption as in sprue, coliac disease, idiopathic steatorrhoea, etc., administration of vitamin B as yeast or better still, Marmite, an autolysed yeast product, will be found to give better results. Somehow, in these cases, highly purified liver extracts, as Anhaemin, Neo-hepatex, etc., do not give as good a result as crude liver extracts, as Campolan, Hepatex-T, etc.

In Addissonian pernicious anaemia, treatment with liver, liver extracts or hog stomach extracts as Ventriculin, by mouth, should be started. All these things give good results. It must be well understood that treatment of pernicious anaemia is not some liver, but enough liver. At least half a pound of liver every day must be given; if this the patients are not able to tolerate, this can be alternated with 250 grammes of extract or 2 tablespoonfuls of hog stomach extract; no one particular dose will suit all cases. Every patient is a type by himself. Not only the need for extract varies from patient to patient, but also from time to time in the same patient. Thus a patient who has not had more than one relapse might need only $\frac{1}{3}$ to $\frac{1}{2}$ the requirements of an elderly patient, who has had many relapses, and who is the subject of arterio-sclerosis, diabetes, etc. Even the same patient needs much more of these anti-anaemic principles when he is suffering from sepsis and acute infections and early symptoms of sub-acute combined degeneration of the cord, than when there are no complications.

The important thing to be kept in mind is, even though these patients feel quite alright with a subnormal blood count as four million R.B.Cs. and 80% Hb. it is absolutely necessary to maintain 5 millon R.B.Cs. and 100% Hb; for it is only in these subnormal people, who are apparently healthy, that sub-acute combined degeneration of the cord occurs. This disease has become much more common now than formerly, since many P. A. people are made to live with a subnormal blood count with liver extracts, who would not have lived to get this disease, if liver extract were not administered. This state of affairs can only be found out by repeated blood examinations.

The advent of potent liver extracts for injection, has revolutionised the treatment P. anaemia. Many of the cases, whose blood cannot be maintained at the requisite level by oral administration of liver and liver extracts alone, were able to do so with simultaneous injection of liver extracts. Most of the patients are not able to carry on oral treatment, either because of gastro-intestinal disturbances, which are invariably present in these cases, or of vegetarianism or of the heavy cost which these things involve. So, in general practice, the oral treatment has been superseded by injection of potent liver extracts.

The manufacture of crude liver extract for injection is so easy that every firm is able to launch a product of its own into the market. Since the method of manufacture does not concentrate the material, very few of these contain more than 5 to 10 grammes of the active principle in one c.c. though they claim to contain the active principle from 50 grammes of liver in 1 c.c. As to the injection, it does not much matter if it is given I.V. or I.M. unless in patients very ill, who cannot absorb enough liver extract quickly and rapidly enough from the muscle, due to failing circulation, œdema etc., when I.V method can be resorted to. But there are some points to be observed, when resorting to this method: (1) observance of

technique as to sterilisation, rapidity of injection etc.; (2) highly purified liver extract only must be given. All liver extracts recommended for I.V. injection can be given I.M. but the reverse should never be the case. Even while giving the purified liver extract I.V. anaphylactic sypmtoms as itching dyspnœa, falling blood pressure and collapse not infrequently occur and must be treated with Adrenalin. When the patient is having treatment with liver extract injections, or shortly after a course, one not infrequently finds especially when inferior brands of liver extracts that flood the market have been used, the kidney becoming involved, as evidenced by albumin in the urine, puffiness of the face etc., and if not detected at proper time and treated, fatal result may ensue. Generally in most of the cases I.M. injection is quite sufficient and the blood regeneration and reticulocytosis are fairly rapid.

As to dose every patient must be studied by repeated blood examinations and the dose adjusted. The following points must be borne in mind: (1) One who has had a number of relapses requires more active principle than an early case; (2) patients who have also developed acute infectious diseases,and especially sepsis, must be treated with more liver extract than an uncomplicated one; (3) it requires more time and more liver extract to raise the blood level from 3 million R.B.Cs. to 5 million R.B.Cs. than from one million to 3 millions. What we generally do is, as soon as the patient notices definite improvement, which is generally the case with 3 million R.B.Cs. and 80% Hb. we reduce the dose, if not completely stop this altogether, the result being, as was formerly pointed out, more cases of sub-acute combined degeneration of the cord. When repeated blood examinations show that cent per cent. Hb and R.B.Cs are not attained, the dose must be increased and even doubled to achieve this result; (4) the disease is one of deficiency and it is almost permanent and as in the case of deficiency diseases as diabetes, the treatment must be continued for life. Enough anti-anaemic principle must be given every day for the first few days to initiate a definite reticulocyte crisis and for the liver to store up its deficient anti-anaemic principle, and once this has been achieved to continue with a maintenance dose, to balance the amount of A.A. principle utilised for the body needs every day; (5) no case is too ill to receive the injections. DR. L. S. P. DAVIDSON, in 'Medical Press and Circular,' mentions of a case, having a R.B.C. count of 600,000, severe heart failure with œdema, double pneumonia and bed sores, responding remarkably to I.V. liver therapy with 46% reticulocytes crisis and rapid rise of R.B.Cs. to normal.

The method adopted is to give the active principle contained in 50 to 100 grammes of liver every day for 5 or 6 days, until a well marked and definite reticulocyte crisis occurs and then to continue the dose, giving the same quantity at intervals of a week till R.B.Cs. come to 5 millions and Hb. 100%. If repeated blood examinations show that the blood does not become cent per cent. normal, the quantity and the frequency of liver extract must be increased to achieve this result. When once this result is achieved, then a maintenance dose must be given to the patient with 20 to 100 grammes of active principle every two weeks. Some require a weekly injection and others monthly ones. It takes much time and repeated blood examinations to find out the optimum maintenance dose, and once this has been properly settled, there is no reason why intelligent patients should not be trained to give injections themselves as diabetics do, with all the difficulties attended with insulin administration.

A word about the depot treatment with liver extracts, which was much in vogue some time ago, when Campolon was available. It consists in giving 4 c.c. of Campolon on admission, and to give 12 c.c. I.M. of the same the next day to form a depot. Subsequent injections of 10 to 12 c.c. are given every week till the blood becomes cent per cent. normal. When this has been achieved, to give the maintenance dose of 8 to 10 c.c. every month. This method claims to have some advantages, in that the number of injections are greatly reduced, a thing of much importance to patients. It is no more painful than giving a single injection of 2 c.c. and no local complications occur. The blood response is as good as, if not better than, the treatment outlined. I do not know whether this kind of depot treatment is advocated with any other liver extract injections that are available in the market to-day.

Though the intelligent substitution of the deficient principles is quite enough to cure the anaemia, the general and adjuvant treatment must not be neglected. Thus rest in bed is essential to limit the wear and tear of the circulatory apparatus. General nourishing food, easily digestible, must be administered frequently. If microcytic hypochromic anaemia does not much improve with proper doses of iron, judicious combination of copper, manganese, vitamin B and often times crude injectible liver extracts bring about rapid improvement of the condition. In the same way, some cases of macrocytic hyperchromic anaemia, do not attain the 100% Hb. and 5 million R.B.C. level, no matter how much liver extract or how frequently the injections are given. In such cases addition of iron, marmite or other yeast products, do the trick.

In conclusion it must be said, if a case is bad enough to be treated for anaemia, it is bad enough for a thorough blood examination, and treatment by proper substitution of the deficient principles is quite satisfactory.

Summary.—The following things are dealt with in this paper, in a concise manner.

1. The physiology of the developnent of R.B.Cs. and the substances necessary in the different stages of the same.
2. How the deficiency of various factors are brought about.
3. How different individuals, men, women and children react to anaemising tendencies.
4. The importance of repeated blood examinations for diagnosis and treatment.
5. Treatment of the two important deficiency anaemias considered in detail. The importance of keeping blood cent per cent. normal, *i.e.*, 100% Hb. and 5 millions R.B.Cs. is stressed.
6. Depot treatment with liver extract, mentioned.

References:

1. F. W. Price.—A Text Book of the Practice of Medicine
2. Cecil P. G. Wakely.—Modern Treatment in General Practice.
3. 'Antiseptic,' 1941 September.
4. Bayer's Medical Diary, 1939.

Comparative Study of Anæmia and its Treatment

BY

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In diseases of blood, the most important point to be borne in mind, concerns red corpuscles (erythrocytes), white corpuscles (leucocytes) and hæmoglobin. In normal blood per cubic millimetre there are 500 thousand red corpuscles in males and 450 thousands in females, and seven to eight thousand leucocytes. The hæmoglobin of the red corpuscles is the oxygen carrier, and hence in order that respiration may go on properly in the tissues, it is most essential that the lungs and heart should be healthy, and the hæmoglobin should be sufficient. If any one of these three requirements fail, shortness of breath readily sets in.

In the strict sense of the word, anæmia means want of blood. Anæmia is a general term used, when blood is defective in quantity, or in quality, or in both respects. Anæmia is generally regarded as being either primary or secondary. Primary anæmia arises without any discoverable cause and is hence referred to a supposed disorder of the blood-forming or blood-destroying mechanism. Secondary or symptomatic anæmia, on the other hand, can be accounted for, by the existence of a recognised cause, such as want of food (bad nutrition) or some digestive disorder which prevents the formation of blood, or a toxic condition which causes destruction of blood or albuminuria. suppuration or hæmorrhage, which impoverishes the blood in some of its constituents. Under primary anæmia is grouped, chlorosis and pernicious anæmia.

According to Indian Medicine, "*Pandu*," "*Sogai*" and "*Kamalai*" correspond to anæmia of allopathy. *Pandu* literally means paleness or whiteness, which word is derived from the illustrious personage "*Pandu*" of the great epic *Mahabharatam* who, it is said, was as white as a lily, without any colour or pigmentation in his skin. *Sogai* corresponds probably to chlorosis, and *Kamalai* to jaundice. In the Indian system of medicine, however, it is not said that chlorosis is a common affection of the fair sex, as it is said in the western system of medicine.

Anæmia, chlorosis and jaundice, are put and dealt with together, in Indian medicine, under one chapter, because the causes and symptoms are more or less identical, and the line of treatment the same.

The general effects of anæmia on the whole upon the body, are imperfect oxygenation and nutrition, which are followed by impairment of function, shrinkage of tissues, softening of the blood vessels, and, in long-standing cases, fatty degeneration of the various organs. Thus begins a vicious circle of retrograde changes, each new failure on the part of an organ increasing the original defect.

Chlorosis.—Is a peculiar anæmia attended with a greenish transparent wax like condition of the skin, generally common in females, and characterised by a deficiency of hæmoglobin. Though the modern scientists are not yet definite about the causes of chlorosis, the following few are considered to be the chief theoretical explanations:—

1. Chlorosis is due to constipation and toxic absorption from the bowels (ANDREW CLARK).

2. Demands of puberty reveal a congenital narrowness of the arterial system, which prevents the proper supply of blood to the various tissues (VIRCHOW).

3. The organic iron compounds of the food are broken up by excessive decomposition in the alimentery canal, and the iron thus liberated, cannot be absorbed into the blood (BUNGE).

4. It is due to excessive loss of blood at the period of puberty, which leads to dyspeptic conditions, anorexia and defective absorption of iron (STOCKMAN).

5. It is due not to an absolute diminution of haemoglobin, but to an excess of plasma. (HALDANE and LORRAIN SMITH).

None of these theories covers all the cases. The chief symptoms are failing strength of vague onset and considerable duration, accompanied by a pallor of the surface. The pallor is marked in the lips, gums and conjunctiva (as may be observed by pulling down the lower lid). The skin presents a greenish hue. Patients generally present themselves either for cardiac symptoms such as dyspnœa on slight exertion, palpitation etc., or for digestive symptoms such as deficient or capricious appetite and discomfort after food, and there may be present atonic dyspepsia, gastric atony or gastroptosis. The blood appears pale and the total haemoglobin is very low. There is an excess of watery constituents of blood or hydraemic plethora. Gradual increase of these symptoms in intensity and gravity with few additional and analagous symptoms, constitute various kinds of anaemia.

According to Indian medicine, the causes of chlorosis are, excessive physical exercise, excessive sexual indulgence, excessive use of wines and spirits, too much use of chillies, pepper, and mustard, and other articles of keen virtues, and the use of burnt earth as food, leads to an excitement of all the three *doshas* (*vadha*, *pitha* and *kapha*) which, in their turn, vitiate the blood and lead to these diseases. Before the appearance of chlorosis, the skin becomes cracked, the mouth frequently waters, the whole body becomes languid, a desire is felt for eating earth and ashes, the eye balls, become swollen, stools and urine become yellow, and indigestion manifests itself. After an attack of chlorosis, if one eats such food in excessive measure as excites bile, the bile becoming exceedingly excited vitiates the blood and flesh further which leads on to anæmia. Enlargement of liver also leads to this disease. A portion of the bilious secretions from the liver, instead of finding a way to the stomach, becomes mixed with blood and produces anæmia. In this disease, the eyes at the outset become yellow. A little while after, the skin, nails, face, stools, urine and the whole body becomes yellow, like a frog in the rainy season. Nausea, indigestion, weakness, disgust for food, and languor are the prominent symptoms. After the appearance of chlorosis and anæmia, the body may become greenish dark or yellow. With such changes of complexion, strength and energy decrease. Sleepiness, loss of digestive fire, fever, distaste for sexual indulgence, pain all over the body, burning sensation, thirst, disgust for food, delusion and similar symptoms manifest themselves. This disease is called jaundice *(Kamalai)*.

Treatment. *Western* :—Consists of rest in bed, administration of iron, attention to hygienic measures, and treatment of symptoms. As for administration of iron, it should be in sufficient quantities in gradually

increasing doses. Liqr. Ferri per Chlor is a valuable remedy, if the stomach tolerates. Ferri Sulphas with or without aloes, is also good, other remedies include Arsenic, Levico water (which contains Iron and Arsenic) Cod-liver oil, Lactophosphates, Malt extracts, Liver extracts and other manganese preparations.

Eastern System of Treatment.—The main and principal line of treatment consists in doing all that is needed to restore the functions of the liver. Leaves of *tinsofora cordifolia* pounded with whey should be given in liquid form. Iron has been considered the most useful remedy for blood production. Therefore any of the iron preparations, that would not cause constipation is advisable. *Loha basmam* (iron oxide) with the powders of the three myrobalams is usefully given. *Mandooram* and Carbonate of Soda, is also given with Saline purgatives. *Punarnavadi mandooram* and *Punarnavasara* are also given with *Thriphaladi lehyam* (confection of three myrobalams). When iron is melted, the impurities that come out are called *mandooram*. In my humble practice of about 15 years, I have found, "Draksha Ferratone," and Liq. Triferrol" of the Cochin Navaratna Pharmacy, very useful and a sure and effective remedy for anæmia, as the combination of various ingredients in both the preparations have been most judiciously and thoughtfully selected and compounded.

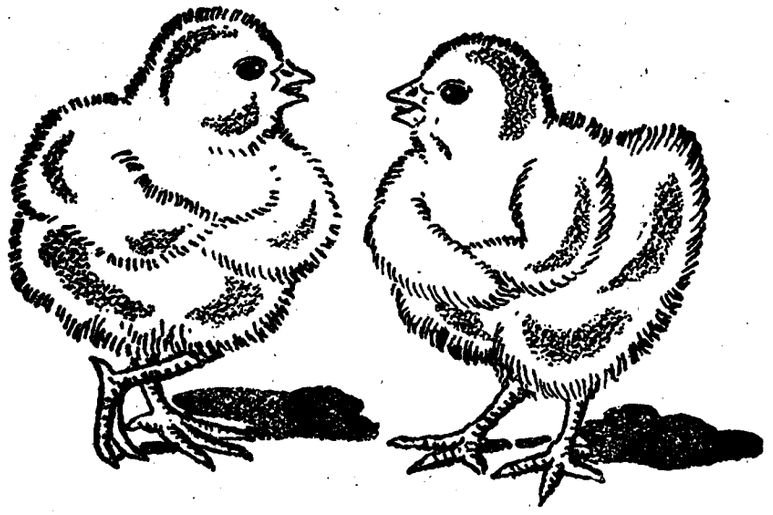
The difference between the iron preparations of the occidental and oriental systems of medicines, is very great. The chemistry of the present day chemists and chemistry of the ancients also differ very much. Just to quote one instance, the fat of cocoanut oil and ground nut oil may be the same from the point of modern chemical science, but their action on the human system is quite different. Some days later on, the researches of RAMAN may enable the modern scientists to understand the hidden secrets of the atomic and molecular world, which makes for the observed difference between a mercurial salt of the chemist and an analagous preparation of an Indian medicine physician, apparently the same as far as chemical analysis reveals, but so very different in their therapeutic potencies. Such a day is in the womb of the future.

In this connection and now, let me say a few words about the Siddha school of Indian Medicine. They have developed their chemistry to such a high perfection as to change the innate quality and characteristics of each material they use as medicine. They have evolved a set of theories and treatment which are the same all over the universe for all the time, because when creation evolved out from chaos, and from that time Man's edition and copyright of man by God, has remained and remains all the same, always, and is yet unchanged. According to this Siddha school, the whole universe is divided into 3 groups, *viz.*, *Dhatu*, *moola*, and *jeeva*. *Dhatu* or mineral group consists of salts with 25 subdivisions, *uparasams* (silicates and others) divided into 112 *Pashanams* (arsenics) of 64 divisions, *Lohas* (metals) of 9 varieties and *Rasam* (mercury), *Gandakam* (sulphur) said to be king and queen respectively of all minerals. The *moola* or the vegetable group is divided into six classes under the six tastes, salt, astringent, pungent, bitter, sour and sweet, with various degrees of strength, according to the kinds of natural growth *viz.*, trees, shrubs, creeps, juicy, juiceless and milk-giving plants. *Jeevas* or animal group are also classified into six classes, as per their originating seeds and germinating faculties.

The Siddha School of Indian medicine prepares its medicines from out of mineral substances, having salt as its basis, *rasam, gandhakam* and *pashanam* as ingredients for the mineral and *metallurgical* medicines. The universe is composed of five primordial elements of earth, fire, water, air and ether known as *Pancha Bhutas*. They have taken salt as the basis of earth and creation, and as the earth crust formation of the universe, they first chemically treat the same to stand the test of fire, to be melt as any metal, and then alkalize the same. Their test and mode of testing all the different minerals was, by natural and god-given agencies of water and fire alone, and not by acids got of salt and sulphur, as it is in the western analytical science. Salt is that which is soluble in water, and volatile in fire having, at the same time, the innate nature of bursting, smoking and burning. *Uparasam* (silicates) is that which is neither soluble in water; nor smoking, volatalizing, or burning in fire. *Pashanam* (arsenic) is that which smokes in fire, but nonsoluble in water. Metals are those which melt in fire, and last fixed, insoluble in water. Mercury is that which is being atomised and vapourized in the smallest degree of fire, and non soluble in water. Sulphur is that which smokes, burns, and volatalizes in fire and insoluble in water. The innate quality of each material is first changed. For example, salt which is soluble in water and volatile in fire, is to be changed to melt in fire, and non-soluble in water. In the same fashion, the nature of *pashanam*, which will waste in fire, and not soluble in water, has to be transferred to withstand fire and become soluble in water. *Uparasam* which is neither wasting in fire, nor soluble in water, has to be totally changed as that of a salt class of material. This process of transforming is called binding. After the process of binding, these materials will be turned into *basmams* (oxides), *chendurams* (sulphides) and *churnams*. *Churnams* are virulent and powerful oxides. These are fit to be administered as medicines for various maladies. The vegetable kingdom is useful in this course and process, as per the nature and class of medicines we want. By changing the birth innate nature of each material, we transform them into a substance acquiring higher nature and potentiality, and having the property and quality of becoming assimilable in the very tissues of the body.

References :

1. Usman Committee Report on Indigenous Systems of Medicine.
2. Kaviraj Nagendranath Sen Gupta—Ayurvedic System of Medicine.
3. Munro—Manual of Medicine.
4. Jack—Wheeler's Hand Book of Medicine.
5. Savil—System of Clinical Medicine.



First Chick: *"Talking of sacrifices for My DeMocracy we save lives of thousands of patients in the country".*

Second Chick: *"You forget the casualties on the Front and in the AIR RAIDS".*

Observations on Anæmic Conditions

Due to Mal-nutrition, in Tea Garden Coolies

BY

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IT is idle to conceal the fact that in my practice the number of cases treated for anæmic conditions due to mal-nutrition amongst tea graden coolies during recent years is much higher than that treated during the thirties of this century. The incidence is steadily going higher and higher and mal-nutrition is undoubtedly playing an important part in causing this condition amongst them.

This populace belong to the lowest economic stratum and cannot get for them a diet containing all the principles required for proper nutrition—the chief defects in their dietary being animal protein, calcium and vitamins. The situation has now been further worsened by the fact that due to scarcity of food-grains they cannot now take even two full rice-meals and cannot brew 'handi' for their drink, which has a definite food value and was so long the source of their vitamin supply. Consequently, they are becoming devitalised and falling an easy prey to minor diseases which they could fight to some extent previously. It is obvious then, that the preblem, at least of minium nutrition, for prophylaxis, is the problem of problems requiring immediate solution. The nutritional problem has now become a world problem, and if it can be solved, it will save this section of people—the back-bone of the society—in tea areas and in rural areas, where the present condition of the majority of the ryots can easily be compared with that of the tea garden coolies in many respects. The question of treatment of this condition comes next—for, what can medicines do in a hungry stomach?

I am sorry that I have been obliged to take some space in describing the present deplorable condition of the coolies, which seems to me the chief factor in causing such anæmic condition. I also express my regret, that for want of facilities and time, I could not study the problem more scientifically and record it as such. My observations and plan of treatment have, therefore, been made by assessing the value of different forms of treatment given to my cases successively or at the same time, and it is hoped it would be helpful to those who have no facilities for hæmatological examination. My suggestions to supply adequate nutrition to these 'haggard faces and desiccated bodies' are fervent appeals to the authorities concerned. It would be helpful if local medical associations kindly represent the cause of these dying precious souls to proper authorities for their consideration.

Symptomatology and Diagnosis.—Unfortunately, the coolies do not seek any treatment until they find that they feel too weak to do their daily work or get their swelling of the feet and/or face. They sometimes come with diarrhœa as the chief complaint and overlook the slight œdema of the face or feet. As a matter of fact, they usually come for treatment in a somewhat advanced stage, when there is marked pallor of the mucous membranes of the mouth, conjunctivæ, and nails. Some even complain of shortness of breath and palpitation. Hæmic murmur is audible in these cases. Oedema of the feet and/or face was the rule in my cases. In more severe cases, there are œdema of the whole body and dead white colour of

the mucous membranes. The mouth was sore in some cases. Hook-worm infection, chronic malaria, and kala-azar cases are not so rampant in my practice and are efficiently treated in their acute stages in the Dooars, so that we have a very low splenic index. These tropical affections, therefore, should not arouse confusion in respect of the causative factor of this anæmic condition—specially when those tropical diseases could be carefully excluded. It has also been found that the anæmic condition caused by the common tropical diseases readily responds to specific treatments and iron therapy. With the knowledge of the substances consumed as food and with careful exlcusion of other possible factors, this anæmic condition can easily be diagnosed.

Suggestions for the supply of improved dietary for prevention.—1. The rice supply by their employer should be on a higher scale in consideration of the energy they lose through day to day labour. If possible hullers should be installed in every tea factory (in villages there are *dhenkis)* for supplying 'atap' rice in place of milled rice; or rice polishings may be stocked in sufficient quantities to supplement the present milled rice. They should also be supplied with some quantities of pulses and cereals. It would be beneficial if a little quantity of rice is replaced by '*atta*'.

2. Tea garden coolies should be granted small lands and encouraged to produce green vegetables for their own consumption.

3. They should be made more milk-minded and should be educated to drink more milk. If necessary, all sweet meat shops should be banned so that liquid milk could be conserved for the use of the common mass of people. They should also be given facilities and encouraged for animal husbandry.

4. In tea areas where there are reserved forests and waters, the coolies should be allowed to hunt and fish with necessary restrictions at least one day in a fortnight. (In villages fish are available yet to some extent).

5. Their huts must be more hygienic.

Though 'handi' was the source of their vitamin supply and has a definite food value, I have purposely omitted it, as it was usually drunk to the point of intoxication and many unfortunate accidents were the sequelæ of the bouts. The above suggestions are believed sufficient for prophylaxis and thereby to prevent great economic loss, if translated into action.

Before I write down my plan of treatment of this anæmic condition I should like to stress again that this scheme has been outlined for those who have no facilities for detailed hæmatological examination like me and that this line of treatment was simply assessed on the value of different treatments in improving this anæmic condition. I have also neither the intention, nor the space to academically discuss the merits and demerits of various iron and liver preparations, or the role of vitamins in such conditions. These medicines and diets which are easily obtainable have only been used and noted.

Treatment.—Try to detect first any underlying or associated disease, if any, treat accordingly, keeping in mind that severe anæmias should also be treated intensively, simultaneously with the specific treatment of the causative factor or preferably first.

1. *Dietetic.*—Prescribe adequate diet from the very beginning to make up as far as possible the suspected deficiencies. This will enhance and maintain the improvement effected by medicines. Increase milk (cow's or goat's) slowly according to toleration, at least to one pint daily. In addition, prescribe some items from the following list to supply sufficient proteins, salts and vitamins to make the diet well-balanced, of course with due regard to the stomach and purse of the patient.

Cereals:—Bajra, rice polishings or bran, and atta.

Milk and milk products:—Milk, ghol, dadhi, chana if milk is not tolerated.

Meat and fish:—Duck, fowl or goat's, or any mammalian liver; fat or lean fish, fat fish preferable.

Eggs:—Whole; hen's or duck's, hen's better; yet much available a thing in a coolie or poor ryot's house.

Lentils:—Any dhal; whole gram is the choice when taken germinated.

Vegetables, tubers and roots:—*Beans*, barbati, *cabbage*, *cauliflower*, garlic, dharas, *onion*, *kalaishuti*, *potato*, *radishes* and their leaves, *palong shak*, *tomato*, *shank alu*, unripe jack-fruit.

Fresh fruits:—*Plantain*, baol, *kalajam*, *cocoanut kernel*, *cucumber*, guava, *lemon*, mango (not available in the Dooars) *orange*, papya, *peach*, *pineapple*, panifal, brinjal.

Mineral nutrients, *e.g.*, calcium, phosphorus, iron and copper will be supplied by the underlined items of the foregoing list.

2. *Advise sunshine and fresh air:* To purdanashins give extra vitamin D.

3. *Medicinal:*—Ferri et Ammon. Citras gr. 30 to 40 and Calcium Lactate or Gluconate gr. 15 to 20 is given orally, well diluted, thrice daily after food. Coll. Calcium with vitamin D is given parenterally as a routine to all pregnant women suffering from this anæmic condition. The number of injections is determined by the general improvement. Oral administration of Calcium is stopped, only when indigestion, gastric irritation etc., are complained of. Having no stock, I have no experience with many proprietary preparations of iron. If, at least within a week, no marked improvement is observed, judged by the appearance of mucous surfaces, condition of swelling of face and/or feet and the estimation of hæmoglobin by the Tallqvist method, Liver extract intramuscularly is started with, the dose and number of injections being determined according to the urgency and improvement.

With the above dietetic and medicinal treatment, which is also considered cheapest and practicable in these days of scarcity, most of my cases have done well.

In a very few cases I have been now trying Copper Citrate in gr. $\frac{1}{4}$ doses along with Ferri et Ammon. Citras, which combination appears better. I have intention to try henceforth Ferri Sulph. Exticatus with traces of Copper Sulphate, as that will be more cheap and is expected to be of the same therapeutic value as that of the other Iron and Copper preparations. Dilute Hydrochloric Acid, better with Pepsin (Vin. Pepsin.) which I give with success in full dosage, only in cases with diarrhœa or dyspepsia is also recommended.

NOTE.—Pregnant women were found very prone to this condition and were bad cases to respond quickly.

Summary.—Observations on anæmic conditions due to mal-nutrition amongst tea garden coolies have been made and suggestions for prophylaxis and plan of treatment found beneficial have been chalked out. The line of treatment has been meant only for those who have no facilities of a laboratory and have to treat their cases depending chiefly on clinical symptoms.

References :

1. Chopra; R. N.—A Hand Book of Tropical Therapeutics.
2. Hare, K. P.—Indian Medical Gazette, LXXVI. 531.
3. Chopra, R. N., and others—I. M. J., LXXVII, 295.
4. Napier, L.E., and Edwards, M. I. Neal—I. M. J., LXXVII, 503.
5. Variava, N. S.,—Journal of I. M. A., XII, 314.

Auto-Hæmo-Therapy

BY

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AUTO-HÆMO THERAPY is an injection of one's own blood from the vein into the deep muscular tissue of the same patient. I cannot explain its mode of action but the results obtained by this therapy in some of the conditions mentioned underneath are quite satisfactory.

The field of auto-hæmo therapy is a very wide one so that one of my superiors used to remark that, " whenever you are in doubt as to what line of treatment you should pursue in a particular case, always lay your hand first on the auto-blood therapy and it will prove to be a sure shot in the dark." I dread to make so dogmatic a statement but I have personally noted very good results, following its use in some of the conditions mentioned here, and I shall describe them in an order in which it has been frequently used with the maximum benefit :—

I. Asthma.	IV. Anæmia.
II. Generalised pruritis.	V. Recurrent bleeding.
III. Skin diseases.	VI. Hemiplegia.

I. **Asthma.**—Auto-hæmo therapy combined with N.A.B. injections is the best line of treatment because the relief thus obtained is very rapid and maintained for a very long time. Many practitioners on this side have established themselves as "Asthma Specialists " because of pursuing this line of treatment. The technique of giving the N.A.B. with auto-blood is as follows : Fill up one 10 c.c. syringe with a solution of N.A.B. and keep ready another sterilised empty 10 c.c. syringe nearby to give auto-blood. The patient lies flat on the couch. Prepare first the buttock area for giving auto-blood injection so that one has not to wait long with the blood in the syringe as otherwise the blood will clot in the syringe and make a mess of the whole thing. Some people use 2½% Citrate solution in the empty syringe to prevent clotting. Now inject N.A.B. solution intravenously (I.V.) and the last drop of the solution remaining in the needle is to be washed off by withdrawing and injecting the blood once or twice ; leave the needle in the situ and remove the N.A.B. syringe. Now attach the empty 10 c.c. syringe to the needle with or without the Citrate solution and apply pressure over the vein and ask the patient to open and close the fist till the desired quantity of blood runs down in the

syringe, and inject the same intragluteally ; the assistant compressing the vein has only to mind the I.V. puncture, otherwise there will be an extravasation of blood around the vein if he forgets to remove the pressure from the vein. These are trivial precautions but they are worth remembering and following so as to avoid an ugly scene. The advantage in using a separate syringe for the auto-blood is that not a drop of N. A. B. solution remains in the syringe or needle that may likely be injected intramuscularly with the blood ; otherwise the site of injection on the buttock becomes indurated and painful and the induration takes a long time to disappear. Such two or three N.A.B. with auto-blood injections give a marked and well sustained relief. Some substitute injection Nicotinic Acid with Glucose or Glucose-Calcium-Redoxon I.V. for N.A.B.—of course in combination with auto-blood.

II. **Pruritis.**—The proper course in this case is to find out the cause of itching and treat accordingly, but a marked symptomatic relief is obtained by injecting first 10 c.c. Calcium Gluconate or 10 c.c. Sodium Thiosulphate solution I.V. and at the same time withdrawing the desired quantity of blood in the same syringe and injecting intragluteally. I use the same needle during both the manœuvres. Intractable itching has been relieved very nicely with this.

III. **Skin diseases.**—Auto-haemo-therapy has a good scope in the treatment of skin diseases. In urticaria, it is to be combined with I.V. Calcium Gluconate or Sod. Thiosulphate. I have also used this therapy in a case of psoriasis where all sorts of local remedies were tried but without any beneficial effects. Even 25 to 30 injections of intravenous Sulfarsenol were given, the latter giving but a transient relief and then I was told to incorporate the auto-haemo after injecting the Sulfarsenol I.V. and that gave a rapid improvement. Scabies with pustular eruptions in youngsters has also responded well to this treatment than the course of milk injections and Sulphonamide therapy.

IV. **Anæmia.**—This therapy is a boon to the poor anaemic patients where their pockets do not allow them to have the costly treatment of Liver extracts and Vitamin B therapy. I fail to explain the mode of action of auto-blood in cases of anaemia but I have noted excellent haemopoietic response by its use alone. While I was working as an assistant to Dr. G. B. MANKAD, I had an occasion to compare the good effects of auto-haemo-therapy in anaemic patients. Two very anaemic cases were selected for the purpose and blood-picture of both of them were noted at the beginning of the treatment. One of them was then treated by giving only auto-blood every fourth day without giving any tonic etc., orally and the other was put down on a course of Hepatex 7 injections. I should say that the complexion of auto-blood patient was improving better than that of the other and the blood picture of the former after a month had also improved to a very great extent and maintained nicely for a long time even after the injections of blood were stopped. It does deserve a trial in such cases.

V. **Recurrent Hæmorrhage.**—In cases of prolonged recurrent haemorrhage, such as uterine bleeding or hæmaturia, where all the ordinary hæmostatic agents had their trial without any benefit, it is worth while giving a chance to this therapy ; 10 c.c. of blood to an adult patient must be the rule at the start and repeated every third or second day till the bleeding stops. It can be combined here with I. V. Calcium.

VI. **Hemiplegia.**—I remember one or two cases of hemiplegia benefitted by its use. In one case, the kalin was negative, the blood pressure was normal and the patient was hemiplegic with loss of power of locomotion. I started giving him auto-blood injections in graduated doses, 3 c.c., 5 c.c., 7 c.c., 10 c.c. every fourth day and then continuing the 10 c.c. dose every fourth day till in all ten injections were given ; by this time the patient was moving about and the motor power in the upper extremity had also returned gradually. It is worth trying as a final treatment in the hemiplegics.

Tachycardia

BY

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IN disqualifying candidates for government service, tachycardia is frequently mentioned as the principal cause by medical officers rather loosely. Tachycardia means a considerable increase in the frequency of heart's action. Although it is a temporary manifestation, in many cases it may also be continuous.

Etiology.—(1) In some patients a frequent heart action is normal. I know of a family in whom normal heart action is 100 beats per minute or even more ; (2) in emotinal nervous patients, in hysterical and neurasthenic patients in particular, very slight stimuli produce marked increase in the rate of the heart ; (3) in diseases like influenza, diphtheria, anæmia or such like diseases which cause enfeeblement of the myocardium, tachycardia is the rule ; (4) in over-secretion of the thyroid gland in Graves' disease, tachycardia is the first manifestation ; (5) in mitral stenosis we have undue frequency of the heart, so also in patients with enfeebled heart in whom physical exertion results in tachycardia ; (6) in some obscure toxæmia, such as pulmonary tuberculosis without pyrexia or physical signs, we get tachycardia ; (7) fevers and infections by bacillus coli produce great increase in the rapidity of heart's action ; (8) so also is fright and violent exercise ; and (9) during menopause in women, tachycardia is the rule.

In the above instances of tachycardia the manner of the heart's action is normal though frequent and the contraction of the heart starts in the normal site.

In another series like auricular fibrillation, auricular flutter and paroxysmal tachycardia, this is not so.

1. In auricular fibrillation the tachycardia is continuous or in paroxysms with no co-ordinate contraction of the auricle.

Auricular flutter is characterised by increased frequency of the action of the auricle, the contractions originating in the ventricles (an unusual site). Paroxysmal tachycardia is characterised by spells of heart hurry during which the action is greatly increased, the pulse rate reaching 200 or over. Here the contraction originates in some abnormal place in the auricles, in the ventricles, or in the auricle ventricular node.

Treatment.—In nervous patients cold bath with rubbing of the skin by wet rough towels daily and gentle exercise will give tone to the vasomotor system.

In tachycardia after influenza rest in the recumbent posture and Easton's Syrup answer well.

In tachycarida of mitral stenosis, Bromide with Digitalis may be beneficially combined. In this disease alcoholic stimulants and the amount of tobacco smoked should be curtailed and sexual excesses must be avoided.

In auricular fibrillation and auricular flutter, rest and Digitalis are recommended.

In paroxysmal tachycardia rest and small doses of Digitalis may be administered ; pressure on the vagus may be tried when everything else has failed. Alcohol, tobacco and tea should be used in moderation only.

The following drugs are reported to be specific for tachycardia.

1. Amyl Nitrite :—After inhalation the vessels of the head and neck and then of the whole body dilate. After inhalation there is slight slowing of the heart due to reflex vagus stimulation followed by quickening from depression of the vagal centre.

2. Cactus (Cactina pillets), a cardiæ tonic free from cumulative action.

3. In Digitalis during the first stage there is moderate slowing through stimulation of vagus centre and from increased contraction of the cardiac muscles, resulting in more complete systole and giving more time for the ventricles to be filled up. During the second stage or poisoning stage, due to the over activity of the inhibitory mechanism the pulse becomes slower and irregular and the efficiency of the pumping action of the heart is less than normal ; the ventricles beat at a slower rate than the auricles so that the number of beats of the heart and that of the pulse is different.

Digitalis produces the above circulatory effects through its action on : (1) The sino-auricular node ; (2) the cardiac muscle ; (3) the auriculo-ventricular bundle ; (4) the coronary arteries ; and (5) the systemic arteries.

4. Nitro-Glycerine :—Its action is the same as that of Amyl Nitrite but its effect is more lasting. Administered under the tongue its absorbtion is more rapid than when swallowed.

5. Sparteinæ (Sulphas) :—It resembles Conine, Atropine, Curarine. The heart is slowed and weakened from stimulation of the vagus and at one time it was used in place of Digitalis.

6. Atropine :—The vagus is the inhibitory nerve of the heart. Atropine in small doses 1/150 gr. stimulates the vagal centre causing slowing of the pulse.

7. Strychnine :—Causes slowing of the pulse from stimulation of the vagus centre and a rise of blood pressure from stimulation of the vasoconstrictor centres in the medulla and cord.

8. Parathyroid :—Its administration is followed by vagotonia with slow pulse, hyperæmia of the internal organs, kidneys are congested followed by diuresis.

References :

1. Robert Hutchison.—Index of Treatment.
2. W. H. Martindale.—Extra Pharmacopœia.
3. B. N. Ghosh.—Pharmacology, Materia Medica and Therapeutics.

Proceedings of Associations

Guntur District Medical Association.—The annual meeting of this Association was held on 9-10-1943 with Dr. K. S. Subramaniam, District Medical Officer, in the Chair.

After tea, the annual report was presented by the Secretary and it was unanimously adopted. The report showed a net balance of Rs. 609-8-0 standing to the credit of the Association.

The following were elected as office-bearers of the Association for 1943—'44 :—*President*—Dr. K. S. Subramaniam, District Medical Officer, Guntur; *Vice-President*—Dr. Ch. S. John, Guntur; *Honorary Secretary*—Dr. G. V. Hanumantha Rao, Guntur; *Hony. Joint Secretary*,—Dr. Md. Ayoob Khan, R.M.O., Guntur.

Drs. M. A. Hamid Baig, S. N. Akhilbai, T. Chitanandam, G. Narayana Rao, C. Ramakrishna and Y. Showri Reddy were elected to the Managing Committee.

Drs. G. V. Hanumantha Rao, Guntur, P. H. Vittal Rao, Guntur, and T. Chitanandam, Guntur, were elected to the Indian Medical Association as its representatives.

Drs. G. V. Hanumantha Rao, Guntur, T. Chitanandam, Guntur, (Miss.) G. Dwarakabai, Guntur and P. Subramaniam, Guntur were elected to represent the Association in the Andhra Provincial Council for 1943—'44.

From the list of nominations for 1943-'44 sent by the Secretary, Andhra Provincial Branch, I.M.A., the following were elected : *President*.—Dr. P. Veeriah, Guntur ; *Vice-Presidents*.—Dr. P. Gurumurthy, Rajahmundry, Dr. (Miss) G. Dwarakabai, Guntur, and Dr. B. Tirumal Rao, Vizagpatam.

Resolved that the District Medical Association be converted into the Reception Committee of the Second Andhra Provincial Conference with powers to coopt members The committee was constituted as follows : *President*.—Dr. T. Chitanandnm, (Guntur); *Vice-Presidents* :—Dr. (Miss) G. Dwaraka Bai, (Guntur), Dr. N. Sambasiva Rao, (Tenali), and Dr. C. Ramakrishna (Ongole); *Hony. General Secretary* :—Dr. G. V. Hanumuntha Rao, (Guntur); *Hony. Joint Secretaries*:—Dr. Rao Saib C Hanumantha Rao, (in charge of reception to delegates and other arrangements), Dr. Ch. S. John, (Guntur) (in charge of scientific section); *Hony. Treasurer* :—Dr. S. Mallikarjuna Rao (Guntur).

Besides the above the following were elected to the Working Committee :—Drs. M. A. Hameed Baig, (Guntur), S. N. Akila Bai, (Guntur), K. Ganeswara Rao, (Guntur), G. Narayana Rao, (Tenali), Md. Ayoob Khan, (Guntur), P. G. Nityanandam Pillai, (Guntur), G. Raghavacharlu, (Ongole), S. Krishna Rao Pantulu (Tenali), E. De Remer, (Kugler Hospital-Guntur), T. V. Subbiah, (Ongole), and Arthur G. Bogg, (Ongole).

The quorum for the Working Committee was fixed at six.

Resolved also that the Guntur District Medical Association do entertain at dinner the members of the Conference.

A vote of thanks brought the meeting to a close.

Notice

The Second Andhra Medical Conference, Guntur

The Honorary Secretary has issued the following communique :

The 2nd Andhra Medical Conference will be held at Guntur on the 27th and 28th November 1943. It is by these Conferences alone we will be able to exchange our views on matters relating to the practice of our profession and its upliftment. Hence the whole-hearted co-operation of all the members of the profession is earnestly solicited. Papers on scientific and professional subjects are invited to the Scientific Section of the Conference from all leading members of the profession. Needless to say that the whole success of the Conference depends upon the ready co-operation of the profession.

A Query

Sir,

I would like to have the opinion of experts as to what effect the use of molasses (treacle) *instead of sugar in tea* has on the human physique. This enquiry has been necessitated by the extreme scarcity of sugar now-a-days.

J. K. D.

Addendum

In the Case Notes under the heading "Dagenan M & B 693 in the Treatment of Bacillary Dysentery" by Nanak Chand, published in page 521 of the October issue, after "I prescribed Mist. Ol. Recine 1 oz. 4 hourly," add "1 Tablet M & B 693 T.D.S."

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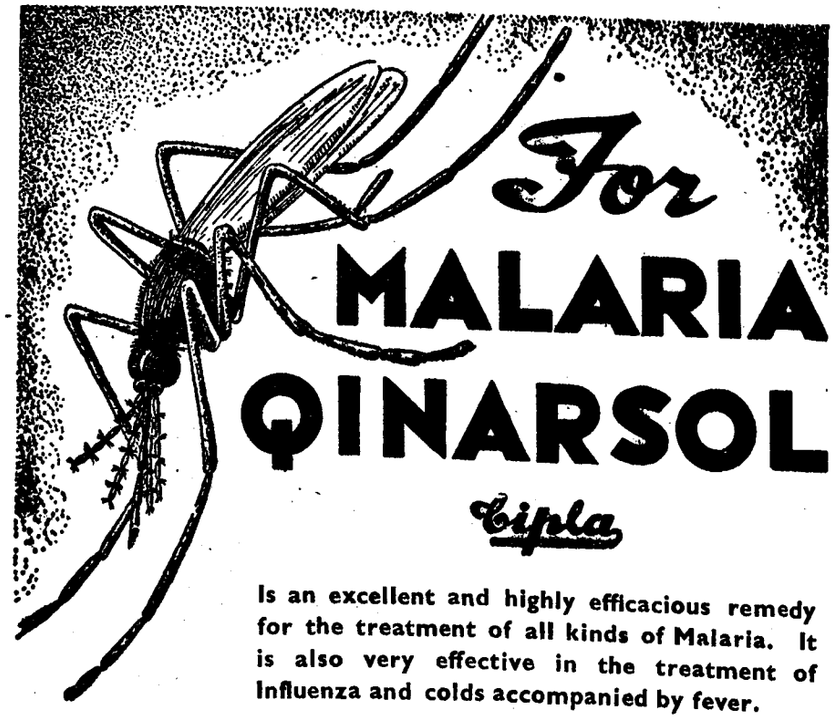

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U. Rama Rau, & U. Krishna Rau, M.B., B.S.

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Some Observations on Addison's Anæmia (Pernicious Anæmia)

BY

K. NARAYANAMURTHI, M.D.,

Hony. Physician, Government General Hospital, Madras.

THE word pernicious anæmia is used to mean Addison's anæmia, but it is not often correct to use this term. In nutritional anæmia, stenosis of the gut, ulceration of the small intestines, intestinal parasites as in Bothriocaphalatus, sprue, sub-acute combined degeneration of the cord, fatty diarrhœa, partial gastrectomy and diseases of the liver as in cirrhosis of the liver, we find a blood picture identical to that of pernicious anæmia. Therefore it will be correct to use the word Addison's anæmia in preference to that of pernicious anæmia. The earlier the word 'pernicious' is dropped and in its place dyshæmopoietic anæmia is used, a considerable amount of confusion can be avoided. [Under dyshæmopoietic anæmia, nutritional anæmia of infants, (anæmia due to prematurity, hypochromic anæmia, due to iron deficiency or some other factor interfering with the maturity of the R.B.C., and Addison's anæmia due to the lack of P.A. factor, can be included. In this anæmia, we get symptoms of sub-acute combined degeneration of cord and symptoms of sprue—the three diseases, Addison's anæmia, sprue and sub-acute combined degeneration of the cord forming the triad. The blood picture in each of them is indistinguishable from one another.] [Thus these anaemias may be classified under (1) megalocytic anaemia due to deficiency in diet, particularly the proteins and vitamins, (2) due to defective absorption of anti-anaemic factors when the intestines are diseased as in dysentery syndrome, and (3) due to defective storage or metabolism of anti-anaemic factors as in cirrhosis of the liver]. In cases of Addisonian anaemia cancer of the stomach is not found to occur, at least it is a rare event. But the development of Addison's anaemia is almost the rule in advanced cases of carcinoma of the stomach. Initially the anaemia may be microcytic in type and later when the intrinsic factor becomes defective, megalocytic anaemia develops, as in cases of partial gastrectomy.

The disease though common betwen the ages of 40 and 60, there are several cases of true Addison's anaemia that have been observed by the author, particularly in children born in a family where the parents are found to be healthy. In that particular family four children, two girls and two boys, were found to be having a megalocytic blood picture. One girl died of sprue and another is suffering from Addison's anaemia. Among the brothers, one is suffering from sub-acute combined degeneration of the cord and the other who recently died had symptoms of pellagra grafted on to the megalocytic anaemia. The age of the boy was 10 years. He had suffered from a very severe form of diarrhœa, dermatitis and dementia. All these symptoms were brought under control by the administration of Nicotonic acid 100 mgs. by injection given for a period of nearly a week. The response of this case to the treatment with Nicotonic acid is so striking that one is apt to think that Addisonian anaemia can be classified under avitaminosis.

Symptoms.—The symptoms of onset of Addison's anaemia are slow and insidious. The body is flabby rather than wasted with an uncomfortable feeling of faintness, and breathlessness on exertion may be evident. The hair is prematurely grey and the skin and mucous membranes are pigmented. The skin may be dry and scaly—as in ichthyosis.

Loss of appetite and slight œdema about the ankles are generally present. The lemon yellow colour of the skin is not now a days noticed as the patient comes to us after taking empirically injections of liver. Temperature is slightly raised, the urine becomes scanty and traces of albumen may be found. Glossitis and dyspepsia, sometimes dysphagia, are present. Nervous symptoms due to sub-acute combined degeneration of the cord are very rarely found in Indian patients. Mental symptoms and anginal attacks, and occasionally violent convulsions (not tetany) are sometimes seen. The blood picture and achlorhydria are the characteristic features of the disease. The disease is not invariably fatal, as the author has followed up in two of his cases under his care for over 15 years with remissions and exacerbations when they were put on a maintenance dose of liver extract given by mouth or by injections depending upon the urgency. It is interesting to note that the response to the injections with crude liver extract is better than the purified extracts as Anheamin and the blood picture is found to vary at different times in the same patient.

The chief feature of the disease is the blood picture which is always a megalocytosis. Hæmoglobin is not reduced to the same extent as that of the total R.B.C., and hence the colour index is more than one. The serum is yellowish in colour and gives an indirect positive Van den Bergh test on account of the hæmolysis of the R.B.C. Sternal puncture reveals a megaloblastic reaction which is typical of Addison's anæmia and this is of much greater value than the examination of peripheral blood. Aplastic condition of the bone is not found in Addison's anæmia, however much the anæmia was severe.

Treatment.—It is always good to give an overdose of the liver extract rather than a smaller dose. Stomach extracts also have some value, but can't be so well depended upon as that of liver extract. Transfusion of blood is seldom necessary when we give liver extract. In urgent cases one can think of giving Liver extract (protein free) by intravenous route. Nicotinic is very helpful in controlling glossitis and diarrhœa. Hydrochloric acid is given if there are no ulcers on the tongue or mouth. Sometimes neuritis yields good results with vitamin B_1 when liver fails. Iron, arsenic and thyroid maybe tried if the case does not improve with liver.

After liver therapy has become the choice of treatment in Addisonian anæmia, the span of life of the individual is not shortened and the individual can lead a happy and useful life.

Valves of the Human Body

BY

R. KRISHNA RAU, F.R.C.S.,

Prof. of Anatomy, Medical College, Vizagapatam.

PART I.

Valves of the Cardio-vascular System.—As one concerned with teaching human anatomy to medical students for a long time I may safely say without fear of contradiction that the medical student most often misses seeing during the course of his dissections the structures mentioned hereunder: small bones such as the sesamoids, accessory bones of the hand and foot, epiphyses in young subjects, bones of Bertin (sphenoidal conchæ), thin and fragile ones such as an entire ethmoid, a complete palatine bone with all its processes, deciduous teeth, venules, emissary veins, venous plexuses emissary and diploic veins, capillary bed, lymph vessels, nerve terminals, nutrient arteries in bones, sympathetic plexuses, nerves traversing bony canals, vasa vasorum, nervi nervorum, end organs, minute ducts of glands such as the lachrymal, sublingual, bulbo-urethral, bursæ, valves of veins, lymphatics. The anatomy museum has, of necessity, to make up for the gaps and deficiencies incidental to dissections by suitable display of specimens prepared by special methods of injection, preservation and so forth. The valves of the human body by reason of their concealed position and small size also come under the category and have not been described in such detail as the other structures of the body; nevertheless they play an important role in the dynamics of the human body. A concise and compact description of all the valves has been given hereunder.

Definition of Valve.—A valve is a fold in a canal or conduit for preventing the reflux or regurgitation of its contents. It temporarily closes a canal or passage and permits the flow of air, fluids or semifluids in only one direction. The word 'valva' means a leaf or a fold of a door, especially one of a pair of folding doors. By long custom and usage the term valve has been used even for insignificant small folds devoid of the function ascribed to it. The numerous folds of mucous membrane of the small intestines which are not obliterated by distension are called 'valvulæ conniventes' of Kerchring or closing valves. The shelf-like folds of the rectal mucosa are spoken of as Houston's valves. Some sphincters are called valves, such as the pyloric valve, O'Bierne's valve (sigmo-rectal sphincter). The anterior or superior medullary velum which forms the upper and anterior part of the roof of the fourth ventricle of the brain is peculiarly enough named as the valve of Vieussens. Numerous small folds of mucosa in the lachrymal passages are designated as valves. In the heart the name valve, according to HYRTL is said to have been used first by BENEDICTUS. The Greeks called them 'hymenes' while VESALIUS

called them membrane. The atrioventricular valves were named 'trisulcas' by GALEN and 'triglochines' by Greeks. The left atrioventricular valve was called mitral by VESALIUS.

Situation of Valves in General.—Valves and valve-like arrangements are met with in the circulatory system—in the heart, in the lumen of arteries, veins and lymphatics, in the alimentary canal, in the extrahepatic part of the biliary apparatus, in the genito-urinary system and in the lachrymal apparatus.

Evolution of the Vascular System.—The complicated vascular system found in mammals and man with its arteries, veins, capillaries and lymphatics is phylogenitically a specialisation of a primitively simple single system. In the early stages of evolution the primitive vascular system is one in which only the white corpuscles and fluid plasma moved through the body in a series of tissue spaces. Such a system in man may be said to be represented by the lymphatic system. At a more advanced stage a respiratory function is superimposed on the system whereby oxygen-carrying elements are borne in the stream in addition to the nutritive ones. This stage is met with in the lowest vertebrates and has been termed a lymphatico-hæmal circulation. Finally there is a more or less complete separation of the hæmal and lymphatic systems. All peripheral vessels in the embryo are at first developed as tissue spaces which later become confluent and form a connected system of channels. These ramify throughout the body and finally communicate with the contractile heart. The primitive vessels destined to specialise into arteries, veins and lymphatics contain all the corpuscular elements; for example, early lymphatics in embryonic life contain both white and red corpuscles. This has been described by HUNTINGTON as the 'hæmophoric stage.' The early plexiform arrangement of the arteries is retained in the nycticebus—retia mirabilia.

Historical Survey of the Vascular System and its Valves.—Though blood-letting was an ancient and time-honoured therapeutic procedure applied in almost every disease, ideas about veins were crude and inaccurate. ALCMAEON of Croton of the latter half of the sixth century B.C., thought that sleep was caused by the retreat of blood to the veins and awakening by its forthpouring. PRAXAGORAS of Cos, about 335 B.C., is said to have been the first to differentiate arteries and veins. HEROPHILUS of Chalcedon, 3rd century B.C., and ERASISTRUS of Chios described the lacteals which they called 'white veins.' Some superficial veins of the body were well-known to the mediæval physicians such as the syele or salvatella or amoris, hepatica, lienaria, cephalica pollicis, black vein, and others.

The highly versatile and prodigious stagyrite philosopher, ARISTOTLE, who was tutor to ALEXANDER the Great of Macedon, about twenty three centuries ago, thought that the heart was the most important organ of the body. Contrary to the belief of his distinguished teacher PLATO he placed even the seat of intelligence in the heart which was 'the first to live and the last to die.' There was not the remotest suggestion of circulation made by him. The aorta, the biggest artery of the body, is named after him.

ERASISTRATUS (CIRCA, 300 B.C.), the contemporary of HEROPHILUS, drew attention to the threefold system of vessels—artery, vein and nerve—the triad of ERASISTRATUS possessed by every organ in the body.

He pointed out that the superficial veins have no accompanying arteries and that the deep veins accompany the larger arteries. He observed the venæ comitantes of the brachial and radial arteries. He described the valves of the heart, the aorta and the pulmonary artery. He considered veins as carriers of the blood and arteries as the carriers of air. He thought that air was first inhaled into lungs and thence carried to the heart where it was worked in some subtle way into the 'vital spirit' which was transformed in the brain into 'animal spirit' which flowed through the nerves to all organs of the body and accounted for their functional activity.

The Great GALEN, "the Prince of Physicians," who flourished during the reign of MARCUS AURELIUS in the second century A.D., wrote a special work 'on the anatomy of the veins and arteries' besides many others exceeding a hundred in number. He taught that the 'arteries came from the heart and the veins from the liver' and that the movement of the blood was of the nature of an ebb and flow. The three pneumas—the natural spirit elaborated in the liver, the vital spirit produced in the heart and the animal spirit manufactured in the brain formed the basis of his physiological system. The lungs cooled off the overheated blood from the heart. Some of the blood from the heart was driven into the lungs where it was ærated and driven back to the right heart. From the right heart it was sweated through invisible pores into the left heart.

LEONARDO da VINCI who may rightly be considered the creator of artistic anatomy of the renaissance age delineated accurately and artistically the heart and the blood vessels. He is said to have disproved the popular theory prevailing in his period that the great vessels of the lungs carried air to the heart to cool the blood by distending lungs with air.

Professor KARL SUDHOFF of the University of Leipzig gives the picture of the blood-letting man from the calendar of Regiomontanus (1475) showing the points of blood letting.

JACQUES DUBOIS called SYLVIUS (1478-1555) named the jugular, subclavian, renal, popliteal and other blood vessels and was one of the first to describe the valves in the veins. The discovery is said to have also been made by GIAMBATTISTA CANANO of Ferrara in 1547.

MICHAEL SERVETUS of Aragon (1509-1553) solved the mystery of 'invisible pores' of Galen by giving a detailed account of the lesser circulation or 'pulmonary circulation' by tracing the continuity of all the 'pipe-lines' from the heart to the lungs and back again. The pulmonary circulation is known as the 'circuit of Servetus'. HORRESCO refers he was cruelly burned at the stake by order of CALVIN for his heretical beliefs and conflict with established clerical authority.

CHARLES ESTIENNE (1564) or STEPHANUS a pupil of SYLVIUS at Paris was the first to mention the valves of the veins as 'apophyses membranorem.'

ANDREAS VESALIUS of Brussels (1514-1564), the author of the great classic 'De Humani Corporis Fabrica', which thoroughly revolutionised the science of anatomy, upset the many inaccurate teachings of GALEN of which the existence of 'pores' in the ventricular septum is one. He found no pore at all which GALEN described to be present in the septum of the heart.

MATTEO REALDO COLOMBO of Cremona (1516-1559) is said to have put forth the claim of being the discoverer of the pulmonary circulation in 1559. He is again charged with the accusation of having appropriated some of the discoveries of his teacher VESALIUS.

BARTOLEMMO EUSTACHI (1524-1574) Professor at the Collegia della Sapienza in Rome discovered the pulmonary veins besides the tubes named after him and many other structures. Some other veins are named after their discoverers, as for instance the veins of Thebesius, veins of Galen, veins of Zuckerkandl by which the ethmoid veins in the nose communicate with the veins of the cerebrum. Others are the veins of Vesalius, the Torcula of Herophilus.

GIULIO CAESARE ARANZIO (1539-1589) better known as ARANTIUS was professor of medicine, surgery and anatomy at the University of Bologna. He gave in his work 'The Human Foetus' published in 1571, a detailed description of the valves of the heart, foramen ovale, ductus arteriosus and bodies of Arantius. The aortic and pulmonary valves are stronger and sturdier than the tricuspid and mitral valves. They need extra strength because they bear the weight of the column of blood and have to resist effectively the pressure exerted against them on closure. The nodules described elsewhere facilitate complete and effective closure of the valves.

ANTONIO VALSALVA (1666-1723) was professor of anatomy at the University of Bologna. He is said to have devoted considerable time to the study of the structure of the heart. He was the first to describe the sinuses of Valsalva.

HIERONYMUS FABRICIUS of Aquapendente, pupil of FALLOPIUS, successor to VESALIUS at Padua and teacher of HARVEY published his book on the 'valves of the veins' in 1600. He was the first to describe accurately the valves of the veins which are named after him. He says, 'In my opinion they are formed by nature to delay to a certain extent the flow of blood and so prevent the whole from flowing at once like a flood either to the feet or to the hands and being collected there. For this would give rise to two evils; first the upper parts of the limbs would suffer from want of nourishment; and second, the feet and the hands would be troubled with a continual swelling. In order, therefore, that the column should be distributed everywhere in just measure and admirable proportion for maintaining the nourishment of the several parts these valves of the veins are formed."

ANDREA CAESALPINO, professor of medicine at Pisa and physician to Pope CLEMENT VIII, is said to have anticipated Harvey's discovery and to have even used the term circulation in 1571.

It was given to the brilliant pupil of FABRICIUS WILLIAM HARVEY of Folkstone (1578-1657) to make the epoch-making discovery of circulation of blood as it were in a circle to describe the correct significance of the discovery of the valves by his teacher which ultimately paved the way to the momentous and epoch-making discovery of the circulation in his immortal classic "an anatomical dissertation on the movement of the heart and blood vessels in animals" which appeared first at Frankfurt in 1628 in the form of a miserably printed unattractive quarto.

Heart and Valves of the Heart:—The heart in the annelids is a contractile muscular tube. It is thicker and better defined in insects and crustaceans. In the amphioxus the sub-pharyngeal vessel represents the heart. In fishes and in all the craniata the tubular heart is divided into the four primary parts, sinus venosus, atrium, ventricle and bulbus cordis. In amphibia the atrium is divided by an incomplete septum into right and left halves. In reptiles the septum is complete. In birds, as in mammals, the right and left hearts are completely separated from each other by atrial and ventricular septa. The heart of man is developed from a tubular structure and is therefore a highly specialised blood vessel. The valves in and about the heart are laid down in the process of division of the tube into the four chambers.

Eustachian valve is the semilunar fold situated in front of the orifice of the inferior cava in the interior of the right atrium. In the adult it is but the persistent vestige of the right sinus valve of the fœtal heart which directs the blood from the inferior vena cava upwards and medially towards the formen ovale. At or soon after birth the free non-muscular part of the valve undergoes retrogressive changes. Lateral traction of the valve in the adult produces a fold on the medial (septal) wall of the right atrium containing a thin band of fibrous tissue called the tendon of Todaro. The fold is directed upwards towards the torus aorticus, an elevation in the upper and anterior wall of the right atrium caused by the root of the aorta.

Valve of Thebesius:—The circular opening of the coronary sinus is situated in front of the anterior end of the valve of the inferior vena cava in the right atrium. It is flanked by a small semilunar valve which is developed in common with the Eustachian valve from the right sinus valve.

Valve of the foramen Ovale:—The foramen primum is the interatrial foramen between the lower edge of the septum primum of born above and the endocardial cushions below. Before this is closed the upper part of the septum becomes absorbed giving rise to the foramen secundum or foramen ovale. A second septum descends down from the roof of the atrium on the right side of the septum primum. The two septa overlap each other in front and behind. The foramen ovale is now a slit-like passage between the free edges of the two septa. "The part of the septum primum which bounds the foramen below and which forms its left wall is sometimes called the valve of the foramen ovale." This can be made out on holding the interatrial septum to the light after opening the left ventricle as a translucent oval area, the upper and anterior part of which is the free margin of the valve of the foramen ovale.

Valve of Vieussens is the small bicuspid valve situated at the sight of opening of the great cardiac vein at the left end of the coronary sinus.

The atrio-ventricular valvular systems consist of (1) a variable number of valves, (2) annulus fibrosus to which the bases of the cusps are attached, (3) chordæ tendinæ, and (4) musculi papillares. The heart skeleton of the French anatomists is the collective name given to fibrous and fibrocartilaginous structures placed at the junctions of the atria and ventricles, the ventricles and the arteries and the walls of the ventricles and apices of the papillary muscles. According to WALMSLEY the heart skeleton comprises (1) the septum membranaceum (2) the trigonum fibrosum dextrum (posterior aortic ligament of Mall) which lies behind the aortic orifice and between the two atrio-ventricular orifices, (3) the trigonum fibrosum sinistrum (left aortic ligament of Mall) which lies on the left side of the aortic

orifice, (4) the conus tendon of Krehl (right aortic ligament of Mall—septum aorticum superius of His) "a strip of tendinous tissue which begins opposite the anterior aortic cusp and runs forwards to the left and upwards in the roof of the conus of the right ventricle to the root of the pulmonary artery where it ends in the posterior spatium intervalvulare." The pointed triangular spaces between the cusps of the semilunar valves are known as the spatia intervalvularia, (5) the arterial roots, the fibrous tissue rings at the roots of the pulmonary artery, and aorta and (6) the annuli fibrosi, the fibrous tissue surrounding the atrioventricular orifices.

The tricuspid valve guards the right atrio-ventricular opening. In the normal position of the heart the plane of the orifice is almost vertical. Though the name implies the presence of only three cusps there may be one or more small accessory ones between the principal cusps. The latter are named the infundibular or anterior which is the largest of the three, the right or posterior and the septal or medial cusp which is the smallest. It is oval in the empty heart and nearly circular in the distended state. Its average circumference is 122 m.m. in the male and 115 m.m. in the female.

The bicuspid or Mitral orifice is the left atrio-ventricular orifice. There are two cusps named the anterior or right and posterior or left. The anterior cusp is also called the aortic cusp. Accessory cusps are not usually met with. Its average circumference is 103 m.m. in the male and 100 m.m. in the female.

Chordae tendinae are glistening strands of fibrous tissue invested by the endocardium. At one they are attached to either the apices of the papillary muscles or mammillary elevations of the ventricular wall. Their attachments to the cusps are variable; they may either be inserted on the free edge of the cusp, or on the ventricular surface of the cusp, or to the base of the cusp. Other smaller chords extend between the ventricular wall to the under surface of the cusp near its base and thence to the free margin.

The arterial valves are placed at the roots of the two biggest blood vessels, the aorta and the pulmonary artery. Their positions are indicated on the exterior by bulges called the aortic and pulmonary sinuses of Valsalva. These enter into the formation of pouch-like cavities opening upwards; when the pockets are filled the valves close. Each valve consists of three semilunar cusps. Their convex margins are attached to the arterial walls while their free borders project into the lumen of the vessels. The pointed triangular spaces between the cusps are known as the spatia intervalvularia. There are small nodular thickenings in the middle of each free edge of the cusp called the corpora arantii. The semilunar areas on each side of the nodule are named the lunulæ. In the normal position of the heart there are two anterior and one posterior in the pulmonary artery, while in the aorta there are one anterior and two posterior. Continental writers describe one pulmonary cusp in front and two behind and two aortic cusps in front and one behind. The difference is a topographical one as the developmental relations of the two sets of valves are maintained. The cusps are transparent in early life but become thicker latter. The aortic cusps are thicker and more tendinous than the pulmonary cusps but the noduli of the pulmonary cusps (noduli morgagni) are larger than those of the aortic cusps.

Veins and Valves of Veins.—A vein has been defined as a vessel that conveys blood to the heart. A more elaborate definition is "a blood vessel neither artery nor capillary conveying blood to the heart having walls of greater tenuity and at the same time less elasticity than an artery." A vein does not necessarily contain 'sang noir.' It is well-known that pulmonary veins carry 'sang rouge' or pure blood. BARCROFT and ROTHSCHILD have pointed out that the uterine and other veins contain arterial blood. Compared with their corresponding arteries, veins have a larger lumen and thinner walls.

Structure.—The vein, like the artery, has the three tunicsintima, media, and adventitia. The circular muscular fibres are well developed in the media of the veins of the pregnant uterus, human adrenal gland and extra abdominal portion of the umbilical cord. They are absent in the veins of the nail bed, erectile organs, splenic trabeculæ, retinal veins, maternal placenta, dural venous channels, most veins of the piamater and veins of the bone marrow. The tunica adventitia consists mainly of white fibrous tissue. The adventitia of large veins contains in addition elastic tissue, longitudinal muscle fibres and collagenous fibres. Lymph vessels, vasa vasorum and nerves are found in the adventitia of the larger veins.

Valves of Veins are present in most of the veins of the body. They are formed by reduplication of the lining endothelium between the two layers of which is a thin stratum of elastic and fibrous tissue. The majority of valves are bicuspid though multicuspidate valves are found in large veins of big mammals. The valves at the entrance of tributaries are called ostial valves, those in the course of veins parietal valves. There are several descriptive terms that are used to signify the different parts of the valve. Sinus is the pouch between the cusp and the wall of the vein. The cusp has an attached margin and cornua. Agger valvæ venæ is the elevation of the wall of a vein over the site of a valve.

Development.—JAGER who worked on embryos of pigs found that the parietal valves in the jugular and anterior facial veins develop by progressive deepening of outgrowths from the inner layers of the vein wall begining near the tributary entries. Valves appear first in the human fœtus at about 3½ months; most of the valves are laid down by the middle of the sixth month of uterine life. Recent investigations have shown that Klotz's statement that valves do not occur in the veins of less than 1 m.m. in diameter is not correct.

SITUATION:—Valves are found in veins which are subjected to pressure from without and in those subject to muscular contraction. It has been observed that the valves of the peripheral veins are formed at a time when the foetus starts muscular movements, while those of the heart are established much earlier. It may not be inaccurate to say that valves act mostly as an antigravity mechanism. On opening up the long saphenous veins, a series of openings placed at intervals of two or three inches of the tributaries could be seen. The valves are mostly placed distal to the ostia. The intima in the relaxed state showed a series of small longitudinal folds in the long axis of the vein. In the neck the external jugular vein is said to be provided usually with two pairs of valves, one at its entrance into the subclavian and the other about 1½ inches above the clavicle. In the vein that was opened up there is a valve containing

(2) the vas (ductus deferens) system comprising the slender artery to the vas most often derived from the superior vesical branch of the anterior division of the internal iliac artery together with its companion vein ; and (3) the cremasteria system consisting of the external spermatic branch of the deep or inferior epigastric artery and the corresponding vein. The mode of termination of the veins is well known but nevertheless mentioned here. The single right spermatic vein formed by the coalescence of the variable number of veins of the pampiniform plexus opens obliquely in the trunk of the inferior vena cava whereas the left spermatic vein joins the left renal vein at almost a right angle. The vein of the ductus deferens is a tributary of the vesical plexus through the vesical veins. The vesical plexus in turn drains into the internal iliac vein. The cremasteric vein is a tributary of the venæ comitantes of the inferior epigastric artery and indirectly of the external iliac vein. The superficial dorsal vein of the penis is a tributary of the external pudendal vein. There is thus a communication between the veins of the penis and the thigh. The superficial and deep external pudendal veins drain a part of the scrotum. The superficial pudendal vein is a tributary of the long saphenous vein ; the deep external pudendal veins usually two in number are tributaries of the femoral vein. There is thus a communication between the veins of the scrotum and those of the thigh. The superficial external pudendal, the superficial epigastric and the superficial circumflex iliac veins are tributaries of the saphena magna. There is thus a direct communication between the veins of the lower abdominal wall and the thigh in the inguinal region. Normally there is no well defined anastomosis between the veins of the cord on the one hand and those of the scrotum on the other. With a view to decide the point the left spermatic vein was opened extraperitoneally in the body. An aqueous solution of Methylene blue was forcibly injected into the vein against the direction of the flow of blood. The scrotum, the cord and the inguinal region were then exposed by dissection. The blue solution filled the veins of the cord and could be seen through its coverings. The fluid did not flow into the veins of the scrotum and the thigh. In varicocele, however, the small venous channels are opened up involving thereby the veins of the scrotum, penis, the thigh and the lower abdominal wall. Another observation made is that there is almost always a vestige of the gubernacular strand anchoring the testis to the scrotum preventing thereby the easy mobilisation of the testis. The strand provides for a communication between the veins of the testis and those of the scrotum. No vestige in the body is exsanguineous. The usual reasons given for the incidence of varicocele more often on the left side of the body are the entrance of the left spermatic vein into the left renal vein at a right angle, pressure of the vein by the iliac colon loaded with scybalœ and the greater contraction of the muscles of the left side of the abdomen owing to the more extensive use of the right side of the body in right handed people. There is hardly any reference to incompetence of the valvular mechanism. RIVINGTON has pointed out that valves are usually found at the orifices of both the right and left testicular veins. When, however, valves are not found at the opening of the left testicular vein into the left renal vein they are generally present in the left renal vein within six millimetres of the orifice of the testicular vein. " A varicocele in an elderly subject should always lead to an examination of the kidney."

Haemorrhoids.—Varicosity of the veins of the anal canal and lower rectus of all grades ranging from simple dilatation of the circumanal veins

to well defined varicosity of the venous radicals of the superior hæmorrhoidal vessels is quite a common condition. Various explanations have been given to account for the frequent occurrence of piles. Rectal veins have *no valves* in the first place. Other causes are inadequate support to the vessels in the loose submucous tissue of the ano-rectal passage, pressure at the site of the anastomosis of the portal and systemic veins, constipation, back pressure in cardiac and pulmonary diseases and portal obstruction. "In all cases of hæmorrhoids developing during middle age search should be made for carcinoma of the rectum or signoid." Portal obstruction should also be borne in mind. The pestinate, white or wavy line of Hilton, is availed of for classifying piles into *external*—those distal to the line, *internal*—those proximal to the line, and *intero-external* at the line. Above the anorectal junction is the communication between the veins of the portal and systemic circulations. It may incidentally be mentioned that another special type of varicosity of the rectal veins is said to occur at a distance of 4 to 6 inches from the anal orifice. This can only be made out by sigmoidoscopy.

Lymphatics.—Lymph vessels were first observed by ASELLI, Professor of Anatomy of Pavia, in 1627 in the mesentery of the intestine of a dog. HUNTER Brothers are given the credit of discovery of lymphatics in man in 1764. The name of BELSHIER of Guy's hospital is also associated with the lymphatics.

Lymphatic vessels are now regarded as modified veins lined by endothelium. They resemble the veins in that they also are thin walled, tortuous and valved channels. SAPPEY in 1874 demonstrated the lymphatics by injecting mercury into them. This has been replaced later by other methods. It is possible to inject lymphatics in a reverse direction in spite of the presence of valves. They also admit of visualisation by roentgenography, It is said that FUNAOKA used lipiodol for injecting the peripheral lymphatics in animals in 1930. This method opens up a great vista of possibilities for investigation of lymph paths in the living. The lymphatics communicate at intervals with lymph nodes. In the upper limb the nodes are mostly situated in the quiet parts of the body ; few are found in the hand, wrist or forearm; just one or more are met with above the elbow; likewise in the lower limb none occur in the foot or in the leg (except very few). The superficial lymphatic vessels accompany as a rule the veins whilst the deep are placed along the arteries. Pulsation of the artery is said to be mainly responsible for the flow of lymph in the direction determined by valves. " In the superior extremity the lymph vessels tend to hug the big pulsating arteries of the postaxial margin; in the lower limb the lymph drainage is concentrated almost entirely along the preaxial margin. In the upper limb the glands are mainly located beneath the deep fascia but in the lower limb *e.g.*, the glands of the groin lie in the superficial fascia in close relation to the cutaneous nerves." Lymph vessels do not reach the epithelium proper, uncalcified cartilage, the sclerotic, bone marrow, depths of the central nervous system, the spleen and the fœtal part of the placenta.

Development of valves :—At about the fifth month of intra-uterine life numerous valves are laid down in the thoracic duct ; it is said that many disappear prior to birth. The valves in lymph vessels are, as a rule, more numerous than in the veins. They are again similar to those in the vein in shape and structure. Usually two valves are found opposite each other

There is a pouch between the wall of the vessel and the valve. These pouches give the characteristic moniliform appearance to the vessels when distended. The thoracic duct has several valves; at its termination it is provided with a pair which prevent the passage of venous blood into the duct.

Another noteworthy and peculiar feature of the circulatory mechanism especially in the hand, foot and sexual organs is arterio-venous anastomoses—a communication of arterioes and venules without the intervention of capillaries. This has been described in detail by POPOFF. The system is however known as the glomic system of SUCQUET-HYER. A rich nerve supply and great muscularity of the walls of the vessels is said to be suggestive of remarkable contractile power. HOYER quoted by FRANKLIN thinks that this arrangement may be concerned with maintenance of the warmth of these parts when exposed to cold.

PART II

Valves in other situations in the Body.—*Alimentary canal*:— Ileo-cæcal valve: Valve of BAULIN FALLOPIUS, TULPIUS, APOTHECARY'S valve. The biggest and best known valve that is met with first in the alimentary canal is situated at the junction of the ileum with the cæcum. The valve is named after JOHANNUS GASPARD BAUHIN, professor of medicine at the University of Basel, who gave a detailed description of the valve in his work Theatrum Anatomicum (1592). He called it the slit-valve. There is a telescoping of the ileum into the cæcum. It is formed by the bulging in of the mucous and circular layers of the ileum; the longitudinal coat does not share in the invagination. The valve presents two lips, upper and lower, arranged almost horizontally, reinforced at its ends by two bands, the frenula of Moragagni. Distension of the cæcum with stretching of the frenula brings about closure of the orifice which prevents reverse peristalsis. The extra competence of the valve is attributed to the obliquity of the entry of the ileum into the cæcum. It is sphinteric in action. RAWLING remarks that the valve may have some relation to the development of intussusception. He is inclined to think that the commonest type of intussusception is the ileo-cœcal and not the ileo-ileo-cœcal type as mentioned in the text books. It is supplied by both the sympathetic and the para-sympathetic (vagus). Stimulation of the former brings on relaxation and that of the latter constriction of the orifice.

Valve of Gerlach:—This valve or valvule was discovered and described by JOSEPH VON GERLACH, Professor of Anatomy and Physiology at the University of Erlangen (1872-1891). It is a small crescentic fold of mucous membrane surrounding the orifice of the vermiform appendix. It is believed, when well developed and competent, to have a protective action preventing the entry from the cœcum into the appendix of food, foreign bodies etc., while it permits the passage of the normal contents of the appendix into the cœcum. Some anatomists and surgeons even go to the extent of saying that appendicitis depends upon the incompetence of the valve. The cœco-appendicular orifice itself is small and narrow but not so narrow as to prevent bacterial infection which however is the main cause of appendicitis.

O'Bierne's valve:—It is more a sphincter than a valve situated at the junction of the movable sigmoid with the fixed rectum. It is affected in pathological conditions of the rectum.

Houston's valves:—Transverse rectal folds: There is a variable number of folds met with in the rectum ranging from three to five above the third sphincter of Nelaton situated at the level of the prostate. The largest and most constant of all is directed backwards from the forepart of the rectum at the level of the fundus of the urinary bladder. The highest is situated at the commencement of the rectum on the right side and the second below it on the left side. Some describe them as a sort of spiral stairway in the rectum. They overlap one another in the empty state and sometimes hinder the passage of the finger or instrument. Their action seems to be "to support the weight of the fœcal matter and prevent its urging towards the anus where its presence always excites a sensation demanding discharge." In pronograde animals support is less necessary; the valves are correspondingly ill-developed in them.

Valves of Morgagni:—They join the lower ends of the columns of Morgagni found in the proximal half of the anal canal. They are better defined in the new born. They are reduplications of the anal mucous membrane containing the terminal radicles of the superior hæmorrhoidal artery and vein. They resemble the semilunar valves of the aorta and open upwards towards the rectum. The position of the valves corresponds to the junction of the ectodermal proctodæum and the entodermal hindgut. RAWLING remarks that they may have some relation to the development of piles. It is peculiar to note that the valves are well marked in lower animals in whom piles are uncommon. The valves are named after GIOVANNI BATTISTA MORGAGNI, Professor of Anatomy first at Bologna and later at Padua (1682-1771). He is looked upon as the Father of Pathological Anatomy.

Spiral valve of Heister:—This is a ridge-like spiral fold of mucous membrane lying partly in the neck of the gall bladder and partly in the cystic duct. "The Italic letter S shaped spiral constriction is assisted further by a series of crescentic folds of the mucous membrane which are carried into the mouth of the cystic duct. Both spiral and crescents add to the competency of the valve." The purpose of this peculiar arrangement is to hold back the bile when the stomach and intestines are at rest and to allow its flow only during the phase of active digestion. The rat-tailed probe was specially designed by MOYNIHAN to negotiate the narrow spiral stairway. The structures comprising the biliary apparatus including the valve were described by LORENZ HEISTER, Professor of Anatomy and Surgery at the University of Altdorf (1683-1758).

Genito-urinary system: Valvular formations:—Valvular formations in the upper part of the ureter have been described as a cause of hydronephrosis. The so-called ureteral valves are merely reduplications of the ureteral mucosa; the bands of muscularis which are contained in the folds tend to make them stand out prominently.

The slit-like orifices of the ureters at the lateral angles of the trigonum vesicœ just serve as valves by the approximation of the upper and lower walls of the oblique intramural course of the ureters. Coffey's technique of transplantation of the ureter in the sigmoid is but an imitation of the mechanism which effectively functions as a valve. There is no fold of mucous membrane in relation to the orifice.

The most important type of congenital obstruction of the urethra is known as congenital valves. According to YOUNG these are mostly limited

to the posterior urethra usually in close relationship to the verumontanum. They are folds of the mucosa of the urethra which baloon out during micturition and hinder urination. They are recognised by urethroscopy. There are considerable variations in the size, shape and position of such valves. Different types of such valves have been described by YOUNG, FRONTZ BALDWIN and other urologists. They are said to be simple modifications and enlargements of the folds and ridges which are normally present in the prostatic urethra. Various other explanations have been given to account for such valves. The chief point of interest of these valves is that, though small, they are liable to impede the free flow of urine.

Guerin's palve is a small fold of mucous membrane occurring in the roof of the fossa navicularis.

Valves of the lachrymal passages:—These were specially studied by AUBARET in 1908. They are small and inconstant folds and are insufficient as valves. Staggering are the eponyms of the valves in the rather short naso-lachrymal passages. They are associated with the names of BOCHDALEK, FOLTZ, ROSENMULLER, HUSCHKA, HYRTH, KRAUSE, BERAUD and TAILLEFER. The most constant fold is situated at the meatal opening of the naso-lachrymal duct. It is the remains of the fœtal membrane closing the lower end of the duct. This olica lacrimalis is named after four anatomists, HORNER, HASNER, BIANCHI, CRUVEIHIER. This is a region of the body where eponymic nomenclature runs riot.

Summary.—A brief description of the macroscopic structure and function of all the valves met with in the human body including a short historical survey thereof has been given in two parts—part I dealing with the valves of the cardio-vascular system and part II with the valves in the other parts of the body. A passing reference is made to varices due to incompetence of the valves of veins. The paper, however, excludes consideration of the "valvular diseases of the heart" which, perse, is an extensive subject coming within the sphere of the physician and the cardiologist.

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References :

1. W. E. Le Gross Clark—The Tissues of of the Body, Oxford Clarendon Press, 1939.
2. Louis R.Effler—Eponyms of Anatomy, 1935.
3. Singer, Kegan Paul Trench—The Evolution of Anatomy, Trubner & Co., Ltd., 1925.
4. Thomas Walmsley—The Heart, Quain's Anatomy, Vol. IV, Part III, Longman's Green & Co., 1929.
5. Kenneth J. Franklin, Charles, C. Thomas, Baltimore, Monograph on Veins, 1937.
6. S. Earnest Whitnall—The Anatomy of the Human Orbit, Oxford University Press, 1932.
7. Longman's Green & Co.—Gray's Anatomy, 1942.
8. B. Rawling and H. K. Lewis, Stepping Stones to Surgery, London, 1930.
9. Professor W. Woodjones—Principles of Anatomy as seen in the Hand, Bailliere Tindal & Cox, 1941.

called the beginning of the optic ganglion. In these animals, therefore, the eye is secondarily connected to the nervous system, although they are of common origin. In still higher animals, in which visual sense has developed, the eye and the central nervous system are so intimately connected functionally that both are developed almost simultaneously from the neural canal; but only to reach light, it has migrated outwards. although buried for the most of its part. "It, *i.e.*, the eye, is an outlying island of the central nervous system with optic tract as isthmus" (DUKE-ELDER).

The highest efficiency as visual end organ is reached in the avians which have more efficient focussing apparatus and higher visual acuity, but, in man, the highest development of associated cerebral-centres makes it a unique organ in the animal kingdom, although visual acuity is not developed to the same extent as in birds.

It might be interesting to note that the whole nervous apparatus from rods and cones to the occipital lobe may be regarded as single "Cell," one end of which is the organ of vision, the other end is the occipital lobe. The rods and cones simply receive and transform the physical energy of light to physiological energy and transmit it to the occipital lobe through various connecting and inter-connecting neurones for the co-ordination of various activities of life. It is quite reasonable to presume that, just as in retina, the whole of the cerebral cortex takes part in the visual process.

In the lowest forms of life, this reaction in the physiological plane alone would have been sufficient for the usual activities of life but, in the human being, as a 'substance' called "super-consciousness" exists, this physiological energy must be transformed in such a way that it may be transmitted to the 'zone of superconsciousness.' In the transference of physiological energy into psychological energy, probably mind is the the first system of relay. But because of its great oscillatory nature, always doing and undoing a thing at a rate far above the rate of vibrations of the physiological waves and being intimately associated with vital activities and so probably lying in the same plane as life, it cannot fix itself to any object unless the superior energy of attention drives it to some particular object. Even at this stage, vision is not possible, for the attention may be fleeting, and the object before us may not be seen clearly. But as soon as discrimination or judgment comes in, that the connection with super-consciousness is made and vision is then possible. The zones of activity of different processes may be imagined as different spheres of energy, beginning in the physical plane to the level of super-consciousness, each of the zones encircling the next higher sphere. As each succeeding quality is steadier than the preceding, it may be supposed for analogy, that the waves constituting each sphere are progressively longer, till they reach the plane of "super-consciousness," where wave lengths are so great, that there almost perfect serenity and calmness prevail, and it is here the vision occurs. Briefly stated the steps may be imagined as follows:—Sphere of physical energy, sphere of mental energy, sphere of attention (epicritic stage of attention), sphere of interest (syncretic stage of interest with its definite conative tendency) and sphere of judgment, super-consciousness. Probably the visual perception of images remains there buried in the depth of consciousness to be brought

up again to the level of mind from time to time and transformed to some figure which is seen either consciously or unconsciously as in sleep, just like light waves are being transformed to corpuscles and vice versa.

The site of the super-consciousness is not clear, but it might be interesting to remember in this connection that a certain quantum of energy is obtained by each individual in the form of vibration of the spermatozoa, which on entering the ovum, loses all its vibrations. But as exchange of chromosomes and cell division proceed, the energy must be there to start the spark of life. The spermatozoa apparently loses its vibrations, but probably creates a covering for the vibratory energy brought from the father. Early formation of the neural canal seems to indicate that probably the energy resides here. This is also supported by the fact that the nervous system is the seat of the driving force of life. But this is philosophy and need not be taken notice of here.

Blood-Vessels of the Eye.—It comprises two distinct systems (1) the ciliary, and (2) the retinal.

1. *The ciliary vessels*:—These are arranged in two groups:—(1) Posterior ciliary arteries—These divide into (*a*) short posterior ciliary arteries which supply the choriocapillaries and a few form the circle of Zinn, and these anastomosing with the central artery of the retina supply the neighbouring part of the retina, optic nerve, pial sheath and lamina cribrosa; (*b*) two long posterior ciliary arteries supply the ciliary body and anastomose with anterior ciliary artery and with one another. (2) The anterior ciliary arteries, usually seven in number, spring from the muscular branches of the ophthalmic artery to the rectus muscles and after supplying the retii enter the ciliary muscles and anastomose with long ciliary arteries. The venous return from the uveal tract is by three routes (*a*) Vartex veins; (*b*) anterior ciliary veins, and (*c*) posterior ciliary veins.

2. *Retinal circulation*:—The central retinal artery arises from the ophthalmic artery at the apex of the orbit. It is accompanied by the central retinal vein and a sympathetic plexus (Nerve of Tiedemann). After its entrance it divides into superior and inferior retinal arteries, each of which gives a temporal and nasal branch at some distance from the disc. Besides these, there are two more nasal arteries and one or two macular arteries. The veins do not follow the course of the arteries peripherally. They empty into the central retinal vein which flows directly into the cavernous sinus. The blood vessels are generally confined to the cerebral layers immediately behind the internal limiting membrane. The retinal vessels like vessels of the C.N.S. are end arteries. Vasomotor nerves are derived from the cervical sympathetic. They can be traced to retinal vessels through the nerve of Tiedemann, the stimulation of which generally constricts the vessels of the retina, although not invariably so, a reverse effect has been noted, and sometimes, no change can be described. Vasodilator fibres have not been traced to retinal vessels, although some evidence has been brought forward to show that the sympathetic nerves contain vasodilator fibres, by paralysing the constrictors with ergotoxins and stimulating the sympathetic. It might be that it is simply a reversal of effects on the constrictor fibres themselves. Such examples may be seen in the melanophores of the fish, fundulus, in which the melanophores are contracted by Adrenaline, but if previously treated with ergotoxin causes an expansion.

Vasodilation is caused by the sensory and the trigerminal, mediating the vasodilation through antidromic activity.

Vascular reflexes of the eye are of two types : (1) axon reflex ; (2) more general reflexes which involve the mediation of the central nervous system. The former is mediated through the sensory nerves or the sympathetic. The direct action of light seems to have a constricting effect and is independent of light sense and size of the pupil. Reflexes of the spinal type are mediated through sensory neurones as afferent path and sympathetic as efferent. They may involve an inhibition or increase of tone of vessels. Thus the stimulation of the cut central end of the sixth nerve causes a vasodilation of the eye (Leven reflex). The naso-ocular reflex, whereby if the nasal mucous membrane is stimulated, there is a hyperemia of the conjunctiva, the reflex being mediated through the sixth nerve and the sympathetic, *via* the bulbar centres.

Retina is the only part of the body, where the condition of the blood vessels of the interior of the body are directly observable. Therefore changes in these vessels are likely to give a fair index of the systemic vascular condition, both functional and anatomical with this reservation that as it is an important sense organ and a part of the brain, it is specially protected. While its widespread connections with the entire body, through the autonomic nervous system as well as anatomically makes it prone to be affected in any lesion in any part of the body, it might not always be so.

Hyperemia of the Retina.—(1) Active hyperemia consists of fullness and tortuosity of the arteries, pinkish appearance of the optic disc with a veiling or blurring of its margin. The causes are varied, such as high blood pressure, persistent exposure to strong light, refractive errors, etc. The best thing is to regard it as an index of a complicated neurosis.

Passive hyperemia or venous congestion:—Veins become dilated and tortuous to a greater extent than arteries.

Causes are papillœdema due to increased intracranial pressure, cardiac insufficiency, a media-stinal tumour, emphysema, epilepsy, obstruction in the orbit.

Cyanosis of the Retina.—When engorgement becomes so marked as to change the colour of the retina, cyanosis occurs ophthalmoscopically—intensely congested tortuous veins are seen, arteries resemble normal veins in appearance, occasional hæmorrhages and purplish hue of the fundus may be seen. Causes—congenital heart diseases, with stenosis of the pulmonary artery, polycythæmia, erythromelalgia, emphysema with generalised venous stasis, acquired heart disease. *Complications*—Thrombosis, massive venous hæmorrhages, glaucoma.

Anæmia : Ischæmia.—It may be due as a part of general syndrome, *e.g.*, anæmia, cerebral anæmia, fall in blood pressure.

Retinal Ischaemia after exsanguination :—Visual symptoms usually occur after medical bleedings, and repeated small bleedings are more effective to bring about this condition, *e.g.*, hæmatemesis, melenæ, uterine hæmorrhages. The resulting blindness is usually complete and comes on between the third and seventh day after bleeding.

Clinically the pupil is dilated and fixed. Ophthalmoscopic changes may be normal, or there may be attenuation of vessels and pallor of the optic disc., optic neuritis with peripapillary œdema, retinal oedema, retinal hæmmorhages may occur. Associated symptoms : sensory and motor anomalies.

The prognosis is uncertain.

Obstruction of the retinal arteries :—The obstruction of the retinal arteries may be functional or organic. The functional type is due to spasm of the normal retinal arteries and the organic due to closure of the retinal arteries by an embolus or closure of a diseased artery by endarteritis or thrombosis. In all cases they come on suddenly and may be fleeting and the eye may regain its function, in others complete destruction of sight may occur.

CLINICAL PICTURE :—The large arteries are reduced to thread and smaller vessels almost invisible. There is fragmentation and beading ot veins. Retina rapidly loses its transparancy. During the first day fine opaque stria appear along the course of the nerve fibres, overlying and near the main blood-vessels. By the second day, the whole retina becomes opaque and in the macular area, a cherry-red spot appears. Even in cases of complete obstruction, an area of normal retina may be retained in the central area, due probably to the cilio-retinal artery. If the obstruction is limited to one of the branches, identical changes are found near the blockage. In all cases some circulation is regained due to anastomosis of the ciliary and retinal circulation near the nerve head. The underlying pathology is uncertain. Two views are held as to the opacity of the retina. Probably the early opacity is an œdema of the ganglion layers followed by ischæmic neurosis. In the early stage, the condition is recoverable and the change is due to "increased osmotic alteration initiated by catacytic breaking down of the retinal tissues by enzymes which flourish in the acid medium, created by the state of anoxæmia, a process which culminates in antolysis and complete atrophy." The red spot is due to the shining through of choroid through a transparent retina.

SYMPTOM :—Loss of vision, which may be complete and permanent. If the obstruction is gradual, some visual field may be retained. Macula, however, remains permanently functionless. Return of vision depends on the duration of the obstruction. If it is for an hour or two, central vision may return. When a branch vessel is obstructed, a sector defect occurs. Late complications are retinal hæmmorhages : (1) as a result of newly distended anastomosis ; (2) resumption of circulation, damaged capillaries, and secondary glaucoma.

Angiospasm.—Spasm of the retinal arteries can be produced by injection of Adrenaline, serum of hypertensive patients, tobacco smoke inhalations, oral administration of Ephedrine and in persons susceptible to cold.

AETIOLOGY:—(1) Those occurring in young individuals who have hyperexcitability of the autonomic nervous system and (2) those occurring in those elderly individuals who have organic retinal arterial diseases.

Frequently in the former group there are other symptoms of vasomotor neurosis, such as migraine, and the phenomenon may be excited reflexly, as in menstruation, vaginal douching. Sometimes endogenous and exogenous toxic factors which bring on a severe strain on the autonomic system, may bring on an attack, *e.g.*, lead-poisoning, malaria, influenze, etc.

The spasm may continue for some days (ELCHING, 1898) and there may be associated with it spasms in other regions.

The mechanism of the spasms and the attending hyperpysis is not quite clear.

The spasm of the retinal vessels seems to indicate that primarily there is a sufficient fall of intra-sinusoidal pressure which causes a reflex dilation of the cerebral and ocular blood vessels and this causes an increased output of epinephrine (HEYMAN, quoted by WIGGERS, p. 541) for maintaining adequate supply to the brain and this causes a spasm of cerebral and retinal blood vessels. This angio-spasm (and such spasm is known to occur in the retina by Adrenaline), causes anoxemia in the retina and the brain and alters the PH and thus stimulates the vasomotor centre (WIGGERS p. 613, p. 537). Although increase in the concentration of adrenaline in the blood has not been demonstrated, it is conceivable that initially, adrenaline gland is stimulated to secrete epinephrine in order to set the vasomotor mechanism at a higher level to counteract the altered circulation of the brain and to obtain adequate supply of food material and oxygen to the brain. Having done its work, it quickly disappears from the circulation, not to appear again in abnormal amounts in the blood.

The increased amount secreted at a particular moment is also quickly destroyed in the blood. Probably the cause of the initial low pressure in the carotid sinus is due to a systemic low blood pressure induced by vagus stimulation; since, according to WIGGERS, low pressures induced in this way cause a supernormal blood pressure which he supposes to be due to a continuation of the vasomotor activity induced in this way (p. 537, WIGGERS).

The exact mechanism of its stimulation is not clear. Probably emotional strains cause an hyper-excitable condition of the autonomic and hence vagus also; and as afferent depressor fibres are contained in it and these are more easily stimulated by lower strength of current than its presser fibres, small impulses originating in the gastro-intestinal tract (which is also not functionating properly being supplied by jaded nerves) or any other part of its supply, may cause a fall of blood pressure. Most possibly the impulses originate mainly in the gastro-intestinal tract or the sacral autonomic, which also contains afferent depressor fibres and may be the source of this low pressure. During the phase of angiospasm, probably the vasomotor activity is in abeyance; since injection of Adrenaline has been found by ADRIAN (WRIGHT p. 334) to cause an inhibition of vasomotor centre and there may be stoppage of vaso-constrictor impulses in the sympathetic for as long as 5 to 10 minutes. Thus, probably in the maintenance of the hyperpiesis, the following chain of events occur:—

Exhaustion and hyper irritability of the autonomics → stimulation of the depressor fibres of the parasympathetic, specially vagus → fall of intra-sinusoidal pressure → alteration in the cerebral circulation → secretion of epinephrine → spasm of the arterioles of the brain and the eye → anoxemia of the brain → stimulation of the vasomotor centre → rise of blood pressure.

Super normal pressure is probably due to the hyperexcitability of the sympathetic which over-shoots its mark; or the vasomotor centre works at a higher level. Probably both factors are at work, since it is likely,

that in nervous exhaustion, this centre is also easily excitable. So long as the centre and the nerves can work at this high level, it does not take the help of the Adrenaline, but as soon as the pressure tends to fall below the normal level epinephrine steps in and relieves the vasomotor centre; thus a vicious circle is established. If there are frequent failures, the help from the Adrenaline will be frequent and if there is almost complete failure, the spasm will be continuous.

Once the vasomotor system becomes accustomed to work at high pressure, it continues to do so with more exhaustion of mind and body. Apparently, the evanescent type of angiospasm occurs in those who have an almost normal autonomic system.

The tonus of the eye and indirectly that of the autonomic nervous system can be measured by photometric examination, the details of which will be given later on.

It should also be remembered that there is a phasic variation of the action currents, the discharge being intermittent as well as a three-hourly variation as is observed in the rise of intra-ocular tension of glaucoma.

This disease is therefore a wasting disease, as much as phthisis, but here there may not be an external infection, but an infection of the mind with grief, sorrow, poverty, stress and strain, high ambition and excessive venery etc., which drives the mind at a high speed day and night, giving no period of rest. The external infection of any type also puts a great strain on the cellular and nervous mechanism of the body, but the toxin is here acting for a short period of time and of one type, and is mainly limited to those parts where the brunt of the infection falls. But if the mind, whose inherent property is to be in constant oscillations at a high rate, be infected with those baser qualities *viz.*, anger, pride avarice, sex, etc., in supression of its nobler qualities, the vibration becomes many million times multiplied and as the mind works through the nervous system, the latter is unable to withstand such oscillations for any length of time and becomes wrecked. The nobler qualities may be regarded as defensive machanism of mind. Increase them, the blood pressure falls. But unfortunately we are born with both sets of qualities.

The treatment of this condition should therefore consist of (1) giving adequate nourishment, specially in the form of milk, avoidance of all animal foods and onion; (2) securing periodical rest to vasomotor centre by administering Ephedrine (gr. $\frac{1}{4}$) to secure inhibition of the vasomotor centre, since the action of this drug is analogous to epinephrine; (3) hyper-irritability is to be controlled by such measure as cephalic cold, administration of Bromide, Liq. auriet arsenic Bromide, ultra violet rays, the last also helps to secure cutaneous vasodilation and has got metabolic effects and calcium; (4) keeping the bowels free by some oils or sena in the form of pulv. glycerhezzala; (5) mental rest can be secured by meditation at some period of the day for some time; and (6) in case of persistent hyperpiesis with angiospasm, injection of a specially prepared absorption compound of Mercury seems to bring down the blood pressure quick. It is still under trial. Other measures as may be necessary may have to be adopted.

THE SECOND TYPE:—It is associated with organic vascular disease and tends to occur in elderly people, who have a high blood pressure. The machanism seems to be essentially the same as in the young and it carries

an element of danger to the life. It is sometimes associated with hemiparesis and angina pectoris. Acute angiospasm is common in severe hypertensive and renal disease. Narrowing may be transient, but too frequent an occurrence or persistent for a long time may lead to permanent damages. It is an arteriolar disease.

CLINICAL PICTURE:—This depends on the duration and extent of occlusion. Pupils are dilated and fixed, the arterioles involved are reduced to thin white streaks invisible for any distance beyond the disc, segmentation of blood column with beaded appearance in the veins are seen. If the spasm is prolonged, the clinical picture of obstructions *viz.*, a milky white retina and a cherry red spot in the macula may appear. Usually attacks are transitory and full restoration of the visual function occurs. In arterio-sclerotic cases, the prognosis is worse.

Embolism:—It is a rare phenomenon, the reason being probably the two right angled bends in the course of the artery, one at the origin of the ophthalmic artery, another where the central artery leaves the ophthalmic artery. The obstruction may be complete or partial, the latter may become complete by thrombosis and is proximal to the embolism, the artery becomes collapsed and obliterated by proliferation and adhesion of the endothelium from the vessel wall. The veins show concentric narrowing owing to thickening of its walls and distal to the obstruction, the vessel is occupied by an organised thrombus.

The frequent site is in the region of the lamina cribrosa.

Endarteritis and arterial thrombosis:—It is a more common disease than embolism. There is a slow and progressive obliteration of the lumen of the artery by a proliferative endarteritis.

The complete closure comes on suddenly by a terminal thrombus or spasm. Such a lesion is the most common cause of arterial obstruction in old people. The obstruction may be bilateral. The usual clinical picture is that of embolism.

TREATMENT:—This consists of (1) Inhalation of Amylnitrate; (2) immersion of patient in hot bath ; (3) retrobulbar injection of Atropine or Acetylcholene; (4) as general vasodilators, cobra venom, intravenous injection of typoid vaccine (10 to 25 millions Papevarine Hydrochlor gr. $\frac{1}{4}$) ; (5) massage of globe repeated parcentesis and eredectomy to dilate the arterial blood vessel; (6) sedatives to the nervous system ; (7) avoidance of tobacco, exposure to cold and fatigue ; (8) careful observation of peripheral arteries ; and (9) ultra violet rays applied to the closed lids.

Retinal arteriolar thrombosis.—This is rarely mentioned in literature. Clinically, there is a localised area of œdema associated with vascular disease. There might or might not be any sign of arterio-sclerosis, but in the affected region of the fundus, a minute arteriole shows extreme sclerotic changes. The affection comes on suddenly, with appearance of a haze before the eye which persists as scotoma, *majority die within* next few years of *uremia* and cerebral hæmorrhage.

Central angiospastic retinopathy.—This occurs in young individuals or middle aged persons, particularly in men, in which an œdema is limited exclusively to the macular region, which is characterised by recurrent transient attacks of visual failure with complete or almost complete restoration of function, probably due to spasm. These are not subjects of

arterial hypertension but there is frequently some vasomotor lability in the extremities. Ophthalmoscopically there is a swelling in the central area, surrounded by a ring-shaped light reflex and dots varying in colour from yellow to Gunn's dots. It may leave behind pigmentary dots.

Obstruction of retinal veins :—It is characterised by gross venous disturbances and profuse retinal hæmorrhage. The general mechanism may be described in four stages.

The predisposing is, (1) slowing of the blood flow and (2) formation of a roughened area on the endothelium upon which deposits may collect.

AETIOLOGY:—Great majority occurs in arterio-sclerotics over middle age, few of them are albuminurics with high blood pressure. In the younger ones, a toxic factor enters into the causation by causing endophlebitis. There may be septic anæmia, endocarditis influenza, pneumonia, meningitis, gonorrhœa, too liberal removal of septic tooth, amaurosis of quinine poisoning. It is not uncommonly bilateral.

PROGNOSIS:—With regard to vision not good, if the macula is involved, prognosis to life in the arterio-sclerotics, its occurence is ominous but not to the same extent as in arterial obstruction.

TREATMENT :—This consists in administering Miotics and combating the general hypertensive arterio-sclerotic condition. Mercury and Iodides may be exhibited. Cautious eradication of septic focus is in order, but there is no treatment for the restoration of vision.

Oedema.—This is one of the most common conditions occuring in most circulatory disturbances and inflammatory conditions. Two factors are probably at work. (1) Increase of capillary permeability in toxic conditions and inflammations, whereby fluid albuminous matter and fibrinogen escape into the tissues and form exudates and hæmmorhages. (2) An alteration of molecular constitution of retinal tissues whereby large protein complexes are broken down, in which case they imbibe fluid from retinal and chorio-capillaries. The first condition is reversible. (3) Upon roughened area, cells and fibrin from relatively stagnant blood stream are deposited, so that a nodule or an organised thrombus protrudes into the lumen of the vein.

CLINICAL PICTURE:—This is dramatic and is essentially the same whether the central vein is occluded at the lamina or a branch vein is occluded. In the first case, the veins become engorged, tortuous and enormously dilated, doubling themselves with great loops, at one spot buried in the retinal tissues, and at another standing out from them. There is relatively small amount of oedema in the beginning In some cases, the oedema may form a macular star and later on macular hole may form. The whole retina is bespattered with hæmorrhages, specially the central region lying mainly in the nerve-fibre layer. After a little time, they become fringed with white exudate like areas which are probably albuminous in nature. Branch thrombosis occurs generally in the superior temporal vein at the arterio-venous crossing.

COURSE OF EVENTS.—The circulation is restored to a certain extent, rapidly clot becomes canalised and collateral branches are established. The tension in the beginning may be subnormal, latter on rises and the most dangerous thing is the occurrence of hæmmorrhagic glaucoma after some time.

SYMPTOMS:—Sudden loss of vision, but without dramatic onset of arterial obstruction. As time goes on, there is little visual improvement, although there is improvement in retina. The whole tissue becomes boggy and thickened and most marked at the optic disc, spaces appear in the ganglion cell layer, so that cells lie in distended lacunæ. In the nuclear layer there is a tendency for elements to separate.

CAUSES.—1. Circulatory—(*a*) Venous obstruction, arterial obstruction; (*b*) Trauma—such as contusions to globe; (*c*) Electric shock; (*d*) Optic neuritis and papilloedema; and (*e*) Trauma to the skull.

2. Tonic Oedema—due to local causes—in all retinal inflammation, and most chorodial ones; and intra-ocular inflammations of the anterior segment.

3. General—hypertension, arterio sclerosis, renal retinopathy. Most interesting is the appearance of œdema, usually transient in nature and limited to the posterior pole in extra-ocular infection *e.g.*, sinus infection, acute dental sepsis, acute febrile diseases, chronic anæmia or cachetic states. The œdema is limited to macula with symptoms of micropsia, metamorphopsia and a central scotoma.

Ophthalmoscopically:—In the early stages, the retina looks thicker and more opaque than normal with a somewhat granular appearance shimmering with irregular reflexes. The symptoms may be the appearance of a yellow veil before the object looked at, a reduction of adaptation and development of a difficultly detectable scotoma. In more advanced stages, the blood vessels are lifted, become very irregular and sinuous, the reflexes disappear. Finally, a milky translucency may set in. Visual acuity may fall to perception of light or may even be lost.

Central Serous Retinopaltrics.—It occurs in young adult males as annular swelling of a darkish red colour round the macula usually less than the size of a disc. The oedema is preretinal and is surrounded by a ring-shaped light reflex with small dots varying in colour from white to yellow.

PROGNOSIS:—It is transient.

TREATMENT:—Elimination of toxic factors and correction of metabolic disturbances.

Retinal haemorrhages:—In contradistinction to their frequency in the brain, hæmorrhages from the arteries or arterioles are rare. Only conditions in which it is likely to occur are (1) advanced atheromatous degenerations of the vessel walls and (2) acute septicæmia and pyemia.

Hæmorrhages from veins occur when venous return is sufficiently obstructed. Generally hæmorrhages occur from the capillaries and is most probably due to capillary dysfunction and are the result of injurious processes affecting their walls; or are expressions of defective circulation through them, so that endothelium is impaired, thus allowing fibrinous exudates or leakage of whole blood in a manner analogous to the formation of plasmoid aqueous. Hæmorrhages from the capillaries may occur as a result of trauma, obstruction, local inflammatory conditions, toxic states, vascular retinopatheos as diabetes, arteriosclerosis, nephritis in senile arteriosclerosis, diseases of the hæmopoietic system, *e.g.*, anæmias, leukaemias, purpura, etc.

CLINICAL PICTURE:—Varies according to the site of extravasation of blood. They are most numerous centrally, where the retina is thickest, and vessels are largest, and is generally confined to the cerebral layers. In the nerve fibre layer the shape of the hæmorrhage is flame-shaped. In the deeper parts of the retina they are round. The colour is red and is retained till the hæmorrhage disappears. Unless the external limiting membrane is lacerated usually they disappear.

Preretinal haemorrhages:—Occur on the inner surface of the retina and do not penetrate the vitreous body. Usually they are derived from the veins and owing to action of gravity assumes a hemispherical shape, central vision may be lost. Causes are the same as inter-retinal hæmorrhages.

Vitreous haemorrhages.—Any inter or preretinal hæmorrhage may burst through the internal limiting membrane and invade the vitreous. It is detected when the red fundus reflex is abolished. The vision may be reduced to perception of light. Prognosis—guarded. Fibroblastic proliferation may occur if syphilis, tubercule or chronic sepsis are present leading to retinitis proliferens. Treatment—Removal of cause, injection of Saline, Infra Red rays, Calcium.

Recurrent intra-ocular haemorrhages in young adults (Eale's disease).—It is the clinical manifestation of many diseased conditions. (*a*) Primary retinal hæmorrhages in young man (EALES).

ETIOLOGY:—According to EALES it is associated with constipation and epistaxis. The former is due to vasomotor contraction and subsequent muscular inhibition of the alimentary tract, and the retinal hæmorrhages to a compensatory dilatation. Of the many cases—(1) tuberculosis; (2) septic focii and (3) thromboangitis obliterens are known to be operative. Male about the age of 23. Sudden in onset, macule may be spared, vitreous hæmorrhages occur.

The mechanism seems to be the same as the angiospasm. In a vasomotor unstable condition, there is sudden sympathetic stimulation; the afferent impulses arise from the sacral nerves plexus. Many of them give a history of excessive libido. Treatment—Ultra-violet Rays, Ephedrine, Bromides, Calcium, and treatment of causes specially psychological. Recurrences are common and the vision may be lost.

Retinal manifestation of vascular diseases:—The most important ophthalmoscopic evidences of sclerosis of retinal vessels are as follows:—(1) Translucency of the vessel walls is lost; and (2) the vascular reflex suffers three significant changes. (*i*) Copper wire arteries-the retinal arteries—assume a burnished metallic appearance with a broader and softer reflex resembling a copper wire. (*ii*) Silver wire arteries—the whole thickness of the artery appears as a bright white reflex like a silver wire. (*iii*) Irregularity of reflex shows dots or leading of increased bightness. (*iv*) Sheathing of the vessels—white lines first appear running along side the walls of the vessels. In extreme degrees, the entire vessel is converted into a while fibrous looking cord (*v*) Arterio-Venous Compression—most easily seen where the arteries and veins cross. (*vi*) Irregularity of lumen. (*vii*) Tortuosity and enlargement of vessels. (*viii*) General attenuation of retinal arteries.

Vascular sclerosis: *Diffuse arteriosclerosis*:—This disease is independent of blood pressure. In the eye they show themselves relatively

slight in extent and late in appearance: so long as the blood pressure remains within normal limits, it does not cause a pathological picture. The only effect is decrease of functional and metabolic activity.

The changes in order of time are:—(1) Increased translucency, (2) the larger branches are full, tortuous, copper-wired, and (3) arteries harder with a moderate degree of arterio-venous constriction.

Hæmorrhages or exudates do not appear in the absence of complication.

Hypertensive sclerosis:—In this condition, the high systolic pressure is not so dangerous to the eye as high diastolic pressure, as the rupture of the arteries in the eye is never great, but the latter, by permanent strain on the capillaries, damage them.

1. *Simple hyperpiesia*:—(*a*) Absence of light reflex on the *veins* near the arterial crossings; (*b*) the arteries may be engorged and their light streak broadened; and (*c*) arteries may become small in size and pale in colour.

Intermittent Spasms. *Engorged arteries are not associated with hypertension.*

2. *Diffuse hyperplastic arteriosclerosis*:—In this group, a large number show exudative and hæmorrhagic changes like "albuminuric retinitis" without albumin in the urine. (*a*) In the large arteries—differences in calibre, irregular tortuosity, copper wire reflex, arterio-venous constrictions and gross sheathing are seen; (*b*) Smaller arterioles may show cork-screw appearances; and (*c*) Hæmorrhages and exudates are common.

Involutionary arteriosclerosis with hypertension:—The most characteristic sign of raised tension is a narrowing and straightening of the arteries. The signs are:—(*a*) arteries are straight and branch at acute angles; (*b*) reflexes harder, changing to silver wire; (*c*) light streaks become broken up and beaded; (*d*) parallel sheathing may proceed to pipe stem sheathing; and (*e*) compression and deflection.

It may be noted that while sclerosis can give no safe indication of sclerosis elsewhere, its occurrence in eye certainly indicates its presence generally. The relation between cerebral and retinal arteriosclerosis is close, but there is no question of uniformity of the pathology and the arteries of the calibre of which usually are associated with cerebral hæmorrhage are unrepresented in the eye and the external support received from the intra-ocular tensions and the danger of close association between the arteries and veins are absent in the brain.

Vascular retinopathics:—This group is characterised by the appearance of hæmorrhages and exudates in addition to the factor of vascular changes; hypertension and toxæmia are added.

1. *Arteriosclerotic retinopathy*:—(*a*) Vessel shows signs of diffuse hyperplastic sclerosis; (*b*) Disc—normal or slight haziness; (*c*) *Complete absence of œdema*; and (*d*) Exudates—small bright spots mainly in the central area: small in size, circular, sharp-edged without surrounding œdema.

Significance—Severe vascular. Sclerosis associated with hypertension without any danger to life, the death being due to cerebral or cardiac in contradiction to renal retinopathy.

2. *Renal retinopathy*:—According to VOLHARD, pathogenesis of retinal changes depend on hypertension and arteriolar constriction.

It is common in chronic form of renal disease. Age 30 to 60.

CLINICAL PICTURE—Four characteristics: (1) Vascular changes—arteriolar in nature—attenuation in calibre to become almost invisible, other changes are less constant; (2) Oedema—blurring of the optic disc, irregular greyness and striation of retina to detachment of retina; (3) Hæmorrhages—they are superficial and generally found near the large vessels and near the disc; (4) White exudative masses of diverse appearance and origin, with a preference for central region within the œdematus areas; (5) Formation of sharply defined white spots always lying deeply underneath the vessels and occurs most frequently between the macula and the disc; and (6) Most characteristically exudates are arranged like a star with fine radiating margin.

In general, œdema and cotton wool patches are the characteristic of acute intoxication, while discrete patches and the star are associated with a chronic process.

Toxaemic retinopathy of pregnancy:—Acute and sudden onset, exudations and haemorrhages are marked and massive œdema. Prognosis as to vision and life is good.

ÆTIOLOGY:—Most frequently occurs during the 9th month. Previous vascular sclerotic changes may be absent.

In all cases hypertension is present. When systolic pressure is above 150 mm. Hg and diastolic above 100 mm. Hg the retinal changes occur and are most marked when 200/130 is reached and run parallel with hypertension and does not depend on the degree of renal pathology.

CLINICAL COURSE:—(1) Stage of spastic and arterial irritation; (2) Stage of sclerosis; and (3) Stage of retinopathy. Complete recovery usually results on treatment provided no organic changes have occurred.

CLINICAL SYMPTOMS—(1) Attenuation of retinal arterioles with hard reflex and high diastolic pressure and the change usually first occurs at the *nasal periphery*; (2) frequent occurrence of angiospasm; (3) retinal detachment; and (4) œdema, exudates and hæmorrhages, which are very marked, frequently resulting in macular star or macular detachment.

PROGNOSIS:—(1) If the changes are confined to the arterial attenuation, the pregnancy may be allowed to continue under closest supervision. (2) If angiospasm appears, graver view should be taken of the case. (3) If vascular sclerosis and retinopathy develop pregnancy should be terminated. If there is no advanced nephrosclerosis, a rapid resolution of retinal changes occur. In about 50% of cases, some amount of optic atrophy remains occasionally, there may be progressive loss of vision. (4) Prognosis with regard to life is also good. Recurrence in future pregnancies are not great, if relief has been obtained before permanent damage to the vessels has been done.

Malignant Hypertensive Retinopathy:—This is not necessarily accompanied by nephrosclerosis except as a terminal event. It differs from nephritic retinopathy in having an extreme degree of papillary and peripapillary œdema. This papillœdema is of special prognostic and diagnostic significance. They are associated with narrow attenuated arteries and may be preceded by angiospasm. There is hyperemia and marked œdema of the disc, profuse superficial patches and soft cotton wool exudates.

Pathologically, there is an actual arteriolonecrosis.

The picture suggests an acute and perilous toxaemia with symptoms of vomitting and its appearance is generally considered as a death warrant, and few patients live for two years.

Diabetic retinopathy:—Doubt still exists whether true diabetic retinopathy occurs. Two views contrary to each other are held. The chief fundus changes are (1) Spots—hæmorrhages; (2) retinal hæmorrhages; and (3) pigmentary degenerations; each of the above following a clinical group. The vital prognosis is good. There is no relation of the clinical picture with the severity of the disease and occurs specially in old age; high tension, or nephrosclerosis may be absent. Probably a *metabolic toxic factor* is important in the production of the condition; changes in the kidney or arteries may occur in a diabetic patient and alter the clinical picture accordingly. Females are much more affected. It affects the older patient only.

Ophthalmic changes.—*Arteries* may show changes characteristic of arteriosclerosis and hypertension. There is early engorgement and congestion of the veins.

Haemorrhages.—(1) Small and the entire fundus may be bespattened with it; (2) They are deep and round. Massive hæmorrhages generally occur in those who are free from sugar and are associated with sepsis and sclerosis.

The exudative spots usually occur in the central area. They are solid, soapy or waxy, looking with *clear cut edges*, and arranged circularly round the macula. The patches are usually discrete but may be confluent. They are inert and persistent.

Oedema is rare.—Disc is usually unchanged, macular star is usually absent. The *macula* may *remain free for a long* time.

Prognosis of diabetic retinopathy with regard to life is better than the renal one. If arteriosclerosis or hypertension is superadded, prognosis with regard to life and vision is bad. Death often occurs by cerebral hæmorrhages. With regard to vision, prognosis is bad as the lesion is progressive in spite of treatment. *Insulin* should be administered with *great caution* in massive *haemorrhagic* cases. Elimination of sepsis is very important.

In treating these patients, caution should be the guiding principle and overzealous treatment may lead to disastrous results.

***B.* Blood Diseases.**—1. *Anaemias*:—(*a*) Pernicious anæmias. When red cell count falls to 25 to 30% small superficial and flame-shaped hæmorrhages appear in the posterior pole. Sometimes these spots have white centres due to degenerating leucocytes. (*b*) In subacute combined degeneration, the hæmorrhages are rare. (*c*) In aplastic anæmia, retinal hæmorrhages occur. (*d*) Chlorosis—papillœdema is common. (*e*) In secondary anæmias, when red cell count falls below 50% the following changes may be noted: a general pallor of the fundus and of the vessels; a distension of thev eins; a faint oedema like veil of the fundus; multiple superficial hæmorrhages associated with wooly patches. They tend to clear up without leaving any trace.

2. *Erythremia*:—Some engorgement and tortuosity of veins, arteries normal. Hæmorrhages thrombosis of central vein.

SYMPTOMS.—Photophobia, photopsia, scotoma, hemianopsia and mistiness of vision and complete blindness.

3. *Leukaemia*:—In the earliest stages—engorgement of veins with marked tortuosity. Later on, veins and arteries become yellowish, become turgid and segmented into sausage-like formations, being deeply dented by arteries at their crossings. Deep or superficial hæmorrhages appear with a central white area. Exudative white spots specially in the central region are seen.

In fully developed condition.—(1) The retina takes on an orange or pale green hue; (2) the disc may become œdematous; (3) perivascular sheathing of dilated and tortuous vessels sometimes as wide as the vessels themselves; and (4) hæmorrhages and marked contractions of visual field and night-blindness may occur.

In chloroma.—Retinal hæmorrhage, exudative spots and papillœdema may occur.

4. *Haemorrhagic diathesis.*—Purpura hæmorrhagica, small, superficial hæmorrhages near the disc appear, œdema of the disc, white spots and macular star.

Haemophilia:—Rarely hæmorrhages are seen.

Scurvy:—Is rarely associated with retinal hæmorrhages, although hæmorrhages in other situations are common.

The commonest retinal disturbance is night blindness due to disturbed metabolism of the visual purple.

5. *Lipaemia*:—Marked retinal changes in this condition occur particularly in diabetics with marked acidosis and is known as lipæmia retinalis.

CLINICALLY:—The blood ve-sels take on a milky appearance and become flat and ribbon like. Light reflex becomes diffuse or lost and yellow white strips accompany the vessels. Disc and ground of fundus remain normal.

Bibliography:

1. Wiggers, Carl J.—Physiology in Health and Diseases. Henry Kimpton, London.
2. Wright, Samson.—Applied Physiology.
3. Duke-Elder, Sir W. S.—Text Book of Ophthalmology.

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Intramuscular Use of Whole Blood in Treatment

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BLOOD is the vital juice of life and as such its potentialities in the therapeutics have not been, I am afraid, sufficiently explored. My aim in presenting this preliminary paper is only to indicate the wide scope for its successful use in practice.

Blood is a fluid of complex constitution. Its chemical, biological and immunological nature is not yet completely known. Its uses in practice will multiply as its true nature is revealed more and more. It is well known that the blood is made up of plasma and corpuscles. The corpuscles are bags of semi-permeable membrane containing a complex ferruginous substance, hæmoglobin, in varying combination with oxygen aud carbon dioxide, and other blood proteins. The membrane itself is made up of some lipoid substance. The plasma contains proteins, fats, carbohydrates, salts, fibrin ferment and other enzymes, immune bodies, endocrine secretions and water. With all this, many phenomena having bearing on the tissue fluids like anaphylaxis, allergy, idiosyncrasy, nephrotic œdema, still remain a mystery. The use of blood in the therapeutics depends upon the utilization of the qualities of some of the known constituents of blood.

Blood has long been given intravenously as a transfusion in hæmorrhage,shock, anæmia, thrombocytopænia, and in a host of other diseases. Its effect is rapid but the operation is too technical to be carried out by the general practitioner. The necessary facilities for grouping and matching of blood are not available everywhere, and even then, the operation itself carries with it a definite degree of risk. It is also difficult to find a donor who is prepared to part with a large quantity of blood as is usually required for an intravenous transfusion.

All these inconveniences are obviated if whole blood is used intramuscularly. The greatest advantage in this method is that the compatibility test of the blood is not required. The technique is very simple—in fact, it is only an intra-muscular injection. Large quantities of blood are not required and hence very little difficulty is encountered in finding a donor. There is not the least risk to life, and the reactions are usually absent or negligible. Anaphylaxis and serum sickness have not been encountered so long. In a hospital, in particular, it is very easy to find a donor in a patient in whom blood-letting is indicated. But I refrain from selecting a patient of essential hypertension as a donor because its etiology is still in the dark.

For intramuscular use, blood can be taken either from the patient himself, *i.e.*, 'auto-blood' or from another healthy person. I always prefer the latter because that sample is bound to have the full complement of the healthy constituents of the blood, while the former is likely to be deteriorated in quality as a result of disease. In selecting a donor, care should be taken to see that he has no disease that can be transmitted by blood *e.g.*, syphilis, malaria etc. In giving blood to a patient suffering from acute infectious diseases, *e.g.*, typhoid, pneumonia etc., the blood of a person who has recently recovered from that infection should be preferred. If

such a person is not at hand, any healthy person may be used with advantage.

Human whole blood can be used intramuscularly for a number of conditions. I will mention below a few of them where I have met with remarkable success.

I. **As a hæmostatic.** Whole blood has been used for this purpose on the same lines as the horse serum. It is superior to horse serum in that: (1) It is a better hæmostatic because of its content of platelets and fibrinogen ferment; and (2) It is not found to give rise to serum sickness or anaphylactic shock. I will quote two cases treated on this line:

CASE 1:—Mr. K., aged 22, had profuse intestinal hæmorrhage as a complication in typhoid. I was called to see him about 16 hours after the bleeding had started. The usual remedies like Calcium, Coagulen and Opiates had failed. When I saw him he was profusely perspiring all over the body with the temperature 95°F., pulse 130 per minute, and respiration 28. One intramuscular injection of 10 c.c. of whole blood stopped the bleeding and improved the patient generally. The patient made an uneventful recovery.

CASE 2:—Mr. C., aged 24, had oozing from the tonsilar bed for over 48 hours after tonsilectomy. After the usual remedies had failed, I was called in to consider the advisability of a blood transfusion, I preferred to give intramuscularly 10 c.c. of whole blood with an order to repeat it after six hours if the bleeding continued. There was no occasion for the second injection and the patient made rapid recovery.

As a hæmostatic, the dose I use is 10 c.c., intramuscularly, to be repeated after six hours, if necessary.

II. **As a protein shock treatment.**—It is specially useful in rheumatoid arthritis and fibrositis. It may be used in chronic gonorrheal arthritis with some advantage. The dose used has been 5—10 c.c., every third day. A course of at least 12 injections should be given as these conditions are often very resistant to treatment.

III. **In allergic conditions.**—I have used it successfully in asthma, urticaria and angio neurotic oedema. The dose is as mentioned above.

IV **In acute infectious diseases like typhoid, pneumonia and their complications:**—As already referred to above, in these cases blood of a person who has recently recovered from the disease is to be perferred. The treatment is useful during the uncomplicated course in diminishing the toxæmia and bringing about general amelioration in the condition of the patient. It is particularly useful in the inflammatory complications like parotitis, arthritis and the like. There is no doubt that in pneumonia, treatment with the chemotherapeutic drug Sulphpyridine is a great success. But sometimes a peculiar condition appears under the treatment. The general condition of the patient together with the high temperature improves but the sign in the lung persists and resolution is long delayed. The reason perhaps is that as a result of the bacteriostatic effect of the drug the activity of the pneumococci is paralysed but the reparative mechanism does not come into action *pari passu*, with the result that the pathological condition of the lung imitates a slow motion picture of pneumonia. It is in such a condition that the injections of whole blood are

useful in expediting the resolution. The dose used is 5-10 c.c. on alternate days.

I have found this treatment useful particularly in the lingering low hectic temperature that sometimes follows the usual course of the typhoid fever. Three injections of 2-5 c.c. of whole blood intramuscularly on alternate days are usually enough to control the temperature. During the course of the typhoid fever the dose used has been from 2 c.c. to 10c.c., rising by one c.c. for each injection, on alternate days.

V. Lastly I want to stress the intramuscular use of whole blood for anæmia. I have found that the patients who do not respond to iron or liver therapy and where nothing but a transfusion seems to be indicated react marvellously to this therapy. The total red blood cell count and the hæmoglobin percentage increase rapidly. I have seen hæmoglobin percentage rise from 42 to 75 per cent. during a course of ten injections. The effect is probably due to the stimulation of the hæmopoietic system as a whole. The results are particularly marked in iron deficiency anæmias. The usual treatment of this group of anæmias is by oral administration of large doses of iron. It is well known that iron in such large doses is either not well tolerated or assimilated. Iron by usual injections can be given only in minute and inadequate quantities as large doses are painful and irritating. In the whole blood we have a non-irritating and painless iron compound that can be given in adequate doses without any harmful effect on the organism.

In anæmias that do not respond to iron or liver therapy, there is probably some other deficiency that is hindering the hæmopoiesis. Vitamin C, Thyroxin, Copper, Manganese are some of the known such substances. As regards vitamin C, it has been shown that it augments the effect of liver therapy to a great extent. Such known and unknown deficiencies are probably adequately made up by the use of whole blood with all its content of internal secretions, vitamins and various organic and inorganic substances. The dose I use for cases of anæmia is from 5 to 40 c.c. Upto 10 c.c. the injections can be given twice weekly and then weekly. The doses should be increased by 5 c.c. every week. While using large doses of blood, anti-coagulent like 2% Sodium Citrate 1 c.c. for each 10 c.c. of blood. should be used.

The doses mentioned above are those used by us with success and are empirical. We are further investigating the possibility of extending this therapy to other conditions and our results, which are promising, will be given in a subsequent paper. In the meantime, I hope that this preliminary paper will encourage wide trial of this simple and inexpensive treatment at a time when the drugs we use are so costly and their potency doubtful. The author will be pleased to hear how this treatment fares in other hands.

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The Therapeutics of Circulation

BY

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FEW people know how doctors die. In a recent survey by DR. A.H. GOSSE, analysing over 8,884 deaths, it was found that in 100 consecutive deaths 33 died of cardiac and cardiovascular diseases. In fact coronary thrombosis had in some quarters come to be regarded as the "Doctor's Disease." Very few are fortunate, amongst the profession, to become grand old men. A good many are gathered in the prime of their lives in one or other of the numerous wars, as well as peace time casualties. In our own country typhoid, tuberculosis and septic infections, gather not a few, even while yet "in statu pupillari."

The same analysis furnishes the fact, that on an average every doctor goes ill for a week and stays in bed for that period every year almost of his professional life, between 25 and 65 years. About 40% suffer from influenza and respiratory affections. Only 57 take seriously to bed with cardiac and cardiovascular affections, a fact that is significant that in this group, the rest which the doctors prescribe so readily to others, is seldom enjoyed by them or falls to their lot to practise their own precepts!

The above is a painful enough reflection for the reader about conditions in the profession in the West, where several favourable factors are present to promote longevity, where epidemics are fewer, where more protein food is eaten and where long established conditions of gainful occupation by medical men and women, are ably assisted by healthy traditions of co-operation, holidays and ample, unfailing remuneration. Conditions in the East are relatively harsher, and the therapeutics of circulation for the "physician patient" as well as his patient "patients" are perhaps not so auspiciously aligned. It will be my endeavour to indicate in this paper, certain salient features only, as time and space do not permit entering into the vast details of recent clinical and laboratory minutiæ, which are, however, of very absorbing interest.

The general practitioner is the first custodian of the sufferer from heart and vascular disorders. It is "D. A. H," "disordered action of the heart" and his following it up with Bromides, Digitalis, Strychnine and a host of tonics, including "Cactina pellets," various "Glycerophosphates" Hæmatinics, Nervines" are too well known to need recounting. The fear of the "murmur" is still too strongly entrenched in his bosom. To persevere with timorous doses of digitalis, is another common failing. The practitioner is in difficulties with his refractory "heart" case and the "heart" itself is in difficulties with its own internal and external foes, the erring physician being alas! at some time or other, unfortunately one of them.

A clear grasp of this peculiar situation is essential for good therapeutic results. The clever general practitioner will proceed methodically and take a good long while to practise the "by-now-well-worn adage," to look into the "stomach" of a young man complaining of heart and to look into the "heart" of an elderly patient complaining of stomach.

A *diagnosis* therefore is of the greatest importance in the therapeutics of the circulation. The more standardised it is, the better. Cardiac cases

form a first large group owing their origin to rheumatism, especially juvenile rheumatism. Next comprise the various failures traceable to hypertension in all its forms. Acute conditions occur in the course of the specific fevers like pneumonia, influenza, typhoid, etc., and they form a separate class by themselves. The heart in anaemia, nutritional myocarditis, the "beri-beri" heart will bring up the rest. The progressive picture in congenital heart conditions, like septal defects, coarctation of the aorta, patent ductus arteriosus, and the heart in myxœdema and in hyperthyrodism, need not detain us for the present, as their therapy largely falls to the lot of the cardiologist under institutional surroundings and with the uptodate facilities for rœntœnology and electro cardiography.

A compensated and functionally efficient heart has to be distinguished from the failing. These failures may be slight to extreme and the compensation, while apparently existing, may be actually on the brink of sudden and complete dramatic collapse. While it would be unnecessary and injurious to impose any restriction on rest, diet, exercise, tobacco, alcohol, work, pleasure, pregnancy, etc., in cases where this delicate factor of compensation is to all intents "maintained," the greatest care has to be exercised where they have obviously failed or commenced to fail. A heart can fail in this dramatic fashion. "The patient, seized and throttled before he could cry out, sprang up livid to wrestle with death. The desperate conflict made the fell enemy almost visible to us. Now this way, now that, springing up in bed to fight from the edge of it, to sink back in utter exhaustion, but only to rise again panting, with the sweat streaming from him, desperately to renew the battle, the scene was almost as distressing to the byestandars as to the victim." From this picture to the fore-doomed, who neglect warning after warning and ultimately succumb, spreading out their defeat in about two years, there are all kinds and degrees.

Chief signs are dyspnœa with or without exertion, occurring nocturnally or after food, brought on after emotional excitement or quietly, sometimes every evening. Prœcordial .pain with night cough and an occasional blood tinged sputum, with cyanosis, sweating, fine tremors, dryness of the mouth and palpitation are common. Swollen ankles at the end of the day, dull heavy limbs, water-logged skin and flanks, to actual pitting œdema and displaceable swellings are noticed. In actual practice the acute congestive failure subject presents the signs of extreme orthopnee and water logging, anxious look and fear of impending dissolution.

The next step is to distinguish between a left sided or right sided failure of the heart. Often the task is difficult and combined failure occurs. The left is more common but sooner or later the right will supervene. The left sided failure makes itself felt chiefly in the pulmonary field, while in the right sided. congestion in the systemic and portal field is prominent. There is that large failure where the peripheral circulation is at fault. Its consideration demands attention as a variety of causative factors in its production will each need attention, *viz.*, whether it is due to traumatic shock, post-operative collapse, toxæmia, etc.

Coming to the therapeutics, whatever the review of the pathology of the condition may dictate, all schools are agreed that the present day cardiac patients' out-look is more hopeful. Rest in bed from one week to 3 weeks,

should be enjoined and the transition to work gradual. This is where in Indian practice, except for the heavily decompensated hospital class of patient, the medical men find *domiciliary treatment* very difficult to achieve. At least a noon day 2 hours rest should be insisted upon the chronic heart patient. Most better class Indian patients have to win their bread while visibly struck down by a failing heart. Often compulsory retirement from a job might have better salvaged the family fortunes than fool hardy striving to earn a little and honouring all medical and dietetic regimen in the breach. Often emotional life needs equal control. It is the early middle aged with hypertensive failure that faces the bulk of the family responsibility. Often worries over marriageable but undisposed of daughters, official complications in the profession, bring down to an untimely end many a useful career, which would have carried on for years, had an earlier suggestion to give up work been acted upon. Every senior practitioner can remember a couple of tragic cases of this kind and the professional honour is at stake to suggest and insist on no half measures.

Systematic baths, massage by an expert, visit to watering stations such as exist in the vicinity, graduated exercises are all helpful means. Much of the benefit is due to regularity and improved appetite, sleep, excretion, quiet which regularly in itself and by itself is capable of assuring. Scientific massage is still in its infancy in the profession as a powerful aid to therapy. Whereas it is the mainstay of the obese and the opulent and the leisured, and was systematically in vogue with the better class of people a century ago and even now in princely establishments, as an auxilliary to therapy in institutions other than orthopœdic, and even there it is a rarity. Once the crude native talent in this direction is harnessed to a better effort and scientifically allayed, immense good will follow to the cardiac therapist. Especially in disposing of venous stasis and bringing about drainage in lymph-logged and corpulent extremities and easing the right heart, there is no equal to this, when judiciously employed and in early cases.

Coming to drugs, Digitalis in the form of Tincture by mouth or Digonin by the intravenous route will be used in almost every case depending on urgency and severity. No dose less than 15 minims for ordinary and not more than 60 m. for massive therapy per dose will be a useful mean average for digitalisation. Complete digitalisation and quick is a goal, but in attaining it a moderate half way house is the safest. Whether the disease is mitral or aortic, digitalisation with caution will be found life-saving, except in very low pulse cases and grave damage to the heart muscle as in the acute affections. It should be pushed to gastro-intestinal upset. It is even said that MACKENZIE was even sadly satisfied that by its action on the stomach, a proof was obtained that a reliable preparation was being used and not an inert one ! Strophanthin is a competitor to Digonin but in an emergency there is no choice. A mildly acting but useful for its other properties as a hepatic, diuretic, carminative,mildly laxative property is *Punarnavasava,* in its various forms and combinations. When Digitalis by mouth disagrees, this comes as a handy substitute.

Diuretics will have to be used, when the diuretic action of Digitalis has ceased and its maximum amelioration has been secured. The mercurial diuretics, like "Mersalyl," "Salyrgan," "Drurin" have all their settled theraputic value. Often when they are reported to have been followed by disastrous results, it is the timing and the advanced stage of renal failure

that are responsible and not their place in the scheme of therapy. Often the older physicians swore by the "Blue Pill" at night and the saline purgatives or Jalap Co with additional ½ drachm of double tartrate of Potash to enhance its action the next morning and if mercurial medication intravenously has come to stay as a mainstay in cardiac diuresis, it is because mercury in some mysterious way acts as a magic, specific for the cardiac dropsy. Diuretic is best administered first thing in the morning after concentrating Ammonium Chloride in 30 gr. doses in capsules three times a day previously to get the best results.

Venesection for acute right sided failure in subjects of hypertension, with threatening pulmonary œdema has been life saving and is being revived. Often tiny nick, with a small lancet or bistoury at the tingesceril vein at the bend of the elbow, is more efficacious than the closed method with a large bore needle. The tiny stab closes immediately with firm pressure, bandage and elevation. A quick escape of 10 ozs. of blood at a minimum is followed by welcome relief, restful sleep and almost equivalent to averted death in carefully selected early cases of sudden breakdown. The height to which the tingid veins above the manubrium, stand up on the neck is an indication direct to the recourse to venesection. The point to emphasize is the intrepedity and resourcefulness with which this should be done and the time factor as in a successful tracheotomy. Another returning ancient therapeutic procedure is the multiple puncture and Southey's tubes for the swollen extremites of the cardiac patient. With increasing recourse to this it is often surprising what great quantities can be drained by the leg and foot into the receptacle and how seldom there is any suppurative complication.

To briefly mention other trusted friends in cardiac therapeutics the use of Morphine and its derivatives is now shorn of all its terrors, use of fruit—flowered Glucose solutions by mouth and concentrated solutions by intravenous methods, and cardiac stimulants like Coramine and Anacardeon, have all come to stay.

By far the most encouraging thing is most of the therapy of the cardiac patient can now-a-days be checked up by eletrocardiagraphy and maintenance treatment can be carried out by tablets already initiated by injections *e.g.*, in Cardiophyllin, Euphyllin, etc.

In conclusion it is a worthy endeavour to prevent cardiac diseases by preventing rheumatism. From care of school children, elimination of the septic tonsil, looking after the nutrition and re-educational clinics, should proceed the freedom from disability on this account. Sudden deaths and due inefficiency on a national scale and the alarming increase of hypertensive disorders can only be then avoided.

Agranulocytosis

BY

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AGRANULOCYTOSIS,' even though a definite disease, is very rarely seen in this country and a review of Journals proves its rarity. Recently a case in a patient of kala-azar has been reported in the *I. M. G.*, Vol. 78, No. 1. The disease was recorded in several patients of kala-azar receiving antimony in China. I had the opportunity to come across two cases which I take to be cases of agranulocytosis, and I am giving these hereunder.

CASE I.—Guman Singh, 50 yrs., H. M., was admitted into the hospital on 13—6—'42 with fever—15 days, extreme prostration and dysphagia—2 days. He came for treatment for the dysphagia. Exam :—toxic appearance, sunken and apathetic, talked with difficulty, Temp.—102°F. P/R 116/24. Spleen—two fingers below costal margin. Liver—not palpable. Heart and Lungs :—N. P. Rash—none seen. Abdomen—soft and not tender. Tongue—coated and dry. Tonsils :—Small greyish black areas with dirty-looking necrotic matter here and there encroaching on the fauces. Pharynx :—Small ulcerations and irregular small vesicles with necrotic matter in their centre :

Blood Exam :—

Hb.	... 65%	Lymphocytes	... 80%
R. B. C.	... 3·6 Millions.	Turk cells	... 10%
W. B. C.	... 1248.	M. P. :—None seen.	
Polymorphs	... 2%	A. T. :—Ve.	
Monocytes	... 8%	C. T. :—Ve.	

M. P.—none seen.

Inspite of treatment with Nuclein, Liver Extract and Glucose the condition was worsening every day. On 15—6—'42 a black necrotic mass was noticed in the mandibular gum opposite the right premolars extending rapidly in size and involving the adjacent part of cheek, margins brawny but no actual pus. Pyrexia was of remittent type, dysphagia was extreme, toxæmia more marked and delirious.

Blood Exam. on 16—6—'42.

Hb.—65%	W. B. C.—936
R. B. C.—3·5 Millions.	Polymorphs—Nil.

17-6-'42. Comatose, dyspnœic, could not swallow anything. Glucose 50% 50 c.c. was given I. V. In the forenoon condition got alarming. Pulse 160 ?, panting for breath, unconscious, afterwards the case was hopeless. He expired at 5 p. m. on that day.

CASE II.—Kishan Singh, 35 yrs., H. M. (resident of Nepal), was admitted on 5—5—'43. He was suffering from fever for the last 6 months, irregular, he said, at the onset but for the last two months there was no remission. Chill was noticed every evening but rigors only occasionally. He complained also of weakness for the last two months. He had anorexia, burning sensation all over the body, and attacks of diarrhœa now and then but not troublesome.

EXAM :—He looked much depressed and worried, emaciated and walked as if dragging himself. Hairs were fallen and lustreless, no rash or pigmentation was seen anywhere, no history of bleeding from any orifices of the body.

TEMP :—102·6. P/R—116/22. Conj.—icteroid, pale ; no pallor ; spleen —3 fingers below costal margin ; Liver—just palpable ; Abdomen—sunken, no tenderness anywhere ; Heart and Lungs—N. P. ; Tonsils—not enlarged ; Gums—spongy ; Tongue furred and fissured.

Blood Exam. on 5—5—'43.

Hb.	... 55%	Lymphocytes	... 60%
R. B. C.	... 3·2 mil.	Abnormal cells	... Nil.
W. B. C.	... 3744.	M. P.—B. T. ring a few.	
Poly	... 30%	A. T. :—Ve.	
Monocytes	... 9%	C. T. :—Ve.	
Eosinophils	... 1%		

Treatment was started with Alkalies and Quinine by mouth after a preliminary Saline purge, but little response was noted. So three consecutive intramuscular injections of Quin.-bihydrochlor were given. The temperature came down to normal level on 12-5'-43, but the general condition was not much improved. Then he was put on the following :

℞ Quin Sulph	... gr. v	
Cinchona Feb	... gr. ii	
Acid N. M. dil	... ♏ xv	II Inj. Liver extract 2 c.c. I.M.
Liq. ars hydrochlor	... ♏ ii	III Radio-hæmogen—one tea-spoonful after meals.
Ferri Sulph Excic.	... gr. iii	
Tr. Nux Vom	... ♏ x	
Aqua Chlorf.	... ad ℥ i	

Mistura, T.I.D. P.C.

Easily assimilable diet rich in vitamins with 24 oz. of milk was also ordered. With this course he was improving, but cinchonism was now prominent and in spite of it on 16-5-'43 the temperature shot up to 102° F.

Blood Examination on 16-5-'43 :

Hb.	... 55%	M. P. None seen.	
R. B. C.	... 3·2 mil.	II Urine—N.P.	
W. B. C.	... 2496	III Stool—N. P.	
Polymorphs	... 22%		

Even though the smear did not show parasites, Quinine was continued to check the pyrexia ; in addition Soamin gr. i. was added perenterally, and T.C.C.O. for the falling W.B.C. count. Condition of the patient was same, weakness continued as it was, pulse was weaker in tension and volume in addition he lost more flesh and weight and he looked a little toxæmic; cinchonism marked. Noting the condition another blood examination was made on 20-5-'43.

Hb.	... 60%	Polymorphs	... 20%
R. B. C.	... 3·4 mil	Abnormal cells	... Nil
W. B. C.	... 2184	M. P.—None seen.	

Next the following treatment was adopted to fight the disease. Quinine was stopped for cinchonism and failure to stop the pyrexia.

(1) Atebrin—·1 grm. T. I. D. for 5 days.
(2) Abidol—c (P. D.) 1 tab T. I. D.
(3) Injection—(*a*) Liver extract—2 c.c. daily.
(*b*) Neuclein solution 5% 2 c.c.
(*c*) Glucose—25% 25 c.c. B. D.

Atebrin also had no effect on the course of the disease. The general condition was much worse, he got bed-ridden and looked toxic. On 25-5-'43 he complained of dysphagia in addition and a tender swelling appeared on the gum, breath was offensive. Spleen 2 fingers below costal margin, liver just palpable. Heart rate—140 per minute, 1st sound weak. Tonsils and pharynx showed ulcerations and dirty grayish areas.

Blood examination on 25-5-'43 :—

Hb.	... 60%	Monocytes	... 10%
R. B. C.	... 3·4 mill.	Lymphocytes	... 72%
W. B. C.	... 1560	Turk cells	... 16%
Polymorph	... 2%	M. P.—None seen.	

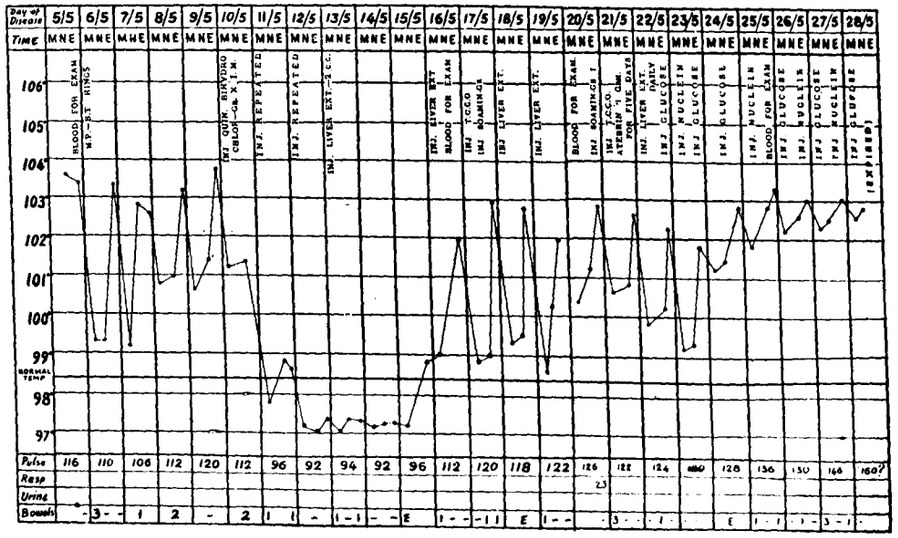
26-5-'43. Condition still worse, a pathetic appearance, toxæmia—intense, temperature—as chart, pulse—feeble and high, dysphagia—more acute, he could swallow only a few tea-spoonfuls of milk. The gum showed a black fungating mass with brawny margins rapidly increasing in size, there was no pus but only dirty sloughs. Liver Extract, Nuclein and Glucose were given daily along with stimulants. Next day he was lying semiconscious and dyspnœic which passed on to coma with feeble rapid pulse (166 ?), gasping which ended at 7 p.m. on 28-5-'43.

The above cases can be reasonably taken as acute agranulocytosis ending fatally. Both of them showed identical symptoms and signs towards the end *e.g.*, a febrile course, dysphagia, enlarged spleen and necrotic lesions in the mouth and gum. Blood picture was also characteristic in both showing extreme leucopenia and absence of neutrophils. Note also the gradual fall of leucocyte count in Case II. In Case II aplastic anæmia was excluded by (1) rising hæmoglobin and R. B. C. count which was unaltered till the end ; (2) absence of pallor ; (3) absence of hæmorrhages ; and (4) blood picture. It is reasonable that prolonged anæmia and protracted illness may have caused complete aplasia of the bone-marrow and all the more possible because these cases go untreated for absence of facilities of scientific medicine. They are mostly agriculturists, merged in poverty and live exclusively on cereals and potato and a little greens. They already suffer from sub-clinical deficiency diseases notably in vitamins. Any prolonged illness or any virulent infection leads to sad result owing to already run down condition, lack of scientific treatment, proper diet, adequate rest and nursing. (He was taking chapaties morning and evening in spite of fever—chapaties mostly of "mandua," sometimes of wheat). This prolonged malnutrition and disease would lead to various morbid states it is well to keep in mind. Aplasia of the bone marrow is one of the states that is likely to develop. "It has been suggested that aplastic anæmia may develop as a result of long-continued anæmia and consequent exhaustion of bone marrow. There are no facts to support this suggestion"—PRICE. Also aplastic anæmia is mostly primary but secondarily may occur but only rarely.

Etiology of the condition is still obscure, exact cause is unknown, administration of certain drugs like Amidopyrine is said to be a potent cause, but in most cases no such noxious agent is seen in actual practice. Poisonous potentialities of certain drugs, however, arise in the mind of an observer and in addition some unknown factor usually superimposed on an infection as lieshmaniasis where leucopœsis is already below par due to blockage phenomenon of drugs Sulphapyridine and Sulphathiazole are known to produce granulocytopenia. Evaluating the toxity of Sulphanilamide and Sulphapyridine Brown et Al in their investigation found that Sulphapyridine caused granulocytopenia in 3 out of 100 cases receiving the drug. KENEDY and FINLAND reported a case of agranulocytosis ending fatally during administration of Sulphathiazole in a case of bacterial endocarditis.

The bone-marrow examination could not be done on account of lack of facilities in this out-of-way-place, corner of the Himalayas, nor could the the post-mortem examination be done. Certainly the result of these examinations would throw much light on the actual state of affairs in the marrow and the condition could be studied in fuller detail. So I had to remain content with clinical and hæmatological study only.

These two cases had not had any of the drugs because they had no treatment at all, especially Case I. This one can be accepted as a case of primary agranulocytosis where no noxious agent can be traced nor it was a complication or sequelæ of some other infection. Nor any drug may have caused it as he received little treatment here as he was brought too late. Case No. II was in the hospital for 23 days, and he had several drugs. Before admission he was treated by a "Vaidraj" of his locality



with indigenous drugs, nature of which is quite unfamiliar to the party and to me. It was definite that he did not take Amidopyrine or Sulpha group of drugs. It is really interesting to study the clinical progress of the case and his blood picture. The blood picture on admission shows parasites and leucopenia as we find in malaria, response to Quinine per-enterally was also notable. On 16—5—43 he had rise of temperature again, blood examination showed a further decrease but it would culminate in serious diminution was not thought of, parasites were not seen as he had enough Quinine. For this he got T. C. C. O. injection to prevent a further fall and also liver extract injection for anæmia and general condition. But the effect of these drugs was far from satisfactory, pyrexia continued (*vide chart*) another blood count was done on 20—5—43 and a further decrease was noted and this was alarming judging from general condition of the patient which was steadily deteriorating, the treatment was entirely changed in favour of Atebrin for the fever and Nuclein and liver extract daily for the rest. During the administration of Atebrin other symptoms *e.g*, dysphagia and necrotic lesion on the gum appeared

making the picture finished clinically. Blood on 25-5-43 showed extreme granulocytopenia corroborating the diagnosis. Also, note the hæmoglobin content and R.B.C. count were almost unaltered after the initial rise of 5% from 55% to 60%. This is a case of agranulocytosis devoloping in a case of malaria; the drugs he had are shown in the chart, how far they have contributed to its incidence, it is difficult to settle. 'Whether it did arise as a complication of malaria or it was the result of the drugs used to combat malarial infection or it was a disease superimposed on malaria of unknown agent, I leave it to others.

References:

1. Brown et Al—Journ. of A. M. A. Vol 114, 17.
2. Das-Gupta C.R. and Sen Gupta P.C.—I. M. G. 78, 1.
3. Kenedy P.C. and Finland M.—Journ. of A. M. A. 116, 4.
4. Price F. W.—A Text-Book of the Practice of Medicine.

Arterio-Sclerosis: Its Causes and Effects

BY

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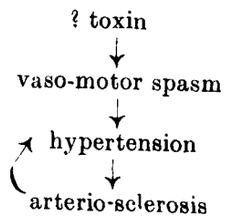
IT is a common experience for medical men to find a thickening of peripheral arteries, usually the radial and the brachial, in hypertensive subjects as well as in elderly individuals with or without hypertension; and much confusion exists as to the value of such palpatory findings and their relation to actual structural alterations in the blood-vessels. Thickening and hardening of an artery is literally known as "arterio-sclerosis," a term first introduced by LOBSTEIN of Strassbourg in 1938, and a term which has created much dissension regarding its pathological significance. Without going into the details about the controversial points surrounding this generally accepted terminology we can agree with ROY (1943) in using the term as signifying a thickening and hardening of an artery due to no obvious inflammatory process, thus excluding acute or chronic arteries from its orbit. Stripped of its terminological burden "arterio-sclerosis" includes: (1) Diffuse hyperplastic sclerosis or myo-hypertrophy, an essential change in hypertension, idiopathic or nephritic; (2) athero-sclerosis, a term introduced by MARCHAND (1904) to give a more scientific bearing to the atheromatous process; and (3) Monckerberg's sclerosis, the least common of the three and better known in its relation to diabetes mellitus.

The problem of exact pathogenesis of arterio-sclerosis is far from being a settled affair and inspite of the huge amount of work done until now, and the host of materials released in the literature as incriminating agents we are perhaps still as wise as the pioneers like GALEN (A.D. 103-193), because we have hardly advanced much in our way to prevention or cure of the disease, which alone would prove real achievements of the modern medical science. Thus, for example, we do not know yet the causative factor or factors of essential hypertension, though the pathological changes, including the arterio-sclerotic process are so constant. Diet, habits, intoxications, mental and physical strains, endocrine influences and sundry other factors have been blamed, but they have only increased confusion. Even the revival of the "renin" theory by GOLDBLATT (1934), HOUSSAY and BRAUN-MENENDEZ (1942) and others has not simplified matters as was fondly expected by many. We are still to think in terms of some unknown toxic factor acting by producing an angio-spasm, or rather a

vaso-motor spasm, which results in a state of hypertension, the latter being directly responsible for the arterio-sclerotic changes in the long run. The cycle can be schematically represented as follows:—



The arterial changes further increase the arterial blood-pressure and thus a vicious circle is started.

Regarding the pathogenesis of athero-sclerosis similar diversity of opinions is present, without any material benefit from the prophylactic or therapeutic point of view. There are still the infective, the degenerative and the metobolic theories sponsored by VIRCHOW (1856), MARCHAND (1904) and ASCHOFF (1910) respectively with their supporters. Observations by feeding cholesterol to rabbits with or without other accessory measures, have increased our store of knowledge, indeed, but whether such factors are actually applicable to human subjects is yet to be decided and whether the same factors would apply to all races and in all environments is doubtful. MUKERJEE and TRIBEDI (1943) have already briefly hinted at the difficulty in accepting the western views of hyper-cholesterolæmia as the essential pre-disposing factor in the causation of atheromatous changes specially in our country.

Monkeberg's sclerosis, usually a peripheral condition, consisting of medical calcification in the vessel-wall, occasionally precedes surgical complications like gangrene in diabetic subjects; but its mode of production is not known. Strangely it simulates greatly the medical calcification produced experimentally in rabbits by feeding activated ergosterol or viosterol.

To enumerate the effects of arterio-sclerosis the first thing that we have to remember is that the condition may not be generalised through the arterial tree and accordingly the clinical manifestations may be very much varied. Thus according to the site of affection we may get cerebral arterial-sclerosis with a multitude of symptoms and signs starting from giddiness, headache, insomnia, fainting fits etc., to major cerebral vascular accidents like cerebral thrombosis and hæmorrhage. In hypertensive subjects one may also come across what is known as "hypertensive encephalopathy" which is more often due to a cerebral arterial spasm. As a part of cerebral arterio-sclerosis retinal arterial changes are very frequent in the shape of "silver-wiring" of the central artery to the retina, and associated retinal changes, like cotton-wool patches, and even hæmorrhages, may complete the picture of "hypertensive retinopathy."

Similarly coronary arterial sclerosis may be the chief event with the resultant well-known coronary syndrome or the popular "heart-attacks." "Angina pectoris and coronary thrombosis are becoming more common incidents in the present civilised world and increasing numbers are being observed among the diabetics who die rarely now-a-days of acidosis. Coronary sclerosis may incipiently lead to cardiac failure without any acute evidence of coronary insufficiency.

Nephro-sclerosis, an inevitable after-effect of essential hypertension, accounts for the polyuria in hypertensive subjects, and the maglignant type is characterised by the evidence of renal failure, as shown by the retention of non-proteinous nitrogenous products in the blood.

Peripheral arterio-sclerosis may not be associated with any local symptoms except in the lower extremities where intermittent claudication is sometimes a distressing symptom.

In certain cases the arterio-sclerotic process may be universal through out the arterial tree and such cases would clinically present a composite picture.

Incidence of arterio-sclerosis is fairly common in the province of Bengal and possibly it is the same in other provinces too. Compared with the incidence the amount of original work of investigation done in our country is not up to the same standard as in other countries, and we hope to get more information about all plausible factors in this connection from our own workers.

References:

1. Aschoff, L. (1910)—Beitr. z. Path. Anat. u. z. allg. Path., 47 : 1.
2. Goldblatt, H. et al. (1934)—J. Exper. Med., 59, 347.
3. Houssay, B.A., and Braun-Menendez, E. (1942)—Brit. Med. Jour. 8, 179.
4. Mukerjee, A. B. and Tribedi, B.P. (1943)—Jour. Ind. Med. Assoc. 10. 285.
5. Marchand, F. (1904)—Verhandl. d. k. f. inn. Med. 21 : 23.
6. Roy, H.K.(1943)—Cal. Med.Jour. 8, 289.
7. Virchow, R. (1856)—Wein med. Wchns. chr., 5, 809.

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Surgical Possibilities in Coronary Inefficiency

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THE coronary vessels of the heart are subject to the same diseases as the other blood vessels with far greater devastating effect on the lives of mankind. Atherosclerosis is the commonest condition met with. Changes in the coronary vessels are found in diabetes and rheumatic disease. In tuberculosis, the arteries may be obstructed either by inflammatory tissue or by thrombosis. Syphilis seems to eschew the coronary vessels as emphasised by HERXHEIMER, SAPHIR and TURNBULL. The most frequent lesion is a constriction of the intramural part of the arteries by a fibrosis of the aortic wall. A gross atheromatous condition of the aorta may encroach and occlude the orifices, or even occlusion for 10 to 12 m.m. along the vessels may be found without any change at the orifices. Formation of miliary gummata, calcification of thrombosis of a vessel sometimes occurs. Buerger's disease or thromboangeitis obliterans in these vessels has been noted by BUERGER, PERLA, SAMUELS and FEINBERG. POWELL and PRITCHARD have showed that more than half the cases of poliarteritis nodosa involve the coronary arteries. Involvement of the vessels by metastatic cardiac tumours is rather rare. Embolism is an important cause of blockage of the artery.

Anatomy of the Coronary Vessels.—It is but natural to suppose that a muscle which is unceasingly active from its birth to its death will have provision for a large blood supply and be sensitive for deficiencies thereof.

The heart is supplied by the right and left coronary arteries belonging to the visceral systematic circulation. The right arises from the anterior sinus of Valsalva and passes between the pulmonary trunk and the right auricle and then runs in the coronary sulcus round the margo acutus on to the back of the heart as far as the posterior inter-ventricular groove where it divides into two unequal branches. The smaller continues its course to the left in the coronary sulcus and then ends by dividing into two or three branches, rami ventricularis sinistri, which descend on the posterior surface of the left ventricle. The larger branch descends in the posterior intraventricular grove to the apex of the heart where it anastomoses with the anterior descending branch of the left coronary artery. In addition to the unnamed small twigs given off in its course, the artery gives; (1) an infundibular branch which ramifies over the conus arteriosus anastomosing with a corresponding branch of the left coronary artery; (2) lateral or marginal branch which follows the acute margin of the heart; (3) two main branches which descend on the anterior surface of the right ventricle giving off a number of more or less horizontal twigs; (4) three or four small branches supplying the right atrium; and (5) several delicate twigs supplying the roots of the aorta and the pulmonary trunk.

Left coronary artery, generally larger than the right, arises from the left aortic sinus of Valsalva. After a short forward course between the pulmonary trunk and the left auricle it divides into a larger anterior descending and a smaller circumflex branch. The former descends in the anterior longitudinal sulcus to the lower margin of the heart where its terminal branches wind round to anastomose with the terminal branches of the posterior descending branch of the right coronary artery. In its course this branch gives off a series of rami collaterales and some branches which pass to the interventricular septum. Since this branch is found to be the seat of extensive sclerosis or embolism or thrombosis, it is sometimes called "the artery of sudden death." The smaller circumflex branch runs along the coronary sulcus as far as the posterior longitudinal sulcus where it anastomoses with the branches of the right artery. At its commencement the left coronary artery supplies branches to the root of the aorta and the pulmonary trunk. These branches belong to the group of vessels called the *arteriae telae adiposae cordis* which form a rich network in the subepicardial fat.

DISTRIBUTION.—1. *Atria*:—The atrial branches of the coronary arteries are not constant in their arrangement. Six or seven stems are found ramifying over both surfaces of the atria freely anastomosing with one another. But any one or any combination of two or more may become larger than others and form the source of arterial blood supply. According to CAMPBELL, in the most common type four stems will be contributed by the right coronary artery and the other two by the left.

2. *Ventricles*:—The right coronary artery supplies the whole of the right ventricle except the left third of the anterior wall posterior third of the interventricular septum and the posterior wall of the left ventricle as far as the attachment of the posterior papillary muscles in whose supply it shares. The left coronary artery supplies the remainder of the left ventricle, the anterior part of the septum, left third of the anterior way of the right ventricle and shares in the supply of the anterior papillarll muscle of the right ventricle.

3. *Atrio-ventricular bundle*:—The greater part of the bundle is supplied by the following branches from the right coronary artery; (*a*) ramus septi fibrosi which supplies the node and the main stem as far as its division. This branch reaches the upper edge of the ventricular septum after piercing the back part of the trigonum fibrosum dextrum; ramus septi ventriculorum superior which ramifies in the posterior part of the septum and supplies the posterior branch of the left limb. The anterior branch is supplied by the left coronary artery. The right limb is supplied by branches from both the arteries.

Age changes:—The following changes have been observed in the coronary vessels as age advances: (1) Progressively increasing tortuosity commencing in the third decade of life; (2) progressive relative anæmia of the right side commencing by about the end of the second decade due to increased demand of blood supply by the left ventricle; (3) increase in amount and width of the anastomoses of the branches of the coronary arteries; and (4) increase in development of rami telae adiposae which establish connections with myocardial vessels.

It is proposed only to discuss the rationale of the various surgical measures that are adopted in treating the coronary inefficiency. The essential effect of the various diseases of the coronary vessels will be diminished blood flow leading to cardiac anoxæmia with all its sequelæ. It is possible that one or more of the branches may be either partly or completely occluded. The gravity of the case depends on the branch that is occluded and on the suddenness of the obstruction. The methods of treatment should aim at either (1) increasing the blood flow to the heart by opening up normal channels of anastomosis or by augmenting the blood flow from artificially established collateral circulation or (2) reducing the general metabolic rate of the body to a level the diseased arteries can cope with by thyroidectomy; (3) in addition to these there are some palliative measures attempted to relieve pain.

SPALTEHOLZ has shown that there is a rich anastomosis between the right and left coronary arteries and between the branches of the same artery. Old saying that the branches of the coronary vessels are end arteries is an exploded myth. Secondly, there is an anastomosis between the vessels of the coronary tree and the vasa vasorum of the aorta and the pulmoray artery. Thirdly, there is the reverse Thebesian circulation. Fourthly, there are anastomoses between the coronary arteries and the vessels of the adjacent parts, *viz.*, the pericardial, diaphragmatic and bronchial arteries. A detailed knowledge of the coronary vessels and their anastomoses has been the outcome of the observation made by a number of workers using one or more of the following methods: (1) Dissection of normal and pathological specimens: (2) injection of the vessels with Gelatine, Celloidin, Mercury, salts of heavy metals or pigments; (3) observations of cases with autopsy; and (4) experimental methods where the extent of infarction is noted after the coronary arteries and their branches are ligated. Study of injected specimens is facilitated by dissection, clearing, preparation of casts, serial sectioning and reconstruction and by sterioscopic roentgenography.

Sternberg's classical case of "pericarditis episternocardia" case of fugiami, cases reported by KOCH and KONG, histories cited by MONCKEBERG and report of Sir CLIFFORD ALLBUTT'S doctor patient, who returned to active life after a severe attack of angina complicated by pericarditis,

clearly show that given time, the heart is able to supplement its blood supply from the parieties by forming adhesions between the infarct and parietal pericardium. Vascularity of pericardial adhesions was demonstrated. HOCHÆIN in his monograph (1937) states that "pericarditis is not a complication of coronary thrombosis but a natural attempt at healing its presence is to be welcomed rather than deplored." The remarkable extent to which collateral circulation can help is shown by Thorel's case, where the patient died of carcinoma. He had old adhesive pericarditis side by side with a complete and long-standing obliteration of the main stems of both left and right coronary arteries. There was no history of cardiac distress during life.

The above case reports have stimulated workers on the field to experiment on the animals and to try the same on the human beings at a later stage. Dogs, cats and monkeys have been used as experimental animals. Vessels have been obstructed either by ligation (SMITH, LEWIS, OTTO) or by use of metal clips (BEAK). Most of the individual vessels have been ligated—even those to the interventricular septum, and the effects studied. Various operations to augment the blood supply to the heart have been tried after occluding the vessels. It was shown experimentally that both the coronary arteries can be more or less completely occluded, if it is done gradually and that omental graft attached to the heart is compatible with highest degree of exertion. Adhesions between heart and pectoral muscle, mediastinal tissues and parietal pericardium and the lung (LEZIUS) have been successfully produced. It would seem from the experimental aspect that the production of a collateral circulation is not only practicable but is a rational and desirable method of treatment of coronary occlusion. The possibility of improving the circulation of the heart by obstructing the venous return was suggested by GROSS and his co-workers: The following methods of increasing the blood flow to the heart have been tried in man :

1. Cardio-omentopexy.
2. Pedicle graft of pectoralis major.
3. Transpleural pericardiotomy.
4. Extrapleural pericardiotomy.
5. Cardio-pneumonopexy.

1. *Cardio-omentopexy*:—The pericardium is exposed by transpleural route by opening up the fifth left intercostal space. Phrenic nerve is crushed. The pericardium is opened, a pedicle graft of greater omentum is brought through an opening made in the tendinous part of the diaphragm and is attached th the heart after scraping the epicardium.

This method has the following advantages:—(1) It brings a new blood supply from the abdominal aorta. (2) It supplements the normal collaterals in the mediastinum which will be brought into contact with the omental vessels near the inferior sterno-pericardiac ligament. (3) Omentum is the only structure in the body having the specific property of vascularisation. It has been pointed out by RUTHERFORD MORISON that the only type of fibroids that grow to enormous size are the retroperitoneal type as the omentum can nourish them with vessels which have been shown to grow to the size of the brachials. (4) "Bridge action" between the branches of supply of the right and those of the left coronary artery. (5) Exact placing of the graft in relation to any localised area of ischæmia is not essential, as its vessels anastomose with the branches of the coronary tree and are distributed to all parts of the heart. (6) The lung often adheres to the graft reinforcing the vascular adhesions.

Some surgeons advocate introduction of the Aleuronat paste inside the pericardial cavity to stimulate intrapericardial adhesions. It may be suggested that the pericardial cavity can be approached by the extrapleural route eliminating the risks of opening up the pleural cavity.

2. *Pedicle graft of Pectoralis major*:—This is the classical operation performed by CLAUDE S. BECK in a patient who was having anginal pain for a period of nine years. A pedicle graft of left pectoralis major was sutured to the inner surface of parietal pericardium. This and the epicardium were roughed with a burr. The medial edge of the pectoralis major was attached to the outer surface of the parietal pericardium. Three months after the operation, the patient resumed work as gardener.

3. *Transpleural Pericardiotomy*:—Pericardium is opened by left transpleural exposure, Aleuronat paste inserted and the pericardium closed.

4. *Extrapleural Pericardiotomy*:—This method has the special advantage of not opening up the pleural sac. Seventh costal cartillage and part of xiphoid are resected in Larrey's angle, pericardium opened and the sac treated with Aleuronat paste.

5. *Cardio-pneumonopexy*:—LEZIUS in 1937 has shown that the lung can form extensive vascular adhesions with the heart when the fibrous pericardium is opened. The heart is approached by the transpleural route on the left side.

II. The relationship between hyperthyroidism and angina was noted by PARRY. Improvement of cardiac condition after removal of thyroid gland either in part or in whole was reported by KOCHER, HAMILTON, and LAHEY and HAMILTON. In 1927 LEVINE observed considerable improvement after removal of the gland. BLUMGART LEVIN and BERLIN in 1933 proposed complete removal in uncontrolled cases. Cases of angina pectoris were treated in this way by CUTLER and SCHNITKER. Further studies on myxœdematous patients by BLUMGART helped him in advocating this therapy. The rationale of this therapeutic measure lies in the fact that reduction in metabolic rate might indirectly compensate for the inadequate supply of coronary circulation. Beneficial effects were also partly due to interference with the sympathetic nerves in the neck during the operation (COHEN and HERRMAN, WEINSTEIN and HOFT) as shown by the fact that pain on the side of operation disappeared when it was bilateral. The following are definite contraindications for thyroidectomy: (1) inability to stabilise a congestive failure with rest; (2) status anginosus; (3) cases with low basal metabolic rate; (4) definite coronary occlusion; (5) hypertension; and (6) respiratory or renal disorder.

III. **Palliative Measures.**—These are measures adopted for relief of pain either by excision or by injection therapy of the sympathetic. The heart is supplied by the cardiac plexus situated at the base of the heart. The plexus is divided into a superficial and a deep part, though both are inter-connected. The superficial cardiac plexus lies in front of the right pulmonary artery beneath the arch of the aorta. It is formed by two nerves—one a branch of the sympathetic, the superior cardiac branch, and the other a branch of the left vagus, the lower inferior cervical cardiac branch. A small ganglion, the ganglion of Wrisberg, is found in this plexus. The deep cardiac plexus is situated behind the aortic arch, in

front of the bifurcation of the trachea. It is formed by all the other cardiac nerves derived from the cervical ganglia of the sympathetic and the cardiac branch of the vagus and recurrent laryngeal nerves which do not join the superficial plexus.

Our knowledge of the nature of the sympathetic supply to the heart even up to the present remain an open field. Histological investigations of sympathetic nerves by RANSON, BILLINGSLEY and STOHR showed that they contained fibres similar to those of the somatic nerves. They are distributed by the cervical cardiac nerves to the cervical ganglia and thence down to the thoracic chain. In addition to these, fibres passing directly across the mediastinum to the thoracic ganglia have been demonstrated (BRAUECKER, IONESCO and ENASCHESCO, KUNTZ and MOORHOUSE). LERICHE is of opinion that there are also sensory sympathetic fibres which are part of a reflex arc—the stellate ganglion being the centre of control. The motor fibres leave the central nervous system through the motor roots of the upper five or six thoracic nerves (LANGLEY) and pass through the white rami communicantes to the corresponding sympathetic ganglia. The post ganglionic fibres run in the cervical cardiac nerves as well as in the thoracic branches. According to ANREP, SEGALL, KUNTZ and others vasal fibres carry vasoconstrictor and sympathetic fibres vasodillator impulses, while COX, ROBERTSON, LERICHE and FONTAINE are of the quite opposite view. RANSON and BILLINGSLEY regard the superior cervical nerve as being motor whereas HEINBECKER considers that it contains some sensory fibres. According to RANSON the afferent path for the heart lies in the vagus and the sympathetic, the vagal being afferent for cardiac reflexes and the sympathetic for the path for pain.

On account of the imperfect state of knowledge it is of no wonder that, previously, so many types of operations on the sympathetic were in vogue. Sympathectomy was first suggested in 1899 by FRANCOIS FRANK, though it was actually performed only in 1916 by JONESCO, where he removed either on one side or both the sympathetic chain including the stellate ganglion. Other modifications such as removal of the first ganglion (BACON, COFFEY), second by HALSTEAD and CHRISTOPHER and third or combinations of first and third, or second and third, removal of the stellate ganglion either with cervical chain (DIEZ JONESCO, KAPPERS), or with lower ganglia only (TUFFER), removal of the 'depressor' nerve, or the nerve of Cyon, and sectioning of posterior nerve roots especially the second thoracic (DANIELOPOLU and HRISTIDE) were also practised. In view of the uncertainty of motor distribution, it is but desirable to destroy as little nervous tissue as will be compatible with relief of symptoms. HEAD and MACKENZIE have shown that pain is referred to the area supplied by the upper four dorsal nerves. So excision of only the upper four thoracic ganglia is feasible, in so far as it relieves the pain.

Paravertebral Injection :—Just as in other parts of the body, injection treatment has replaced the operative treatment owing to the greater ease with which it is performed and lesser risk involved. As early as 1922 LAEWEN performed these injections. Local anæsthetics of the novocaine type were employed. In 1926 SWETLOW used alcohol, which later became very popular. Recently Procaine has been employed by PARAF and DREYFUS LE FOYER.

The patient lies on the right, as for spinal puncture. Intracuticular wheals are made two fingers' breadth lateral to the seventh cervical to

fourth dorsal spine corresponding to the first to fifth ribs. Needles of 8 to 10 c.m. in length are introduced first perpendicularly to a depth of 3 c.m., then caudally passing below the respective transverse process and the neck of the rib a further distance of 3 c.m. at an angle of 20 degrees towards the middle line till it strikes the side of the body of the vertebra. The needle is slightly withdrawn and aspiration attempted. If no blood or fluid is obtained, 2 c.c. of 2 per cent. Novocaine or Procaine is injected. If Horner's syndrome with anæsthesia in the axilla developes in about 15 minutes a further 3 c.c. of local anæsthetic is injected following which 4 c.c. of 95 per cent. Alcohol is introduced (SMITHWICK). WHITE uses 80 per cent. Alcohol. Results of this procedure are reported to be fairly satisfactory for relief of pain. Care should, however, be taken not to injure either the intercostal nerves or the pleura or the lung.

Summary.—A short account of the various methods of surgical treatment of cardiac ischæmia has been given with a discussion of their rationale and relative merits.

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Bibliography :

1. Beck, Claude, S.—The Development of a New Blood Supply to the Heart by Operation, *Annals of Surgery*, Vol. 102, 1935.
2. Davies, Daniel T. Mansell, H. E., and O'Shaugnessy Lawrence—Surgical Treatment of Angina Pectoris and Allied Conditions, Lancet, Vol. I, 1938.
3. Fulton, Frank T.—Coronary Artery Disease, A Historical Sketch. Annals of *Internal Medicine*, Vol. XI, 1937-1938.
4. Gask and Ross.—Surgery of the Sympathetic Nervous System.
5. Gross, Louis.—The Blood Supply to the Heart, 1921.
6. King. E. S. J.—Surgery of the Heart, 1941.
7. O'Shaugnessy, Lawrence — Surgical Treatment of Cardiac Ischæmia, Lancet, Vol. I, 1937.
8. Parsons-Smith, Basil, Treatment of Angina Pectoris, Lancet, *Vol. II, 1936.*
9. Quain's *Anatomy*, Vol. IV, Part III, The Heart, 1929.
10. Ranson, Stephen Walter—The *Anatomy of the Nervous System*, 1937.

Syphilitic Aortitis

BY

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IT is known to the clinicians that the blood vessels and the heart are frequently involved in syphilitic infection from the very birth of the medical science. That the blood vascular system is most commonly affected in syphilitic infection of the system has been definitely established by pathologists. MANOHAR (1935) reported from a detailed examination of 882 post-mortem cases at Bombay that the evidence of syphilis was found in 21·5 p.c. of cases. RUNEBURGH has found the involvement of heart and vascular system in 35 cases out of 81 fatal syphilitics. COCHEMS and KEMP (1937) from a study of 1,000 patients of syphilis found that the incidence of aortic involvement in the entire group was 12·7 per cent. and found the incidence of syphilitic aortic disease was slightly less in females (10·8 p.c.) than in males (13·4 p.c.) Syphilis of the aorta was found only in 21·5 p.c. postmortem cases by MANOHAR (1935). The frequency of syphilitic aortic disease, and particularly its more serious forms, increased equally with advanced age in both males and females. Among 7,000 autopsis done in 10 years there were 125 individuals with syphilitic aortities as was found by HOOD & MOHR (1937). Amongst my patients in the hospital the incidence of syphilitic affection of the heart and blood vessels are much less and constitute only 3 p.c. of cases because cardiac syphilis attend medical out-door and are treated on admission in the medical indoor and one can see at any time at least 3 cases in the medical indoor due to syphilis amongst heart cases.

Pathology.—BOYD (1940) has observed that aortitis is one of the commonest and most important of syphilitic lesions. The lesion begins in the aortic wall just distal to the aortic cusps, and spreads horizontally around the root of the aorta and distally as far as the mouths of the great vessels springing from the arch. Even more frequently the whole arch is diffusely involved. As a rule the abdominal aorta is free from lesions. Marked transverse wrinkling is very characteristic of syphilitic aortitis. The disease does not spread along the coronary arteries but the openings of the coronary arteries are reduced to pin-points. Atheromatous lesion is absent in a pure case. The adventitia is thickened and the cut edge shows thickening of both intima and media. Owing to the destruction of the elastic tissue by the spirochætes there is dilatation of the aorta and the aortic ring, giving rise to aortic incompetence. ALMKVIST (1937) thought that in the blood capillaries there is proliferation in the form of buds from which new capillaries originate together with certain increase in the endothelial and perithelial cells and the "budding formation" occurs only in the primary lesions whereas in the great vessels there occurs a combination of proliferation in the form of the usual infiltrative chances of the connective tissue and degenerative process. HOOD and MOHR (1937) studied two groups of patients with syphilitic lesions of the aorta and found that one group of 17 patients who received Arsenical and heavy metal therapy showed microscopically thickening of intima, media, and adventitia, the location of cellular infiltration and the amount of fibrosis and the degree of destruction of elastic and muscular tissue present, whereas in the other group of 32 untreated cases microscopically no difference could be found in the wall

of the aorta as compared with treated cases. CAMPBELL (1941) has observed that syphilitic mesortitis is a focal inflammation but may involve the whole of aorta and the inflammation extend from the adventitia.

Symptoms. The symptoms that result from syphilitic vascular diseases depend upon the organ affected. In the aorta aneurism is the common result. The symptoms of necrosis or fibrosis of the myocardium are severe anginal pains often resulting in death.

Diagnosis.—MAYNARD (1940) thinks that the diagnosis of incomplicated cardiovascular syphilis involves serious difficulties and for diagnosis the following points are important:—(1) The patient must have syphilis beyond reasonable doubt; (2) there must be either a history of syphilitic infection and strongly positive Wassermann reaction; (3) definite evidence of syphilis elsewhere on the body; (4) there must be no evidence of any other disease that may dilate the aorta such as arterio-sclerosis, rheumatic fever or rheumatic heart diseases, hypertension or hyperthyroidism; (5) patient must be 40 years of age or younger; (6) there must be evidence of dilated aorta in the shiagram; (7) in auscultation there must be a hollow, accentuated second sound and a systolic murmur at the aortic area; and (8) uncomplicated syphilitic aortitis does not cause symptoms of circulatory embarrassment, progressive cardiac failure, or paroxysmal dyspnœa. From a general study of 225 cases, and from an intensive personal study of 135 of them, BLACKFORD and SMITH (1938) believe:—(1) The diagnosis of syphilitic aortic insufficiency demands that the pressure of syphilis be proved, that the diastolic blood pressure shall not be elevated, that the pulse pressure shall exceed the diastolic and that calcification of the aortic valve be excluded; (2) syphilitic aortic insufficiency developes at an early age in Negroes which can be explained only in part by their youth at the time of infection; and (3) adequate treatment of early syphilis will prevent the development of syphilitic aortic insufficiency.

Course.—The course of syphilitic arterial disease is very variable and the important and characteristic cardiovascular changes in the first part of the aorta generally follow 15 to 25 years after the original infection.

Prognosis.—CAMPBELL (1941) has observed that the prognosis in the cardiovascular syphilis is bad unless the diagnosis is made early before any serious cardiac symptoms have developed. The incidence of cardiovascular lesion is more in syphilitics without treatment than with early treatment. It has been found by various workers that the incidence of cardiovascular syphilis is twice as frequent as among patients who received some treatment. Patients may die within 4 days of the first cardiac symptoms with syphilitic aortic insufficiency, or they may live at least for 13 years. A sudden onset of grave heart failure, especially when the condition is not controlled by treatment, is a serious omen. In patients with a symptomatic syphilitic aortic insufficiency, treatment with Bismuth and Potassium Iodide seems to prolong life indefinitely (BLACKFORD and SMITH, 1938). Cardiac pain is of great prognostic value.

Treatment.—SCHAMBERG and WRIGHT stated that every patient with syphilis must secure an irreducible minimum of treatment which is based upon the sum total of medical experience, and in regard to cardiovascular syphilis "carry out specific treatment for an extended period of time, even though all clinical manifestations disappear." BECKER (1941) advocated preparatory treatment with Bismuth and Iodides for a period of

10 weeks followed by 3 courses of Arsenicals at intervals of 4 months. Arsenicals are not necessary after the age of 60 years and Bismuth is given in courses of 10 injections at increasingly longer intervals upto one year. If the blood test is negative, the patient is kept on observation, but if positive, a course of Bismuth is given yearly until it becomes negative or the patient reaches the 70th year. If the patient is not a symptomatic but has cardiovascular involvement, the duration of arsenical therapy, in case it is indicated, is for the same period, namely one year.

In a study of 743 syphilitics, receiving varying amounts of treatment for early syphilis it was found that the incidence of cardiovascular syphilis with the duration of the infection from 0·7 per cent. among patients infected for 3 years or less to 23·8 per cent. among those infected for 30 years or more. In their series of 422 patients about whom all the incidence of cardiovascular syphilis among 249 patients adequately treated for early syphilis, 109 of whom were followed for 10 years or more, its completion was 0·4 per cent. The incidence of cardiovascular syphilis among 214 patients who had received varying amounts of treatment for early syphilis examined less than 10 years after its completion was 1·4 per cent. In every instance uncomplicated syphilitic aortitis was the type of syphilitic heart disease encountered. The incidence of cardiovascular syphilis among 208 patients who had received varying amounts of treatment for 10 years or more before their cardiovascular syphilis comprised 71 per cent. of the total cardiovascular syphilis encountered. Among 92 patients who had received little or no treatment for early syphilis the occurrence of cardiovascular syphilis (18·5 per cent.) was twice as frequent as among patients who had received more treatment but who were nevertheless inadequately treated for early syphilis (7·4 per cent.)

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References:

1. Almkvist,J.—(1937) Uro. Cut. Rev., 41: 296.
2. Boyd, W—(1940) Pathology, pp. 429.
3. Becker, S. W.—(1941), Ind. Jour. Ven. Dis. 7: 80.
4. Blackford, L. M. and Smith, C.—(1938), Am. J. Syph., 22 : 146.
5. Cochems, K. D. and Kemp, J. E.—(1937), Idem, 21 : 282.
6. Campbell, M.—(1941), Price's Medicine, pp. 1031.
7. Hood, B. J. and Mohr, C. F.—(1937), Am. J. Syph., 21 : 177.
8. Kemp, J. E. and Cochems, K. D.—(1937), Idem, 21 : 625.
9. Maynard, E. P.—(1940), Med. Times, 28 : 355.
10. Manohar, K. D.— (1935), Ind. Jour. Ven. Dis., 1: 9.
11. Smith, C. and Blackford, L.M.—(1932), Am. J. Syph., 22 : 168.

The Pathogenesis of Hypertension

BY

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BLOOD pressure is the measure of the lateral thrust in the arteries resulting from a number of forces acting in a number of places in the circulation. It is measured by a standard method. It has been fixed arbitrarily that any systolic pressure exceeding 160 must be termed high under ordinary conditions. It must be remembered that in a number of cases transitory pressure changes are met with due to variation in the physical or emotional make up of people. I think that the terms hyperpiesia, essential hypertension, malignant hypertension etc., are the out come of conception of diseases creeping into terminology before the pathogenesis is established. The word hypertension may be left to denote high blood pressure though it may appear to be the resultant of a number of different causes.

Physiology.—The circulatory system consists of a propulsive central organ, the heart, a distributing system of pipes, the arteries, and a mesh work of the fine tubules called arterioles and capillaries, and another system of pipes and tubules which form a passage back to the pump called the veins. In addition to the system of pump and pipes the fluid medium which is the material circulating has certain properties of its own which may or may not constitute some factor or factors towards the augmentation or otherwise of blood pressure. Thus a study of blood pressure involves a study of the organs of circulation and the part played by blood.

I have frequently noticed oil pumps at work. They sprout out water into any receptacle or channel as they continuously work on. The water is ejected out of the pump in a discontinuous manner, in jerks. If the heart were to work like a pump propelling blood in jerks, at times blood flowing and at others not flowing, it is possible to imagine a conducting tube collecting and transmitting the outflowing blood being full at times and empty at others. Naturally one raises the question as to the cause of a continuous flow of blood through the blood vessels in spite of the jerky and discontinuous nature of the cardiac output. Though the heart is comparable to a rigid pump in most respects one should not forget that it is made of muscle which is adjustable to the changing pressures imposed on it. The cardiac output is of the same nature as that from a rigid metallic pump. Then it is evident that the continuous nature of the blood flow in the vessels has to be accounted for by the events connected with the distributing system of blood vessels as the blood pumped out courses through the tortuous tubes.

It is customary to measure blood pressure by applying an armlet made of a rubber bag over an arm and pumping in air which is balanced against a column of mercury in a manometer. The armlet presses on the arteries, and the lumen of the vessels are first obliterated, and the latter gradually relaxed so that as the lumen of the vessels become patent a sound or murmur is audible if a stethoscope is applied to the bend of the elbow. The murmur corresponds to the cardiac systole as conveyed to the arteries in the arm. It is a discontinuous murmur and not a continuous hum. Does that mean that the flow in the vessels is discontinuous? Though the

patent part of the lumen allows passage for some blood, the forcible thrust corresponding to the systole of the heart causes the murmur as an augmented quantity of blood is forced to pass through the narrowed calibre of the blood vessel in question. When the lumen of the vessel assumes its normal dimensions, the blood passes without any obstruction to its flow and no murmur is detected. The blood pressure as measured by the sphygmomanometer comprises the pressure contributed by the arteries compressed, the pressure of the blood due to its viscidity, volume and density, and the cardiac thrust sending in more blood into a vessel which already contains blood and is regulated by an elastic muscular wall.

Arteries are of various sizes from large sized ones to fine capillaries. From the centrally placed large vessels the vessels taper peripheralwards into arterioles and capillaries. Thus the diminishing cross-section of the vessels afford a steady resistance to the onward flow of blood. There is a lag in the blood pumped into the blood vessels, since the whole quantity of blood sent in cannot be sent out as in an empty pipe conveying such fluid. The pipes in this case contain blood and a further quantity is pushed in by the force of the cardiac systole. This phenomenon is noticed because the tapering vessels afford a check to the outward flow and the blood pumped in gets distributed only gradually. It has to work against a resistance. Thus one could imagine a steady resistance to the onward flow of blood producing the diastolic pressure. In any section of the arterial tree between systole to systole there is an interval when the blood vessel contains the minimum quantity of blood and a measure of its pressure is the measure of the diastolic pressure. The central current in any stream is affected to a minimum extent only by the surface resistance exerted, and to a maximum extent by the fluid in contact with the sides or walls of the vessel. Thus the blood flow is mostly checked at the periphery and the central current keeps on circulating without hinderance. The resistance afforded to the peripheral flow causes the diastolic pressure, and at the same time helps the exchange of body fluids and thus facilitates metabolism. The diastolic pressure is the measure of the peripheral resistance.

The arterioles and capillaries are under vasomotor control. The changes brought about by other factors shall be considered subsequently. As McDOWALL points out (in the *B.M.J.* July 12, 1941), it has become apparent that the essential function of adrenaline is the transference of blood from one part of the body to another. Thus it becomes clear that circulation is controlled by the vasomotor mechanism though other influences have to be considered. The rate of flow in the arterioles is greater than in capillaries. The major part of the peripheral resistance is caused by the splanchnic vessels and skin capillaries. It has been recognised clinically that circulatory collapse might occur from the rapid removal of a large amount of fluid which had been compressing vessels in the chest and abdomen, or from excessive dilatation of skin vessels by heat. The total cross-area of the capillaries is great and therefore its capacity is enormous. DALE, RICHARDS and KROGH made it clear that by far the greatest number of capillaries in the body are not usually open, and that when local metabolic needs demand a greater supply of blood, they dilate. Excessive dilatation or opening up of the capillaries lead to a sponge-like soaking up of blood with consequent circulatory failure.

RICHARDS has pointed out that the kidney has 2,000,000 glomeruli out of which only a part is in action at a time, and that explains why in infections the kidneys survive after manifesting symptoms of inflammation. Similarly, it is quite likely, that in the capillary bed in all areas of the human body, while some section is functioning, some other section or sections may be at rest. As ELLIS points out nephritis is a cappillaritis affecting not only the capillaries of the kidneys, but all capillaries (ARTHUR ELLIS, *Lancet*, Feb. 1934). The hot flushed state and œdema all over occurring during onset are supposed to be evidences of a generalised capillary disorder. The active capillaries may be affected, and the capillaries at rest escape. This observation is helpful in tracing the involvement of the total capillary mechanism of the body in the nephritic syndrome more than in anything else. The relationship between pressure alterations and capillary involvement noticed in diseases should be well borne in mind.

The factors controlling blood pressure all act on the vasomotor centre. The sources of impulses are:—(1) impulses proceeding from a plexes over the aortic arch; (2) impulses proceeding from the carotid sinus; (3) impulses reaching the centre due to changes of temperature, action of Histamine, Pituitrin, Adrenaline, and the metabolites like Carbon Dioxide, H-ion, and oxygen lack; (4) irradiation of impulses from the respiratory centre; and (5) influence of emotional and mental changes.

The arterioles have muscle coats and sympathetic enervation. The muscle coat has been modified in the case of capillaries to leave much of the endothelium uncovered and so permit the passage of various substances to and from the tissue spaces. The capillaries are capable of altering their calibre independently of the state of the arterioles and venules. If their tone is high they can resist the distending force of arterial or venous circulation. Sympathetic fibres pass to the Rouget cells of the capillary wall. The stimulation of the sympathetic nerve causes contraction of the capillaries even after the arterioles had been obstructed. The tonic constrictor fibres from the vasomotor centre pass normally to the capillaries. From the above observation it appears that constriction of arterioles or capillaries is effected through the medium of adrenaline secretion, and changes in blood pressure are controlled by the vasomotor centre, acting through the intermediation of the autonomic nervous system, according to the requirements indicated by organs or parts of organs connected with the process.

Adrenaline is normally secreted during mental stress, severe exercise, and exposure to cold and in all sympathetic nerve endings. At the neuromuscular junctions adrenaline or its polymer acetylcholine is secreted, and they serve as transmitters of nerve impulses. The impulses so transmitted go to regulate the peripheral resistance and indirectly blood pressure. Thus at the bottom of the problem of blood pressure the question of contraction of skeletal muscle is involved.

In a case of myotonia acquicita the patient who was a good athlete in his youth, was noticed to respond to high doses of potassium in mixtures. The body muscle which went into a spasm at every movement was noticed to be relieved of tension when he was put on Potassium Iodide mixture for about two months. Once, when he complained of body pain, he was put on Sodi Salicylas. But the spasms returned. Similarly any sodium salt was found to increase the spasm and potassium salts to reduce the same. On

this observation as basis, I gave the patient large doses of Potassium Salts in mixtures and Potassium Iodide injections. The result was gratifying, and the patient is now a very useful member attending to his usual avocations. This instance raises a problem which I have been thinking of discussing ever since 1938 when the above patient came under my observation. It is evident that muscle spasm is relieved somehow by a liberal administration of Potassium Salts.

In cases of myasthenia gravis CUMINGS found that serum potassium was greater than muscle potassium (J. N. CUMINGS, 1941; *Journal of Neurol Psychiat.*, IV, 226). FENN and COBB (1936) showed a loss of potassium from muscles in animals during exercise, and KEYS (1940) showed an increase in plasma potassium after short exercise. Thus evidently the presence of potassium in muscle tissue causes relaxation of muscle, and a series of contractions tend to drive out the potassium. The action currents dislodge the potassium ions. The chemical transmitter at the myoneural junction, while setting up an action current in the muscle fibre, displaces the ionic potassium and produces a contraction. The potassium ion so dislodged is found in the plasma only and by a reversible reaction it may combine with the muscle fibre and bring about relaxation. The muscle contraction is due to the reversible shifting of the potassium ion in the muscle-plasma unit when the chemical transmitter sets the process going. In some diseases with differences in muscle tone like myotonia, administration of excessive doses of potassium ions produces a rapid cure, and thus confirms the conclusion arrived at. The patient in question had polyuria, insomnia and myotonia. The treatment relieved him of all these symptoms. The adrenal cortex, the pituitary gland and the kidneys seem to have some part to play in potassium metabolism. Insulin hypoglycæmic shock seems to help the potassium ion to get fixed to the muscle and administration of large quantities of Glucose displaces the potassium ion. Thus the liver also has a part to play. Myasthenia occurring in Addison's disease is due to an excess of potassium in the muscle. In cases of nephritis there is a tendency to administer potassium salts as diuretics, and the effective result obtained is probably due to the action of the potassium ions on the kidney capillary musculature. Sleep also has some connection with potassium metabolism, and I think that in potassium bromide the hypnotic influence is produced by the potassium ion and not by the bromide part of the salt.

Thus one could see the link between adrenaline, an endocrine product, the potassium ion, a product from a chemical substance, and the major organ involved in the metabolism, liver. In one case potassium seems to initiate diuresis, and in another it appears to arrest it, and thus appears to act peculiarly. But this apparant peculiarity is accounted for by the reversible reaction of the potassium ion in the muscle-plasma combination. In the normal state the chemical transmitter most probably sets the process moving. The healthy condition of the muscle also has to be assured for a normal response. Thus the administration of liver extract has helped to bring about an early correction of the chemical constitution of the muscle. Once the chemical constitution of the muscle fibre is normal, the reversible potassium ion displacement process is determined by the chemical transmitter, which is under the control of the endocrine glands.

Blood, the fluid that passes through the blood vessels, is a viscous material composed of cells and dissolved substances. The composition of

the blood is pretty constant. The specific gravity, viscocity, and composition of the blood contribute to the tension of vessels. The volume of blood pumped in also determines the pressure. The components of blood conveying minerals and other metabolites, and hæmoglobin as an agent of respiratory adjustment, are responsible for changes in the respiratory rhythm. The chemical changes act on the vasomotor centre and bring about respiratory changes as well as blood pressure changes.

Pathogenesis.—Hypertension is said to be absent in the lazy African Natives. In India hypertension does not appear to be so well marked as in the Western countries, where more of protein food and alcoholic drinks are used than in the comparatively vegetarian India. Further the action of cold on skin and the task imposed on the kidneys may account for this greater incidence of hypertension in the West. The blood vessels are subject to the play of temperature changes brought about by the severe external cold and alcoholic drinks, etc., meant for masking the effects of cold. As civilisation advances men are taken away from their native setting, and congestion of town or city life replaces the calm, peace and contentment of rural life. The hard competitions of the crowded life of modern cities give no rest to the mind of people. Their nervous system is continuously subject to the play of adrenaline secretion. The sympathetic system is overtaxed, and the mind is open to unwanted stresses and strains. Thus a faulty habit formation occurs, and the mind is subject to a continuous tension.

DAWSON (1925) emphasised the mental factor, and de WESSELOW (1934) stressed on chemical changes as causative of hypertension. McDOWALL (*B.M.J.*, July 19, 1941) remarked 'some fancy the neurogenic hypothesis, and others a chemical one in spite of the fact that hypertension may be caused by a variety of causes though it is a common symptom.' A physiological approach to the conditions that lead on to hypertension, *viz*, mental stress, severe exercise, adrenal tumours, nephritis, gout, eclampsia, chronic lead or alcohol poisoning, pituitary tumours, hyperthyroidism, and erythrocytosis as in polycythæmia may help to solve the problem. Though the causes appear to be many, should one not think of a single or common mode of action of all the apparently divergent causes in the production of a single response, hppertension? Either an increase in the peripheral resistance aiding an increase in the volume of blood in the vessels by a process of stagnation as further quantities are being pumped in, or an increase in the tonicity of the arterial wall due to hyperadrenalism, or arterial sclerosis, is in essence very similar to the action of metabolites helping to contract the vascular muscle or adrenaline acting on blood vessels. As it has been already pointed out the vascular change is a resultant of physio-chemical changes in the muscle-plasma combination through the mediation of the adrenaline acting as a chemical transmitter. Thus in endocrine, metabolic, inflammatory or other changes the resultant hypertension is caused by a physio-chemical process.

GOLDBLATT and his collaborators (1934) showed by constriction of the renal arteries in animals that hypertension resulted. F. GLENN, C. G. CHILD, and G. J. HELLER (*Ann. of Surg.*, 1938, cvii, 618) concluded from an experiment on the left kidney of a dog which was placed in the groin where renal and femoral vessels were anastomosed quickly, and the blood pressure was recorded for 3 weeks followed by the removal of the right kidney and a further estimation of blood pressure for another ten days,

and when the artery of the transplanted left kidney was constricted with a Goldblatt clamp hypertension developed within two months, that the renal nerves played no part either in the development or maintenance of this type of hypertension. The process described clearly shows that when the blood flow is so restricted, as pointed out, the production of metabolites, from inside the kidney substance, or outside due to faulty excretion, is responsible for the production of hypertension. The experiments with the Goldblatt clamp do not in any way change the view about the neurogenic origin of hypertension.

WILSON and BYROM (*Lancet*, 1, 136, 1939, 1941; Quart. *Jourl. of Medicine*, N. S. 10, 63) have shown that hypertension resulted from the constriction of one renal artery in the rat. If this ischæmic kidney is excised before arteriolar lesions have occurred in the unclamped kidney, the blood pressure falls, but later when arteriolar changes develop in the remaining kidney, hypertension persists. EVANS suggests that in any disease associated with progressive renal ischæmia, such a lesion will operate in a vicious circle. The ischæmia produces anterior changes, and the arteriolar changes produce hypertension. In many forms of renal disorder a similar clinical picture with hypertension and renal failure occur at the late stages.

BOYD states that the two most important conditions causing hypertension are acute glomerulo-nephritis together with the closely related toxæmias of pregnancy, and the form known as essential hypertension, so called because it is not dependent on disease of the kidneys or of any other known organ. The vasomotor system of 98% of the patients suffering from essential hypertension shows excessive reaction. This observation proves the essential part played by the vasomotor mechanism in the production of hypertension.

The observations of J. M. ROGOFF and E. MARCUS (*Jour. Amer. Med. Assoc.*, 1938, ex. 2127) from experiments on dogs, that the concept of hypersecretion of adrenaline as a cause of persistent elevation of blood pressure was untenable is only one sided. Adrenaline is secreted only in minute doses and the changes in the arterioles are brought about not by any hypersecretion of adrenaline, but a persistent secretion of adrenaline from various causes, forming a habit and hence serving like the clamps used in the experiments described and acting over long periods.

Some mention has to be made of the pressor substances which send up the blood pressure. Extracts from meat, when putrefying, send up blood pressure. An iso-amylamine was found in the urine of normal subjects by BAIN, and it was absent in urine when the pressure is high. He thought that it had a pressor action. Methyl guanidine, found in normal urine, sent up the blood pressure on injection. Patients with high blood pressure excreted less of this substance than normal people. Intestinal putrefaction occurs in hyperpietics, and if the products pass the liver barrier, and get into circulation, hypertension may result. Thus the toxins of metabolism may cause liver damage, especially when the metabolism is abnormal, or disordered before the production of hypertension.

There is a close relationship between eclampsia and the hepato-renal syndrome described by T. G. ORR and F. C. HELWIG (1939 *Ann. Surg.*, 110, 682). In the latter condition liver damage produces renal damage with albumin, casts, red blood cells, etc., in urine, and an increase of total

nonprotein nitrogen and creatinine in blood. Since liver damage seems to be the cause of kidney involvement, I tried the effect of liver therapy in cases of nephritis of various ages and types. The amelioration of symptoms occurred in a spectacular manner. The effects of fluid imbalance noticed in these cases all cleared up, and blood pressure changes settled down rather slowly. The pressure was set up by the histamine or other product of tissue destruction, most probably, and the kidney damage was caused by the toxin escaping the liver barrier. The effect of liver therapy was more complete in clearing the renal symptoms than in the reduction of hypertension. Experimentally also liver therapy has been found to be of little use in the reduction of high blood pressure. I think that this kind of resistance is caused by the histamine or histamine-like substances produced by liver damage.

In a recent review H. A. LEWIS and H. GOLDBLATT conclude in experimental hypertension produced by constriction of the renal artery that renin, an enzyme, interacts with pre-hypertension (or pre-angiotonin), a pseudoglobulin, probably formed in the liver by the influence of the adrenal gland secretion to form the final effector pressor substance, hypertensin (or angiotonin). In addition to prehypertensin and hypertensin, another substance hypertensinase has been discovered. It destroys hypertensin in vitro, and it lacks proof of its capacity to reduce blood pressure in animals.

Extracts of kidney have been tried in hypertension with good results. Some alarming symptoms of fall of blood pressure like flushing of the skin, sweating, and slow pulse followed with fever. I think the symptoms are due to histamine from destroyed tissue.

The clamp experiments, based on the pattern of the Goldblatt clamp experiment on dogs, show that there is a general belief that hypertension is primarily of renal origin. But there is a large body of opinion in the opposite camp. In hyperpiesia the blood pressure becomes normal under ether anæsthesia, and there is a diminution of blood pressure in such cases during sleep. Less than 10 per cent. die of renal disease from among cases of hypertension. Capillaries exist all over the body, and there is no special reason why one particular group of capillaries should be incriminated for the production of hypertension. From aught one knows the capillaries work in groups, keeping some in the reserve all over the body, and only when the limit of adjustability and reserve capacity are transgressed will any symptom of hypertension make itself prominently felt.

GULL and SUTTON brought forward the conception of arterio-capillary fibrosis of the arterioles and capillaries, the kidneys being only secondarily affected. Some regarded it as pre-albuminuric stage of Bright's disease. CLIFFORD ALLBUTT introduced the term hyperpiesia to denote hypertension independent of kidney disease. The term hypertension is now largely used. Too many restrictions and definitions, not necessitated by pathological evidences, tend to defeat the motive of the introduction of such terms and complicate the understanding of the subject.

The conditions that lead on to hypertension have been referred to. The attempt in this article is to find out a common factor which produces high blood pressure in all the conditions and hence each condition is not considered in detail. The physiological study of raised blood pressure indicates hypersecretion of adrenaline as the forerunner of the condition.

Adrenaline as the hormonal transmitter of impulses and potassium ion as the chemical element involved while impulses pass through muscle which go into a spasm or contraction at will or out of necessity or disease, are both responsible for capillary or arteriolar contraction in cases of hypertension.

In mental patients, during exacerbation of symptoms, rise in blood pressure is noticed. Emotional changes involve blood pressure changes. If a tame cat is screened after feeding her with a barium meal, the churning rhythmical movements can be noticed. When a fox terrier is introduced into the scene and the cat is held in position over the screen, the cat shows terror and anger and the stomach movements abruptly cease. The churning movements of the intestine cease also, and the gastric juice stops flowing. That is, the whole process of digestion stops during the state of anger. The secretion of adrenaline in this inhibits the digestive organs. Changes in emotion are detected by electrical changes in the skin which can be measured by a psychogalvanometer. The emotional changes make physical changes in the organs of the body through the medium of hormones which bring about physio-chemical changes in the tissues involved and the organ concerned functions adequately. The hormone in question in this case of emotional upset is adrenaline. A large dose of adrenaline makes the subject so treated feel as if in tension. The state is that of an anxiety neurosis. The faulty habit of being subject to the effects of constant secretion of adrenaline brings about the increase of blood pressure from increased peripheral resistance.

Innocent looking emotions like fear, disgust, displeasure, and all sorts of stresses and strains of life leave their mark on the body. They affect the system through the endocrine glands. Thus one notices anxiety symptoms, forming the basis of even hyperthyroidism. The adrenal secretion is the basis of all sympathetic upset consequent on emotional upsets The arterio-capillary constriction following such emotional upsets occurring habitually helps the arteriolar musculature to hypertrophy or to act like a Goldblatt clamp, not only on the blood supply of the kidneys, but also on all arterioles and capillaries. Thus peripheral resistence is enhanced, and hypertension supervenes. The process of muscle contraction involves a chemical process—that dependent on the reversible potassium ion shift, and the healthy make up of the muscle. A method is likely to be found to fix the K-ion on to the muscle so as to produce muscular relaxation at will. It should be akin to the biological process, being helped by methods of relaxation of the emotional stresses and strains. In a case of bronchial asthma, just two days ago, I found the injection of liver extract very effective in the amelioration of symptoms when given in conjunction with a Potassium Iodide mixture. Thus I think that liver has a part to play in the process of fixing K-ions to the tissue.

It is high time that we cast our differences aside and take up the study of hypertension from a biochemical point of view. Life processes while acting normally produce lots of chemical changes in the tissues. The chemical changes themselves involve the common elements of chemistry. If only our views get a proper direction, the method of action of these elements in a biological process can be studied, and by presenting drugs in the proper proportion and combination it may be possible to tackle many a difficult problem in medicine successfully. In this article I have made such an attempt on a small scale, and I hope the physio-chemical aspect of hypertension, when made clear, will indicate the line of approach in the treatment of this difficult problem.

Endocrinic Therapy in Hypertension and Arterio-Sclerosis

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Introduction.—While treating cases of impotency or enlarged prostate with testicular preparations I had been struck with their effect on blood pressure. Patients with supernormal pressure showed not only a lowering of pressure but also relief from its symptoms and improvement in their general health. The blood pressure of those suffering from hypotension always rose producing a feeling of vigour and vitality. At the same time in all cases the weight, if abnormal, showed a tendency to approximate to the normal.

ILLUSTRATIVE CASES:—1. A man, aged 42, was treated for partial impotency. His blood pressure which was 150/102 after treatment which also consisted of nourishing diet fell to 125/84.

2. A male patient, aged about 32, complained of diminution in sexual desire and his pressure was 100/62. At the end of 2 months' treatment it was found to be 115/72.

Fortified with this observation I have now for some years been utilising it in treating cases of hyperpiesia which did not yield to the usual measures *e.g.*, regulation of diet, physical and mental rest, administration of laxatives, purgatives, diuretics and antiseptics, removal of septic foci and toxæmia, use of iodides, nitrites, and other pressure-reducing drugs, etc. Generally I reinforced the above measures with gonadal therapy and have been gratified with the results.

ILLUSTRATIVE CASES:—1. A man of 47 complained of headache, disturbed sleep, irritability of temper, palpitation, etc. His blood pressure (B. Pr.) was 168/108. Enquiry showed that sexual weakness has set in earlier for his age and health. He was given injections of testicular hormone which was also administered orally and after some three months his blood pressure had come down to 132/90 and he was relieved of all his complaints. His B. Pr. was again noted 3 months after cessation of treatment and it was 136/94. After about two years he again complained of lack of concentration and irritability and his B. Pr. was found to have risen to 152/100. This time he had another course of treatment and it came down to 130/86.

2. A male patient of 62 had a B. Pr. of 207/126. He had received various treatments before and was given the usual treatment for over 2 months, and inspite of it his reduced B. Pr. ranged round about 190/125. Enquiry into his sexual life indicated that the so-called male climacteric had set in 10 or 12 years previously. All medication was stopped and hormone therapy instituted which, after nearly 4 months, brought down his B. Pr. to 169/106. At this stage he left the treatment.

Advantages and Rationality.—1. Generally the strict regime of the usual treatment of hypertension dislocates the whole life of the patient and becomes irksome. He may submit for a time to the regulation of his habits and diet but the moment he feels relieved or gets used to the frightening idea of high B. Pr. he gives up the treatment. For a patient of say 50 or 60 when nature becomes inelastic and powers of adaptability limited it becomes next to impossible for him to remodel his habits, to modify his diet, to change his taste, to alter his mentality, and, in short,

to recast his whole life into a new mould. Usually very soon he slips back into his old ways of life. For example, obesity as a cause of high B. Pr. owes its origin, among other things, to overeating and lack of exercise. Treatment restricts the diet and imposes activity. When the treatment is over the patient reverts back to his over-indulgence and laziness, regaining his lost weight and pressure.

ILLUSTRATIVE CASE :—A man of 38 years, 5' 5" in height, weighed 15 stones. Treatment reduced his weight to 13½ st., accompanied with a fall of 30 m.m. of Hg. in his B. Pr. reading. After 1½ years he weighed 14 st. 10 lbs.

Hormone therapy being compatible with lesser restrictions in the habits and comparatively greater latitude in the every-day life of the patient is generally welcome to him. At the same time it reactivates the body and the mind and changes to some extent his outlook and psychology. The energy both of the mind and the body which it revives can be directed into healthier channels. The body and the mind become more pliable and with a little guidance can be moulded into new and healthier ways.

2. From the etiological point of view the hormone therapy has much to commend itself. The etiology of hypertension can be summarised as under :

Repletion due to overeating and insufficient exercise. Focal sepsis, *e.g.*, teeth, tonsils, nasal sinuses, etc. Toxic *e.g.*, tobacco, alcoholic excess.

Renal—Nervous—Mental strain, anxiety, etc.

Each of the first 4 causes will require appropriate treatment. Repletion will have to be counteracted with restricted diet and exercise. In this connection too the utility of the endocrinic therapy has been recognised. In cases of endo- and exo-genous toxæmia further poisoning should, if possible, be stopped. Kidney disease should receive suitable treatment. Here again according to Dr. H. BENJAMIN "...Even hypertension with chronic interstitial nephritis has occasionally been reduced." In nervous cases it is easy to order mental rest and avoidance of anxiety and worry. But in practice patients of nervous and neurasthenic temperament given to worry seldom can have real mental relaxation. In such cases again endocrinic therapy can to some extent prove useful in relieving the nervous tension. Endocrinic disturbance of course will require endocrinic treatment.

After all the possible causes are removed or remedied we are still left with hypertension and arteriosclerosis, the legacy of the causes which had been at work. Raised pressure, when it has lasted some time, always brings about fibrotic changes in the arterial walls (L. BROWN, G. EVANS etc.). The only therapeutic measure which can exert some influence on the arterial sclerosis is gonadal therapy as has been shown by HALLS DALLY and others. (*vide infra.*) Even if the removal of the cause is not possible, as happens in the great majority of cases, endocrinic therapy, by breaking up of the colloids and bringing about regeneration of tissue cells, confers elasticity on the hardened arterial walls. It thus extends the only hope of combating the arterio-sclerosis and hypertension. In my very limited experience it gave surprising results when other measures had failed.

3. In the majority of cases once that hypertension occurs the patient has to live with it and die with it and at the same time he is doomed to the life-long care of it. No treatment can restore him to pre-hypertension

state of health, and the benefit obtained by intensive treatment lasts but a very short time. Endocrinic treatment by reducing the fibrotic changes in the arterial walls provides somewhat lasting relief.

4. Again in the great majority of cases the sudden reduction of pressure by the drastic use of potent drugs can be dangerous. (" A certain amount of hypertension is absolutely necessary to the individual's well-being. Were it possible to reduce the high blood pressure to normal, there would not be sufficient driving force to send the blood to the vital organs in the brain, and cerebral anæmia would result."—L. M. WARFIELD.) The endocrinic treatment is free from such risks.

5. According to R. S. PALMER and E. G. THORP, "the primary factor in etiology is a constitutional susceptibility," and thus the above six factors act only as exciting causes. There is no known drug or therapeutic procedure which can alter this inherent ' constitutional susceptibility.' The endocrines, however, can be expected to influence, to some degree, this ' primary factor.'

6. The rise of pressure and the contraction of the arterioles under the action of adrenalin indicates the influence the endocrines have over the spasm of the arterioles. The vasopressin fraction of the post pituitary extract manifests a similar action of vasoconstriction. In old age the increase of fibrous tissue in the organs of the body (including arteries) is regarded as a part of senility—the result of the dysfunction or hypofunction of the gonads. The age of incidence of arteriosclerosis with hypertension (after 40) coinciding with the beginning of the decline in some of the endocrines (gonads) points to the probability of some connection between the two. Endocrinic disturbance is recognised as one of the etiological factors. Is it not possible that even in those cases where they are not directly responsible they may still be having some connection, however remote and indirect, with the rise of pressure and arterial changes ? Conversely cannot the height of pressure and arterial fibrosis be influenced through the agency of the endocrines ?

7. The retirement of the ovaries causing raised pressure at the menopause is an established phenomenon. This retirement is like a crisis in life-climacteric—and does not admit of being overlooked. In men, on the other hand, the failure of the testes is a very slow, subtle and insidious process simulating a sort of lysis in life and as such does not force itself on attention and recognition. Whether recognised or not it cannot fail to have a definite influence very much similar to that of the accession of the ovaries justifying the application of the endocrinic therapy.

References.—Satisfactory results obtained by me led me to find out the experiences of other observers. The beneficial results of the endocrinic treatment has been recognised by a number of authorities. I give below a few references :

1. LESSER, discussing the treatment of angina pectoris with testosterone in the *New England J. Med.* 1942 : 51 (as quoted by the *J. of the I.M.A.* of Oct. 42), says : " A lowering of the blood pressure was noted in the majority of patients during the course of treatment....."

2. BENJAMIN discussing the results of the treatment has observed : " Among the objective symptoms, the hypertension has responded most favourably....."

3. Dr. PETER SCHMIDT has noted : "Of fundamental importance is the effect on the tone of the arteries.....The high blood pressure diminishes within some weeks or months after operation—and that too regularly....."

4. At another place he says: "I hope I have emphasised strongly the decisive influence of the gonadal hormone on the tone of the arteries....."

5. In an inaugural address at Berlin, BERGMANN observed: "In comparatively young persons suffering from endocrine disturbances, we often see persistent hypertonia. This leads me to think that the hypertonia which so often manifests itself in men when the involutionary period begins (analogous to the climacteric hypertonia seen in women) must be closely connected with the endocrine formula, and especially with the behaviour of the puberty gland."

6. HALLA DALLY in his book "High Blood Pressure" says: "Following Steinach operation for cellular regeneration in elderly males, a lowering of the arterial pressure in hypertonia and arteriosclerosis has been established by several authors. Changes probably occur in the arterial walls in the direction of increased elasticity, metabolic regeneration of tissue cells occurring through the break up of colloids, which has the effect of reducing the thickening of the vessel walls. Even if the hypotonia shows no abatement on sphygmomanometric registration, clinically cessation of epistaxis and of irritation (ante-crawling) of the extremities connected with arteriosclerosis was noted, as well as disappearance of subjective noises of pulsation in the arteries."

7. In his book "*The Conquest of Old Age*" SCHMIDT has mentioned a large number of cases in which the supernormal pressure was reduced to normal as a result of the Steinach operation. In this connection he states: "....Manifestly the hormone of the reproductive gland has a regulating influence upon the tone of the sympathetic vascular nerves. Possibly the hormone in question is antitoxic to certain metabolic poisons which have a bad effect on the sympathetic nerves so that the influence of the waste products of tissue change makes itself felt when the activity of the reproductive gland declines.....There can be no doubt that morbidly increased blood pressure of old age is reduced after rejuvenation and that it often regains the normal of youth."

It must be noted here that, from the therapeutic point of view, vasoligature (Steinach's operation) and gonadal therapy are the same as both provide testicular hormone to the system. One is endogenous and the other is exogenous. In the latter the effect lasts for a short while, whereas in the former it is continuous and lasts for a very long time.

SELECTION OF CASES:—Every case requires thorough investigation, detailed examination and individual study. Eradication or at least the palliation of the cause or causes is of primary significance. Critical enquiry will, in the majority of cases, reveal the surreptitious advent of the involutionary period indicating gonadal therapy. In some it may not be so obvious and the failure of the usual measures justifies the endocrinic therapy. I cannot speak about malignant cases which yield to nothing.

Observations.—I have excluded from this review cases of temporary rise seen at the climacteric in women which are due to a temporary imbalance in the endocrinic system—ovarian insufficiency coupled probably with adrenal overactivity. My observations have been confined to those male patients who presevered in the treatment long enough to allow definite conclusions to be drawn. Thus during the course of some 10 years only 11 cases could be observed. Out of these 11 cases non-endocrinic treatment was first tried in 8 cases and on its failure to do

much good it was supplemented with the endocrinic therapy. One of these 8 did not respond even to this line of treatment. In the other 3 cases endocrinic treatment was given from the very beginning together with the moderate application of the usual treatment. The results were equally satisfactory. It has to be noted that all cases were of some years standing and had had various treatments before coming to me. Even in those cases where the treatment was not continued for a sufficiently long time improvement was observed but was inconclusive.

Treatment.—In all cases it was fouud necessary to continue the treatment for months before obvious benefit could be expected or observed. Testicular hormone was administered both intramuscularly and orally. It compensates for the hypofunction of the testes by artificially providing to the body the testicular hormone. In reality it is a substitution therapy and had therefore to be continued orally for sometime subsequent to the cessation of the active treatment. In selected cases the testes were stimulated by supplementing the above with the gonadotropic hormone of the anterior pituitary and it is my impression that its effects were more lasting. The one subjective symptom after the injections of the anterior pituitary hormone was the feeling of heaviness or of tension in the testes as described by the patients. There was at the same time some perceptible increase in the size of the organ. Thyroid was in some selected cases included depending on the endocrinic study of cases, its action being carefully watched. The habits and the diet of the patients were regulated only to the extent that it did not become irksome and intolerable to them. Bowel action was secured by the use of mild aperients only. Mental relaxation and physical rest coupled with suitable amount of exercise were insisted on. No other pressure-reducing drugs were prescribed while giving endocrinic treatment.

Conclusion.—My own meagre observations have impressed me and with the authorities referred to above I hesitate no longer in recording my results. It cannot be claimed that it is a certain cure for hypertension and arteriosclerosis. But it is a rational line of treatment which cannot supplant but can supplement the accepted methods of treatment with great benefit to the patient.

Serial No	Age	Indications of male Climacteric	Average of several readings of B. Pr. at the beginning of treatment	Average of several readings at the end of 2 months' non-endocrinic treatment	Average of several readings at the end of endocrinic treatment lasting 3 or 4 months	Date	Failure as determined by lack of relief from symptoms and by the height of pressure	
				A	B		of A	of B
1	60	Yes	196/130	180/110	155/100	Jan. '34.	Yes	No
2	58	,,	178/110	160/100	148/100	July '34.	,,	No
3	45	,,	186/115	172/110	166/104	June '35.	,,	Yes
4	43	No	170/112	156/104	142/96	Aug. '36.	,,	No
5	47	Yes	168/108	——	132/90	Jan. '37.	,,	,,
6	55	,,	190/118	170/108	145/100	Feb. '38.	,,	,,
7	50	,,	180/114	166/106	142/93	July '38.	,,	,,
8	48	,,	172/109	161/100	142/95	Oct. '38.	,,	,,
9	52	,,	212/130	——	161/102	Mar. '39.	,,	,,
10	62	,,	207/126	101/114	169/106	Nov. '40.	,,	,,
11	58	,,	195/116	——	162/103	Aug. '41.	,,	,,

References:

1. Halls Dally—High Blood Pressure.
2. Price—Text Book of Medicine.
3. Tice—Practice of Medicine.
4. Dr. Peter Schmidt—Six Hundred Rejuvenation Operations.
5. Benjamin—The Reactivation of Women.
6. P. Schmidt—Conquest of Old Age.
7. Medical Annual 1937.
8. Essential Hypertension by Basu—Antiseptic, January 1940.
9. Bhattacharya—Hyperpiesis — Antiseptic, February 1938.
10. R. J. Lal—Early Detection of High B. Pr.—Antiseptic, July 1940,
11. Chatterjee and Mitra—On the Relation of Intestinal Fermentation to Arteriosclerosis — Antiseptic—Oct. 1941.
12. Raja Ram—Hyperpiesis and old age —Antiseptic October 1941.
13. Ghosh—Treat. of H. B. Pr.—J. I. M. A. October, 1941.
14. Murthi—Occurrence of Essential Hypertension in the Hospital Class of Patients—J. I. M. A. Sep. 1940.
15. Banerjee—J. I. M. A. June 1941.
16. Muir—Text Book of Pathology.
17. Halliburton—Hand Book of Physiology.
18. The Practioner, January 1938.
19. Whitla's Pharmacy Materia Medica and Therapeutics.
20. Majumdar — Modern Pharmocology and Therapeutic Guide.

Book Review

Tables of Food Values By ALICE V. BRADLEY, Associate Professor of Nutrition and Health Education, State College, Santa Barbara, California. Published by the Manual Arts Press, Peoria, Illinois. Price: $3-50.

It is a far-fetched cry to ask for a balanced diet in India when millions of its people are ill-nourished and tens of thousands are dying of starvation in public streets, hospitals and elsewhere. But the problem has to be tackled sooner or later, sooner than later, and a National Government is bound to devote its first attention to this all-important subject. Any literature, therefore, that will guide us in this direction is welcome.

The author has had wide teaching experience in all grades, from the lowest to the highest; she has done County Home Service Work from the University of California and also lectured before professional scientific groups.

The book is divided into four sections. Chapter I deals with the components of the diet, II with diet, meal and menu planning. Part I is a series of 27 tables giving values for the actual serving portion of foods. Part II is a similar group of 27 tables giving values for 100-gram portions of the same foods. The Chapters are self-explanatory that even a lay man can easily follow and profit by them.

The values for prepared foods are based on the recipes given. The functional value of this book is its ease of use and everyday usefulness. All the values for a single food are given in a *single table.*

This new edition is thoroughly revised and considerably enlarged, as to make it appear new. It is completely up-to-date, the recommendations of even the National Nutritional Conference finding a place in it. It is neatly arranged to meet the needs of all. We have no hesitation in recommending it to all those who are interested in the nutritional problem.

Announcement

We are informed by Messrs. Ciba (India) Ltd., Bombay, that they have now received a large consignment of Cibazol which will be available to the Medical Profession from the 15th November '43.

Errata

In Nov. '43 issue of THE ANTISEPTIC in page 604, lines 27 and 28, please *read* "*chunnams*" *for* "*churnams.*"

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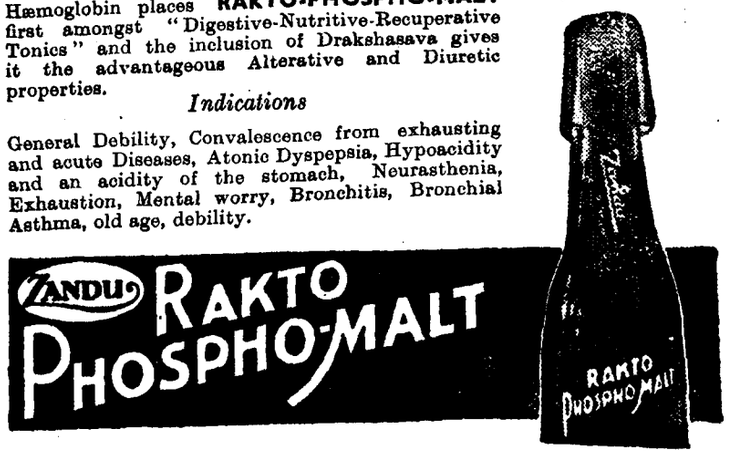

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