OUTLINES

OF

Normal and Pathological Histology

A SYLLABUS OF LECTURES

AT THE

COOPER MEDICAL COLLEGE,

SAN FRANCISCO.

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(FOR INTERMEDIATE COURSE.)

PREFACE.

THE students and alumni of Cooper Medical College have often requested the publication of my lecture notes, hence this syllabus.

To use these outlines to best advantage it will be necessary to use the blank pages for additional matter given in the lectures, and refer to the subjects mentioned in the more elaborate works of Stricker, Klein, Beale, Comil and Ranvier, Delafield and Prudden, etc.

J. H. W.

Oakland, Cal., 1892.

PART I.

GENERAL HISTOLOGY.

PART I. Living Matter in Health and Disease.

I. THE NATURE OF LIFE.

Physicians deal chiefly with life. It is true that the materials of human or other organized bodies are the same as those of the inorganic world, and the knowledge of physics and chemistry cannot be dispensed with, but our patients are living beings. The functions of their bodies are vital functions, not known outside the living world. Physiological activities, as well as psychological, depend on life. Pathological changes are modifications of vital actions. The activities we seek to modify by therapeutics are mostly vital activities. Hence the need of studying biology, or the science of life. The mystery of life is no reason for avoiding its study. It is no more mysterious than any other ultimate fact in nature.

Only two theories possible to account for the nature of things. One is called Monism, and regards the universe as a mechanical evolution of a single substance, which is generally considered to consist of material atoms, very minute and indestructible, with spontaneous motion. Some, however, teach that immaterial force is the only substance. The other theory is called Dualism, because it admits two kinds of substance, one atomic material and mechanical, and the other spiritual and invisible, but both capable of acting upon each other. Under one of these modes of thought we must range ourselves if we think at all. Many physiologists have tried to define life so as to avoid both theories and have been amusingly unsuccessful.

Bichat defined life as "the sum of the functions by which

death is resisted," which is merely asserting that life and death are opposite states.

Dr. Carpenter says that life is the "condition of a being which exhibits vital actions." This is only another way of saying that life is a state of living.

Coleridge called life "the principle of individuation." This is equivalent to separate existence and applies to stones, metals and everything else.

Herbert Spencer says life is "the continuous adjustment of internal relations to external relations," a description which will apply to a steam engine, a burning candle, or a boiling teakettle, as well as to a living thing.

All such definitions evade the real question—"What is the cause of the difference between the living and the non-living?"

The only answer which we deem reasonable is that of a rational dualism, *viz.*, that a living being is the manifestation of a spiritual existence in the sphere of the physical world. In other words, life is the influence of the soul upon the body. This opinion is the most ancient and universal one, held in all ages, and maintained at the present day by the great majority of educated and uneducated men of all creeds and nations. The identity of psychic and vital force is rendered probable if not certain by the intimate relation between organic and mental functions. Anatomy has found no bodily organ for thought, affection or will, yet these mental processes are enfeebled by exhaustion of the bodily powers, except where there is organic defect. The mutual influence of body and mind is matter of daily observation.

II. THE HISTOLOGICAL UNIT.

1. The old division of bodies into organized and unorganized, as synonyms of the living and non-living, from the presence or absence of organs, or distinct parts with definite structure capable of special use, is no longer applicable, since only a small part of an organism is truly alive. A dead twig, or bone, or muscle, may be called organized when no part of it is alive. The organic crystals found in plants, or in patho-

logical conditions, were never alive, although the product of life. The only unexceptional characteristic of living bodies consists in the presence of living matter, or bioplasm. This is a structureless, jelly-like substance, either scattered in minute particles or arranged in fibrils or networks through nerves, muscles, bones, skin and every other tissue.

2. All animals and vegetables, and all their varied tissues, originated in such bioplasm. This jelly-like substance is found in every living thing, and it is not found in any dead thing. It may be properly called the histological unit, since every tissue and organ of every living body is formed by it.

3. To the eye or the microscope all bioplasm appears alike, whether in man, horse or monkey, oak or fungus. There is no way of distinguishing one kind from another but by observing what they do. One kind remains a single mass of bioplasm during all its life history; others will divide and subdivide in various forms, so as to make all the complex organisms of the living world.

4. Bioplasts, or individual masses of bioplasm, used to be called cells, and are still so called in some text-books. It was supposed they were always covered by an integument called the cell wall. In most bioplasts there is a sort of concentration of material called a nucleus, and in some nuclei there are further condensations called nucleoli. Recent histology has shown that many bioplasts have neither cell wall nor nucleus, and that it is probable that most of the bioplasm in a living body exists as a communicating network. In an embryonic condition, however, it is a single particle, or microscopic mass, which we may term a cell, if we are not misled by the name to regard it as a bladder-like vesicle, instead of an indefinitely shaped particle.

III. THE PHYSICAL FORCES IN BIOPLASM.

1. Bioplasm exists in a colloid state; that is, like glue, gum, etc. Professor Graham taught the distinction between colloid and crystalloid material, especially in relation to the physical processes called *diffusion* and *osmose*. These processes are constantly active in living as well as in non-living matter.

2. *Diffusion* relates to the tendency of fluids or gases to mix intimately even contrary to specific gravity. This tendency varies in different substances. Thus a solution of common salt, which is a crystalloid, has a diffusive power of twenty times as great as a solution of albumen (a colloid) of equal strength.

3. *Osmose* refers to the passage, or separation, of fluids or gases by a membranous or porous diaphragm. Thus in Dutrochet's experiment a membrane or bladder was tied over the large end of a funnel containing colored alcohol. This was inverted in a vessel of water, which fluid passes through the membrane, causing the alcohol to overflow. The process of separation of materials by a membrane, etc., is called *dialysis*, and the passage through the membrane, or *osmose*, is called *endosmose* when it passes inwards, and when outwards *exosmose*. For dialysis the membrane must be moist, hence the advantage of wetting the skin in fevers. Alkaline solutions generally exhibit endosmose, and acids exosmose. Since colloid material does not readily permeate a porous diaphragm, while crystalline solutions pass readily, crystalline poisons may be separated, for examination, from colloid animal fluids, as in the contents of the stomach. The colloid state is not peculiar to organic matter, as seen in hydrated silicic acid, soluble alumina, etc. As colloid substances are as permeable to fluids as membrane, the colloid state of bioplasm permits the flow of currents, as in ordinary dialysis, modified, perhaps, by vitality.

4. All physical forces, as light, heat, electricity and gravitation, act in and upon bioplasm as well as non-living matter, yet vital influence so modifies these forces as to show that it is not identical with them. Gravity tends to bring all things towards the center of the earth, yet a living tree grows upwards in opposition to gravity. Different bioplasts differ greatly as to endurance of heat. Some are deprived of life by a freezing temperature, and many by a heat much below that of boiling water. Yet trout's eggs develop well in ice-water, and die at a moderate temperature, while certain confervæ have their habitat in the boiling water of sulphurous

springs. Human bioplasm is so resistant that men can live in the cold of an Arctic winter, or, as the workers in plaster of paris, may endure for a considerable time the heat of an oven when it is over 500° F. Dr. Dallinger shows that certain infusoria adapt themselves to great thermal changes, provided such changes occur gradually. Different persons show different degrees of resistance to an electrical current, and even the same persons at different times.

The differences between man and animals as to diseases and remedies render many modern experiments inconclusive. Most diseases of man are impossible to produce in animals, and the action of drugs upon them likewise differs. Nitroglycerine, which is toxic to man in 10 drops of a 1 per cent solution will not poison a dog or a hare in three-drachm doses.

IV. THE CHEMISTRY OF BIOPLASM.

1. Bioplasm was called sarcode by Dujardin, proteine by Mulder, and by many, protoplasm. As the latter name was applied to it whether living or dead, Dr. L. Beale proposed the term bioplasm to represent it in its living state. In chemical composition it is nearly identical with albumen or white of egg.

2. The elements O, H, N and C, which form the material of bioplasm, are called *essential* elements. Other substances which are found occasionally associated with it, as sulphur, chlorine, sodium, calcium, iron, etc., are *incidental* elements.

3. Organic compounds, which are especially connected with nutrition and which are only found as the result of the vital activities of bioplasm, are called *proximate principles*, or *organizable substances*. Such are glutine, starch and lignine, from vegetable textures, and albumen, fibrin and casein, from animal substances.

4. Substances derived from the destruction of the proximate principles are called *secondary organic compounds*. Such are urea, uric acid, kreatin, hippuric acid, etc. Some of these have been made in the laboratory, but no proximate principle has been formed artificially. Were it possible it would not have the properties of bioplasm.

5. The chemistry of bioplasm is a difficult if not impossible study, since life departs before analysis. There is also in every tissue a mixture of elementary, formative and retrogressive materials which cannot be separated.

6. As all bioplasm appears alike, although its development and transformation produce materials which differ in physical properties and chemical composition, it is probable that the elements do not combine as in inorganic matter, the ordinary chemical affinities being suspended or modified by the presence of the vitalizing power. Bioplasm, for example, is semi-fluid, yet it will not freeze like water, at 32° F. It is doubtful if it will really freeze until life departs.

7. Bioplasm (when not dormant) is in a state of active molecular change, or unstable equilibrium, since it is constantly appropriating pabulum and transforming itself into formed material or tissues. It is doubtful if ordinary chemical combination occurs, the activities being too transitory for real combination. The elementary atoms or molecules constantly pass through the phase of bioplasm, to be rearranged in the composition of organic products.

8. When bioplasm is changed into formed or retrogressive material, more permanent combination of chemical elements occurs. Free oxygen may be absorbed and complex compounds result, often baffling analysis. If the life of the bioplast is suddenly destroyed, the result is water, albumen and fat. Sometimes fibrin is also formed, which differs from albumen by its spontaneous coagulation, while albumen requires heat, nitric acid, etc., to coagulate it. Certain salts, as sodium chloride, etc., may also result from the sudden death of bioplasm. Fatty matter increases for some time after death. In slower transformations, equivalent to slow molecular death, different materials result, depending on various circumstances, especially the quantity of oxygen present. These materials are fat, sugar, amyloid matter, biliary acids, milk, etc.

9. Many important changes may occur in formed material after production. It may undergo condensation, during which structural peculiarities may be manifested. It may dry gradually, and remain long unchanged, or if fluid may split into sol-

uble or gaseous matter at once. It may combine with oxygen and be eliminated. If it be imperfectly oxidized, it may lead to pathological changes. Thus imperfect oxidization of muscular tissue, etc., may result in fatty degeneration, and similar defect in other organs may lead to an accumulation of uric acid, oxalates and fatty matter in the blood, or to leucin, tyrosin, etc., in the liver.

V. THE PHYSIOLOGY OF BIOPLASM.

The special functions of living matter are the vital properties which are common to all bioplasm. They are what the living can do which the non-living cannot do.

1. *Spontaneous motion* is shown by all bioplasm and distinguishes it from the non-living. We are familiar with various movements among inorganic bodies, but they are wholly dissimilar to the motion of living matter. We see motion produced by the impact of one mass against another. We witness the regular movements of the planets. We observe molecular vibrations in consequence of heat, light or electricity. But in all these cases the body is acted upon by a force exterior to itself, while bioplasm is self-acting. It can originate motion and overcome inertia. The movements of bioplasm are molecular or inherent, amœboid and wandering.

(1) The inherent, or molecular, motions must not be confounded with a microscopic phenomenon called Brunonian motion, which is a vibratile movement of fine particles suspended in fluid. The molecular movements of transparent, jelly-like bioplasm may be seen in the microscope by observing accidental granules, or cavities, which are often imbedded in it. The motion is in all directions, upwards, downwards, or sidewise. Max Schultze compares the molecular motions in a thread of bioplasm to the movements of passengers in a crowded street, some of whom go straight on, while others turn or stop and move on again at their own will.

(2) Amœboid movements are so called because first observed in the amœba, an animalcule similar in appearance to leucocytes, or white blood cells, and other bioplasmic masses. Such are continually changing shape by the protrusion or retraction

of threads, knobs, fringes, or other projections, so that the same form is but momentary. Of course this change is only possible to free bioplasts.

(3) In wandering movement a thread or arm is projected from the mass, along which, as a sort of bridge, the semi-fluid material flows and accumulates at the further end. Thus bioplasts move or wander from place to place. Such motions may be seen in the mesenteric vessels of a frog under the microscope, the white blood cells attaching themselves to the walls of the vessel, then penetrating the wall, and passing through the tissues outside. The stimuli of gentle heat, light, or electric currents accelerate all these movements, while cold or excessive heat, etc., retards them. They also respond to mechanical stimuli.

2. *Nutrition* is the appropriation of new material molecules to replace the old ones as they are changed into tissues or become effete.

The chemical composition of the tissues differs from that of the blood, and still more from the food. There is a decomposition of the pabulum, a selection of appropriate molecules and a rearrangement of such molecules in the bioplasm, quite unlike the chemical transformation of the non-living. It differs from crystallization, which is a deposit along certain axes of attraction of a similar substance in solution, which after crystallization may be dissolved and recrystallized, while bioplasm is nourished from dissimilar substances. It differs also from catalysis, or the phenomena induced by the presence and influence of a third material substance, as when spongy platinum induces O and H to combine. In nutrition there is no known third substance present, but the bioplasm itself selects nutrient chemical elements from the pabulum, dissolving their former affinities, and recombining them after the laws of a vital chemistry. We distinguish between nutrition of bioplasm and the building of tissues, although nutrition may have reference to the nature of the tissues to be formed.

3. *Growth* is the increase of bioplasm within normal limits.

Non-living matter, amorphous or crystalline, enlarges by accretion, or deposit of similar matter on the outside, but bio-

plasm grows by accumulation of nutrient matter in the interior. In inorganic matter the surface or outside is the newest or last deposited, but in a bioplast the outside is oldest. In growth there is also a movement of certain parts of the surface in a definite direction. Dr. Beale says: "Bioplasm alone, of all matter in the world, moves towards lifeless matter, incorporates it with itself, and communicates to it in some way we do not in the least understand, its own transcendently wonderful properties." "The rootlets of the plant extend themselves in the soil because the living matter at their extremities moves onward from the point already reached. The tree grows upward against gravity by virtue of the same living power of bioplasm. In every bud, portions of this living matter tend to move away from the spot where they were produced, and stretch upwards or onwards in advance. No tissue of any living animal could be formed unless portions of bioplasm moved away from one another."

4. *Structural power.* The formation of structures and organs with reference to their special uses or functions is a striking example of the presence of intelligence in creation. In some instances a simple mass of bioplasm suffices all the needs of the living being, as in the protozoa. This unicellular mass extemporizes arms or feet or stomach out of its jelly-like material according to its needs. In most organisms, however, a division of labor is the rule, and the bioplasm divides and subdivides so as to make up the entire organism, in which all the bioplasts are coördinated so as to act in harmony. Each has its appropriate place and function, and subserves the general good, unless disturbed by some morbid agency. The probability that all cells are united by a network of bioplasmic threads renders this easier understood.

The manner in which bioplasm changes from structureless jelly into formed material and structures is a generally neglected part of histology. We distinguish several processes.

(1) *Interstitial deposits.* Bubbles of air may form vacuoles, or oil, pigment, etc., may occur in cells. Vacuoles may be so numerous as to form the bioplasmic mass into a network. According to Heitzman this takes place in every embryonic

cell or bioplast, so that a network is generally seen with enlargements at the intersections. See Fig. 1, Pl. 2. Motile contractions and relaxations in these enlargements he deems to be the primary movement of living matter, communicating by filaments from each particle to those nearest to it, and thus throughout the body.

(2) *Fusion of contiguous material.* Thus certain softened epithelial cells on the surface of mucous membrane may become fluid mucus, and thus, according to some, the matrix of cartilage is formed by cell union.

(3) *Gradual transformation towards the surface.* In the skin, the inner layer of cells, or stratum lucidem, are bioplasmic networks, united by fibrous threads—the prickle cells, so called—but the external layers are gradually transformed into a substance analogous to horn, and in the epiderm, or outer layer, there is no living matter left. Yet this effete layer serves for protection. The formation of hair and nails proceeds upon the same method.

(4) *Linear formation.* As a living particle moves onward it may leave behind a fibrous train which may remain alive or be changed into permanent structure. The sheath and axis of nerve fibrils and the fibrous network of voluntary muscle may have been produced by a modification of this method. In ganglionic nerve fibers from a frog's heart there is a spiral arrangement showing that the constructing bioplasm had a movement of rotation as well as of progression. Fig. 2, Pl. 2.

(5) *Division of nuclear fibrils.* Modern microscopy shows the living matter in most cells to be a network, which is finer, or more concentrated, in the nucleus. Previous to cell division the nuclear fibers are subject to great changes. They become wreathed and twisted so as to resemble a star; they then split asunder and form a double star, after which the cell divides, one of the fibrous stars being in each cell. Fig. 3, Pl. 2. This process is called *Karyokinesis*, and in this way a single particle of bioplasm may be multiplied by myriads.

(6) *Molecular coalescence* is a modification of ordinary solid forms when inorganic particles are aggregated in the presence of organic or living matter. Mr. Rainey and Professor Harding

showed that when lime salts are slowly formed in organic colloids, as gum, albumen, etc., masses occur which are similar to those formed in organized bodies. Thus they produced spheroidal concretions of carbonate of lime, like some urinary deposits, discs like those of Bathybius, lamellæ of shell substance, and imitations of cuttlefish bone, etc. These experiments indicate that calcareous and other deposits in tissues, as fish scales, bone and teeth, may be accounted for by a vital modification of the ordinary forms of concretion.

5. *Reproduction.* Parentage is the universal law of living beings. Abiogenesis, or the spontaneous production of living beings from non-living material, has been taught by some. If animal or vegetable infusions are boiled in flasks and hermetically sealed, infusorial organisms will after a time be found in the flasks. This was considered evidence of spontaneous generation, until it was shown that the germs of infusoria existed either in the atmosphere or in the infusion itself. Drs. Dallinger and Drysdale proved that some germs resist a temperature of 300° F. Pasteur showed that if the atmosphere is filtered by plugs of cotton wool in the neck of the flasks, after boiling, the infusion remained indefinitely free from infusoria, and Mr. Tyndall's elaborate experiments respecting purified air tend to the same conclusion. We may therefore regard the question of parentage as settled, and affirm, with Virchow, "*Omnis cellula e cellula*"—Every cell is from a cell.

(1) Non-sexual parentage is seen in tissue bioplasts and in the unicellular forms of animals and vegetables. It is a self-division of the bioplasm, preceded by a vital movement and division of the fibers of the nucleus. This self-division may be a simple fission, a budding or protrusion and separation of part of the mass, or an endogenous growth, which is a sort of internal budding.

(2) Sexual parentage is the union of a germ cell or ovum with a sperm cell or spermatozoid, by which a new individual is produced. In some species these cells are found in the same individual, and in others the sexes are distinct.

(3) In what is called alternation of generations the ovum

produces an intermediate form, so that the offspring is not like its parent, but its grandparent. Thus the jelly fish or sea nettle is first a ciliated germ, then a hydra-like polyp, which produces colonies of medusæ by division or budding. These become free, enlarge, and propagate germs.

(4) Parthenogenesis, or virgin production, is another variety of generation by which one or more broods may occur without sexual union. The aphides, at the close of autumn, are winged males and wingless females, whose ova lie dormant in winter, but the young of summer produce ten or more sexless generations, and a final brood as before. The eggs of male or drone bees are said to be laid by unimpregnated bees, queens, or even workers. Similar instances occur also in other insects. Cases of fœtation by inclusion (an egg within an egg), and other curiosities of embryology in higher animals, may be similar.

(5) The development of the ovum in higher animals presents an extensive field for study, but a few particulars will serve our introduction to histological structure. The germ cell, or ovum, is a globular epithelial cell of the Graafian vesicle of the ovary. The latter is constituted by an infolding of the surface so that the epithelial covering becomes the lining of the vesicle. The ovum is a product of this epithelial lining, and consists of a vitelline membrane, or outer surface, the vitellus or yolk, the germinal vesicle or nucleus, and the germinal spot or nucleolus. Fig. 4, Pl. 2. The sperm cell, or spermatozoan, is in like manner developed from the glandular epithelium of the seminiferous tubules in the male. After impregnation the self-division or segmentation of the vitellus occurs, preceded by separation of the nuclear fibers and other vital phenomena.

In some animals the entire contents of the ovum participate in the segmentation and development, but in vertebrates a layer of cells is formed by subdivision of bioplasm on the surface of the ovum. This occurs on one side, forming the blastoderm, to which all subsequent processes are restricted. The blastoderm separates into three layers, the epiblast, the mesoblast, and the hypoblast. The outer one, or epiblast,

forms the cuticle and its appendages, and, by folding over the primitive streak, as it is termed, forms also the epithelium of the canal of the spinal cord and of the ventricles of the brain. Some histologists think that it forms the substance of the brain and cord. The middle layer, or mesoblast, forms nervous, muscular, connective, and vascular tissues, and the hypoblast the epithelium of the internal organs. Fig. 5, Pl. 2.

Further details are reserved for future study.

6. DORMANT LIFE.

Life may exist potentially without activity. The material changes we have referred to are not essential to the existence of the power on which life depends, since its activity, or functions, may be suspended. This clearly indicates that the cause of life differs from the material organization. The lack of stimuli, or some unknown peculiarity, causes a living being to remain inactive or dormant, with a suspension of all vital functions. Eggs will remain sound and well preserved for a long time before hatching. Rotifers have been desiccated in heated sand, and revived by moisture, a score of times in succession. The hybernation of bears, frogs, and other animals is a well-known phenomenon. The seed from the hand of an Egyptian mummy has been planted after 3,000 years, and produced perfect ears of wheat. Syncope is sometimes so complete that life becomes dormant. There is no circulation, respiration, nor motion. Cases of trance and catalepsy are similar, and premature burial has occurred. Among Indian fakirs instances of voluntary syncope, or human hybernation, have been witnessed under the strictest precautions against fraud. One was buried for six weeks, and another for ten days.

7. DEATH.

Death is the cessation of vital power, to which disintegration and chemical decomposition succeed. In our view life is not synonymous with spiritual existence, but the result produced by the union of matter with spirit. Life has no real existence apart from living matter more than motion can exist without a moving substance. Life is propagated from one

body to another, and from one cell to another, as flame spreads from one torch to another without loss, or magnetism from one steel bar to another.

1. Somatic, bodily, or systemic death is the removal of the vitalizing cause, or spirit, and is usually indicated by excessive syncope, coma, or dyspnœa. Thus we may have death beginning at the heart, the brain, or the lungs.

2. Molecular death is the cessation of vital power in the organic molecules. It is a constant occurrence during life, and without it there could be no renewal of living tissues by nutrition and growth. It does not immediately cease with somatic death, since hair will grow on a corpse, and the secretion of poison continue some time in the fang of a dead rattlesnake.

8. THE PATHOLOGY OF BIOPLASM.

1. General principles.

Living matter, or bioplasm, is quite ephemeral. After manifesting its functions in assimilation, formation, or secretion, it disappears as bioplasm. It may remain as formed material, or as a sort of skeleton of the tissues, or may be dissolved as effete. Sometimes it remains in a state of dormant life, as the pigment cells of the uvea, or as embryonic cells in connective tissue, which under stimuli act in processes of repair, or originate new pathological growths.

Disease may be defined as excess, defect, or alteration of structure or function. Pathological changes in bioplasm usually depend upon excess or defect of pabulum.

1. Excess of pabulum leads to multiplication and morbid growth of bioplasts, as in inflammation, or as the cells in tubercle and cancer.

If an epithelial cell be ruptured mechanically, or softened by fluid, so that excessive growth of bioplasts occurs, we witness the formation of pus. In pneumonia, etc., the nutrient pabulum is diverted to the lungs, as a focus, and bioplasts rapidly multiply in the air cells. In new growths there is merely an abnormal development of tissue elements.

2. Defect of pabulum leads to shrinking, hardening, and

wasting of bioplasts. Thus we may have contraction and condensation of the liver, kidney, and other glands, or waste of the muscular, nervous, and other tissues. Cirrhosis of the liver is an example. The normal liver cell is a soft, moist substance without cell wall. Its bioplasm, as all others, is nourished from the inside. Now if the cells are bathed with improper pabulum, as alcohol, which renders albumen hard and insoluble, then nutrition is interrupted, they shrink in size, less pabulum is absorbed, and they gradually condense, waste and die. This instance shows the action of alcohol and astringents in restricting the growth of bioplasm, and suggests the close relation of histology and therapeutics.

2. Inflammation.

This is a complex process, partly vascular and partly textural, but closely connected with bioplasm.

1. The phenomena of inflammation since the days of Celsus have been described as redness, swelling, heat, and pain, with impaired or arrested function. They may be studied by placing a drop of acid upon, or scratching with a needle, a frog's foot, tongue, or mesentery, stretched over the stage of the microscope. First there will be seen a derangement of the circulation, producing hyperæmia and congestion. Dilatation takes place, first in the arteries, then in the veins and capillaries, so that red blood cells occur in the latter. The flow of blood at first is more rapid, then slower, the white cells are disposed to linger at the wall of the vessel, and the red cells take the place of white ones in the capillaries. Then exudation occurs. A number of the white cells migrate or pass through the walls of vein or capillary vessel, and red blood cells from the capillary. There is also an escape of liquid plasma, rich in albumen. Fig. 6, Pl. 2.

2. The agencies of inflammation are innumerable. (1) The injurious agent may affect the vessels through the blood and the surrounding tissue suffer secondarily. (2) The injury may affect vessels and tissues at the same time. (3) The alteration in the wall of the vessel may be secondary to alteration of tissue.

3. Several theories of inflammation have been advanced.


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Andral defined it as simple hyperæmia. Henle, Stilling, and others refer the dilatation of the vessels, the accumulation of blood in them, and the subsequent exudation, to paralysis of the vessel wall from excitation of the sensory nerves, or reflex through the vaso-motor nerves. This is termed the neuroparalytic theory. Hoffman, Cullen, and others refer the phenomena to spasmodic contraction of the vessels. This is the neurospastic theory. Beale, Simon, Paget, and Virchow ascribe the phenomena to increased nutritive activity of living matter. This may be called the bioplastic theory.

The formation of pus cells, which are the same as leucocytes, indicates that the blood itself is a factor in inflammation, as well as the vessel wall. Cohnheim maintains the origin of pus corpuscles from blood only and not from fixed tissue bioplasts, but Stricker claims their origin from both blood and tissues. The latter is most probable, since excess of pabulum may produce proliferation in the bioplasts of both. The multiplication of bioplasts by increased nutrition is more comprehensible than the vague theory of a mysterious "irritation" strangely propagated through nerves and vessels.

4. The varieties of exudation accompanying inflammation depend chiefly upon the structure affected.

(1) *Serous exudation*, when occurring on free surfaces, is called serous catarrh; in serous cavities it is inflammatory dropsy; infiltrated in tissues it is inflammatory œdema, and under the epidermis it takes the form of vesicles. In albuminuria and dysentery the serous exudate is albuminous and coagulates spontaneously or by action of reagents, as casts and membranous shreds.

(2) *Mucous exudation* is synonymous with mucous catarrh. There is hyperæmia, swelling of the mucous membrane and follicles, excessive production of epithelial cells and mucous elements. If the growth of epithelial bioplasts be excessive, the discharge will be purulent. Catarrhal pneumonia shows increase of the alveolar epithelium of the lobules connected with the bronchial tubes where the catarrh begins. This may become caseous by fatty degeneration and drying.

In desquamative catarrh of the kidneys there is the charac-

teristic proliferation of bioplasm with albuminoid exudation, and granular cloudiness with falling of the epithelial lining of the tubules. Eczema is a chronic catarrh of the skin from hyperæmia and proliferation of the cells of the papillary layer. The horny layer of the epiderm is destroyed, and the multiplying epithelium cast off.

(3) In *fibrinous exudation* the fluid from the hyperæmic vessels coagulates into fibrin, between whose meshes serum is confined. Pus is generally present. This form generally occurs on the surface of serous membranes, and the coagulated fibrin either glues together adjacent surfaces or forms a slightly adherent membrane, as the false membrane of rheumatic pleuritis or pericarditis.

(4) *Croupous exudation* differs from fibrous, according to Wagner, by originating from a peculiar metamorphosis of epithelium, although others think the croupous network to be like the fibrous network of inflamed serous membrane. The croupous exudate appears as a deposit or membrane upon superficial organs, as the air passages in croup, or air cells in croupous pneumonia. Underneath the exudation the mucous membrane is swollen and hyperæmic.

(5) *Diphtheritic exudation* is from a greater degree of hyperæmia in the mucous surface than in the croupous form, attended with a gangrenous separation of infiltrated parts. Some regard it as an exaggerated croupous exudation, and others, as Buhl, consider it an acute tissue necrosis quite distinct from croup.

(6) *Hæmorrhagic exudations* are those which contain so many red blood corpuscles or their coloring matter as to appear red. This may occur with or without visible injury to the blood-vessels, as in hemorrhagic measles, smallpox, scurvy, etc.

5. By the resolution of inflammation is meant its gradual subsidence, and the return of the tissues to a normal or healthy state. The congestion of the vessels lessens and disappears, and the emigration of the cells ceases. Some of the emigrated cells are removed whole by the lymphatics, while others undergo fatty degeneration and lactification and are then absorbed. Necrosed tissues disintegrate and liquefy, and are

then absorbed. Repair of injured parts is effected by multiplication of tissue cells—each tissue after its kind.

6. In reorganization, after a diminution in the intensity of inflammation, the new cells are organized either into cicatricial or granular tissue.

(1) Cicatricial tissue is seen in healing of closed wounds, generally called healing by the first intention, and in chronic inflammation of the kidney, liver, etc. Microscopically, the cicatricial tissue is of spindle-shaped cells—fibroblasts—which, according to some, are first epitheloid in nature, and then become true connective tissue cells. Green writes also of a sort of adenoid tissue of meshes of fibers inclosing lymphoid cells.

(2) Granular tissue is seen after suppuration in an ulcer or open wound, and is termed union by the second intention. The granulation tissue consists of roundish embryonic cells, occurring in nodules or papillæ upon developing loops of capillaries below. The deeper layers develop into fibrillated cicatricial tissue, while the surface cells appear as pus. Near the normal epithelium, or grafts of epithelium made by the surgeon, and under its influence, some of the pus cells, or leucocytes, remain and become new epithelium. This new epithelium is weaker than the normal, being thin and dry. Fig. 7, Pl. 2.

3. Infiltration.

Infiltration is a morbid affection usually depending upon imperfect nutrition. The constitution of morbid fluids may be considered as a kind of infiltration. Thus fluid pus may be regarded as infiltrated with pus cells, serous fluid with granular corpuscles, epithelium, etc., mucus with fungi, pus, or blood, and milk with blood discs, granular corpuscles, etc.

In infiltrations, properly so called, the new material is not derived from the tissue itself, but is deposited from the blood, after producing a change of form or destruction of tissue. Such depositions may occur from adulteration of the blood or from local causes. Peculiarities of the tissues may influence the form of infiltration. Thus the liver and areolar connective

tissue are most fitted for fatty deposits, the lungs for salts of lime, the kidneys, liver, spleen, etc., for amyloid matter.

1. *Albuminous infiltration*, or cloudy swelling, is a deposit of molecular albumen in the tissues. Virchow regarded it as a nutritive change, on account of which the cells take up an abnormal quantity of pabulum. In the liver and kidneys it is often connected with fatty degeneration and fibrinous exudation.

2. *Serous infiltration* is a deposit in the tissues of serous or sero-mucous substance, producing œdema, as in herpes, eczema, or in blisters from vesication.

3. *Pigmentary infiltration* is derived from the coloring matter of red blood corpuscles. Pigments are usually eliminated by the kidneys or liver, but are sometimes deposited elsewhere, as normally in the choroid coat of the eye and the rete malpighii of the skin. Some pathological cases may be due to local blood stasis or extravasation, and others to wandering leucocytes, which take up particles of pigmentary or foreign matter, and transfer them to other places. Thus dark spots in the lungs may be due to soot particles from the atmosphere taken up by leucocytes of the trachea and bronchi, which are either expectorated or make their way to the lungs. In coal miners such deposits of carbon may render the lungs quite black. Workers in iron dust may have lungs infiltrated by oxide of iron, and a deposit of fine sand in the lungs of stonecutters may set up inflammation. As the color of bile is from the blood, jaundice may be regarded as an infiltration of pigment in the blood.

4. *Fatty infiltration* must be distinguished from fatty degeneration. The first is derived from the blood, and the latter is a metamorphosis of the tissue. In fatty infiltration the fat occurs in the cells as distinct drops of oil, which may be absorbed and deposited elsewhere. In muscular fibers the oily drops are seen between the fasciculi, and not in the fibers themselves, as in fatty degeneration. The "fatty liver" is due to infiltration. The ingestion of fats is followed by its temporary accumulation in the portal blood and deposition in the portal zone of the liver cells. In advanced cases of disease,

as tuberculosis, all the liver cells may become filled, and the bounds of the acini effaced.

5. *Calcification* is the infiltration of tissue with granules or crystals of calcium, or of alkaline salts. Free carbonic acid is a solvent of these salts, and, by its capacity for diffusion, it escapes, leaving insoluble salts in the nutritive fluid. True osseous tissue differs from calcification by the intimate union of glutinous and calcium elements, and the vital modification of molecular coalescence into the concentric lamellæ of bone structure. Calcification of arteries is a secondary affection, following fatty degeneration of the connective tissue. Arthritic deposit of urates in gouty persons is most common in cartilage cells.

4. Degenerative Metamorphosis.

1. *Fatty degeneration* is a metamorphosis of the protoplasm or of formed material, marked by molecular fat globules. Its progress may be illustrated by the degeneration of epithelial cells of internal organs. Their molecules change into fat, and they become granular globules, known formerly as "inflammatory" or "exudation corpuscles," or "corpuscles of Gluge." They are identical with colostrum corpuscles thrown off from the mammary gland after parturition. These globules disintegrate to a fatty detritus, and the last act of fatty degeneration is *lactification.* The fatty detritus may be absorbed as milk. If not absorbed it is partly saponified and partly separated in solid form, as margarin, etc. Finally there is a deposit of crystals of cholesterin, which crystallizes in rhombic tablets, with their long sides parallel. In some cases, when the fatty matter is not absorbed, it undergoes a change into a crumbling material resembling cheese, and the process is called *caseation.* It was formerly regarded as the result of tuberculosis, and considered as the separation of morbid matter, or crude tubercle, from the blood. Tubercle may undergo fatty degeneration and caseation, but all cheesy matters are not tubercular. Such masses in the lungs were considered to be inspissated pus, but Virchow and others show them to be the product of fatty degeneration, with but little water present. Sometimes calcification occurs in such masses.

Fatty degeneration in the coats of arteries may lead to *atheroma*, which begins as fatty metamorphosis and ends in calcification. In fatty degeneration of voluntary muscle the metamorphosed albuminous fiber is seen as rows of minute globules of fat in the long axis of the primitive bundles, while the transverse striæ become indistinct.

In pulmonary emphysema the epithelium is so changed that the fatty degenerated elements are more conspicuous than the normal. Fatty metamorphosis is the regular mode of decomposition for tissues liable to rapid change, as epithelium. Decreased nutrition produces it, especially in non-vascular tissues, as cartilage and the transparent media of the eye.

Softening of the brain is largely due to fatty degeneration. Acute cases may be caused by embolism or thrombosis, interfering with nutrition. White softening is a chronic condition of old age from the gradual diminution of blood supply. Yellow and red softening depend on the proportion of blood pigments present. In all these cases accumulations of fat are present between the nerve fibers.

2. *Amyloid degeneration* is known also as waxy or lardaceous degeneration, and vitreous swelling. It is due to nutritive disturbance, and, next to fatty metamorphosis, is the most frequent and most important degeneration. It is a chronic change of tissue, producing a peculiar homogeneous translucent albuminous substance, which becomes brownish red (like mahogany) on the application of iodine, and violet on adding sulphuric acid.

The amyloid cell is larger than normal, and deformed. Such cells often coalesce. This form of degeneration occurs most often in the small arteries and capillaries, more rarely in interstitial connective tissue.

Corpora amylacea are often ranked with lardaceous degeneration, since they become blue by treatment with iodine and sulphuric acid. They are small round or oval bodies, homogeneous or laminated, found in the prostate gland, the ventricles of the brain, and other parts. Some of the tube casts of the kidney resemble them.

3. *Mucous degeneration* is a transformation of albuminoid

tissues into *mucin*, a material of soft, jelly-like consistence. It is a colloid substance, like gum, albumen, etc. What is called *colloid degeneration* differs from this only in the colloid material being firmer than mucus, and being more generally confined to cells. The colloid or mucous condition is the embryonic state of most tissues, and in the umbilical cord and vitreous humor of the eye persists after birth.

The mucus which normally covers mucous membrane is derived from epithelial cells. Certain cup or goblet-shaped cells occur, which some regard as producers of mucus, and others as the result of mucous metamorphosis, which causes them to swell and burst. The effect of chemical irritants, or chronic catarrh, is not only to dilate the vessels, but to produce a rapid new formation of cells, which are as rapidly destroyed by mucous metamorphosis.

In the mucoid degeneration of cartilage the change chiefly affects the matrix, which splits into fibers, whose ends taper to a point and soften to mucus. In bone the solution of lime salts and liquefaction of basis substance may be simultaneous or otherwise. The colloid change is most common in enarged thyroid glands, in lymphatic glands, and in many new formations. Colloid or mucoid tumors, or tumors which have been thus transformed, are sometimes called colloid cancers, although their structure may wholly differ from cancer. Some forms of ovarian multilocular cysts result from colloid degeneration of the stroma of the ovary, and may be termed a cystic colloid cancer of the ovary.

PART II.

NORMAL AND PATHOLOGICAL HISTOLOGY OF NUTRIENT FLUIDS.

I. GENERAL VIEW OF THE CIRCULATION.

Next in importance to living matter itself is the nutrient material for its physical support. The manner in which this is distributed to the various tissues first claims our attention in a general outline, reserving further details to future study.

1. *Absorption of aliment* is first in the train of vital actions. In plants and in unicellular animals this takes place by simple imbibition, but in higher animals the presence of a stomach, or special reservoir for food, is universal. The alimentary canal is lined with epithelial cells, which in the stomach preside over nutrition, exercising a power of selection so that only certain materials may pass inwards, or be absorbed, while the passage of other substances is resisted. Thus wooara, so fatal by inoculation, is harmless in the stomach, not from modification of the gastric juice, since mixture with gastric or intestinal fluids does not destroy its power. The living cells of the alimentary canal can by no means be regarded as inert or passive, but perform important functions in absorption.

2. *Circulating vessels.* In invertebrates nutriment is conveyed from the alimentary canal to the various parts of the body by a general system of blood vessels, but in vertebrates an intermediary set of vessels exists between the nutritive material and the circulating blood. This intermediate apparatus is of two kinds, like two sets of roots from a single trunk. They are the lacteals and the lymphatics. In mammalia these vessels are abundantly furnished with what are termed glands. The vessels for conveyance of nutrient fluids are, therefore, the arteries, veins, capillaries, lymphatics, and

lacteals. Our plan of study permits only a brief account of their microscopic structure.

The arteries, veins, and larger lymphatics consist of a lining of endothelial cells, flat, irregular in shape, joined edge to edge by cement. Next to this lining we find a layer of elastic tissue, then a layer of transverse involuntary muscle fibers, and an external layer of connective tissue. The arteries are more richly supplied with muscular fibers than the veins. The capillary blood vessels and the lymphatics in general, more irregular in caliber than capillaries, consist of a single layer of elongated endothelial plates joined by cement.

3. *Lacteals.* The blood vessels of the stomach and intestinal canal may absorb many soluble alimentary substances which have passed the epithelial lining, and those of the body may absorb some interstitial fluids, but fatty matters, and many albuminoids, or colloids, after mixing with the fluids of the pancreas, liver, etc., are emulsified and conveyed by the epithelial cells in the villi of the intestine to the lacteal glands. This stimulates the growth and multiplication of bioplasts, which are carried with the fluid pabulum through the thoracic duct into the blood.

4. *Lymphatics.* The lymphatics exercise a selective influence on residual material which may have escaped into the tissues, or which, although partially degenerated, as in lactification after fatty degeneration, may serve for reconstruction. This material is a stimulating pabulum for the growth of leucocytes in the lymphatic glands, as chyle is in the lacteal glands, and the combined products enter into the circulation. The lymphatics form rich plexuses in all tissues and organs whatever, and the smaller are termed lymphatic capillaries. Sometimes, as in the brain, the blood vessels are ensheathed by lymphatics, called the perivascular sheaths. The rootlets of the lymphatics begin in the connective tissue of different organs by a communicating system of crevices, spaces, or canals of various sizes and shapes, which are generally without endothelium. The lymphatic vessels are also connected with lymph sinuses or cavities in various organs, as well as with the serous cavities of the body. Thus the subdural and

subarachnoid spaces of the central nervous system, the synovial cavities, the cavities of the tendon sheaths, of the tunica vaginalis testis, as well as the larger pleural, pericardial, and peritoneal cavities, communicate with lymphatics, and form a continuous system connected with the circulation of nutrient fluid. The cavities above named connect with the neighboring lymphatic vessels by means of holes, or stomata, which are often lined by a layer of polyhedral endothelial cells, called germinating cells, producing leucocytes by their proliferation, which are carried by the lymphatics into the system as white blood corpuscles. Fig. 1, Pl. 3.

5. *Continuity of blood fluid.* From the brief outline given it will be seen that the true circulation of the blood is not confined to the arteries, veins and capillaries, but involves a complicate system of blood vessels, lymphatics, lacteals, large cavities and interstitial spaces. In all this system we find the real blood—the fluid portion—carrying in one part milky fluid, or chyle, in another white cells, or leucocytes, and in another both red and white corpuscles.

The fluid of the blood is called *plasma*, *serum* or *liquor sanguinis*. It is the conveyer of nutriment as well as of effete matter or pathological products. It is a germicide in its normal state, and hence a protection against zymotic diseases. In a case of leukæmia I have known it to dissolve red corpuscles, which again acquired resisting power by the use of ferrum et manganese iodidum. This example illustrates the importance of its study.

II. LYMPH AND CHYLE.

The term chyle is given to the milky juice, or emulsion, with which the lacteals are filled during digestion. Its color is due to fat, partially saponified with soda. It contains, also, chloride of sodium. Its milky appearance is shown by the microscope to depend upon very minute fatty granules suspended in the fluid. Varying numbers of leucocytes are also found in it. Lymph, or the fluid contents of lymphatics, is a more or less alkaline, watery fluid. Both lymph and chyle are similar to the serum, or fluid part of the blood, and, like it, con-

tain much albumen. The constituents of fibrin are found in lymph as well as in blood, although subject to considerable variation. Lymph taken from lymphatics of different regions differs in composition. That taken from the thoracic duct contains many lymph corpuscles, or leucocytes, like the white corpuscles of the blood. During digestion fatty and granular matter is present. The lymph corpuscles are of different sizes, ranging from 1–5000 of an inch to 1–2000 in the duct, and 1–1200 in the peritoneum. Some of the larger contain two or three nuclei and have more active amœboid movement than the smaller. A few red corpuscles are seen, slightly tinging the lymph when allowed to stand. Those histologists who consider the red corpuscles of the blood to be formed from the white ones, look upon these as derivatives, but others regard them as accidental.

III. WHITE CORPUSCLES OR LEUCOCYTES.

In 100 parts of human blood it has been estimated that there are 64 of plasma, or liquor sanguinis, and 36 of floating corpuscles. The majority of the latter are colored, but some are colorless. The colored are called red or colored corpuscles, and the colorless white or lymphoid cells or leucocytes. They appear to be particles of embryonic or elementary living matter, similar to other formative cells. In healthy blood there is one white corpuscle to about 500 red ones, although this may vary to one in 300. Under the microscope the white blood corpuscles vary greatly in size and appearance. When a drop of blood is examined fresh on a slide covered with very thin glass, attention will be called to a few corpuscles paler than the rest and generally a little larger. Under a moderate magnifying power they will appear granular, and some of them exhibit one or more nuclei. With a power of 1,000 diameters or more, and the best lenses, the granulation is shown to be a convoluted reticulum, or network, and the nucleus is a denser or finer reticulum. Careful examination will show that there are great varieties in size and shape. Some are spherical or oval, and others quite irregular. In any form leucocytes are simply floating particles of bioplasm or elementary living matter. Fig. 2, Pl. 3.

The amœboid movements of these leucocytes may be seen in human blood by using a warm stage at nearly the normal heat. The blood of a frog, or other cold-blooded animal, needs no warm stage. The movements of leucocytes show varying degrees of vitality. Some are active, others sluggish, and some inert or moribund. Some contain fat molecules similar to the pus cells in inflammation, and many dormant cells may be quickened by gentle stimulation.

Leucocytes absorb a great variety of things, as milk, oil, carmine, aniline blue, etc. Even red corpuscles may be swallowed by them, and they have been seen to devour one another. Some bacteriologists regard them as destroyers of microbes in the blood, under the term "phagocytes," and consider them to promote immunity from many diseases. Their migration through the walls of blood vessels, and their part in the building of tissues, forms an important factor in pathology as well as physiology.

IV. RED BLOOD CORPUSCLES.

First seen by Swammerdam, in 1658, and in human blood by Lewenhœck, in 1673. More observed than any other structure, yet only partially known, since their formation requires perfect objectives and unusual skill. Most of the mistakes made in histology arise from the employment of too low powers. Thus the red blood corpuscles have been variously described as rings and as simple homogeneous flat discs. Better microscopes and greater care teach us more.

1. *Form and color.* Under moderate powers the red corpuscles of human blood appear usually as flattened discs, with rounded edges and depressed centers. Fig. 3, Pl. 3. They are generally circular in mammals, except the camel and llama, which have elliptical discs. They are also elliptical in birds, amphibia, and fish, except a few fishes of the order cyclostoma, which have circular discs. With higher powers both the circular and elliptical discs are seen to be quite irregular, and even polyhedral in outline. The color of the red corpuscles is due to *hæmoglobin*, which is infiltrated in the filmy framework, or *stroma*, and forms more than 90 per cent of their organic

matter. It cystallizes after being dissolved out of the corpuscles. Its composition is C. 53.85, H. 7.32, O. 21.84, S. .63, Fe. .42.

2. *Size.* Many have attempted measurements of the red corpuscles for the purposes of jurisprudence, but to the present the size is quite uncertain, and the measurements only comparative and approximate. In every specimen of blood examined with high powers corpuscles are seen which are one-half or one-third smaller than the rest, and the number of these smaller ones is often quite considerable, especially in anæmia and other pathological states. There are also very minute corpuscles which have been termed microcytes, or small cells, but which do not seem to differ otherwise from the larger globules. The following gives the average variation in size in different animals, the largest being in Siren lacertina, and the smallest in Moschus Javanicus:—

Musk deer, $\frac{1}{12000}$ of an inch in diameter; goat, $\frac{1}{6400}$; red deer, $\frac{1}{5000}$; horse, $\frac{1}{4600}$; sheep, $\frac{1}{4500}$; cat, $\frac{1}{4400}$; rabbit, $\frac{1}{3600}$; ox, $\frac{1}{3200}$; man, $\frac{1}{3200}$; dog, $\frac{1}{3500}$; ape, $\frac{1}{3200}$; elephant, $\frac{1}{2700}$; eel, $\frac{1}{1200}$; frog, $\frac{1}{1000}$; salamander, $\frac{1}{700}$; proteus, $\frac{1}{400}$.

3. *Effects of reagents.* When specimens of fresh blood are examined with the microscope the red corpuscles show a tendency to adhere by their flat surfaces so as to form longer or shorter chains or rolls, like rolls of coin. As this is not seen in the vessels during circulation, it is probably due to some unknown change. Almost every microscopic specimen of blood contains also red corpuscles, which present the form known as crenate. This is a stellate, or jagged and uneven form, as if a number of minute granules or points projected from the surface of the corpuscle, which changes from a discoid to a globular form. This crenate form is known also as mulberry shape, horse-chestnut shape, rosette and thorn-apple forms, etc. Under high powers the projections are readily seen. Whether due to external agencies or the vital power of the blood is unknown. Water, acid, alcohol, electricity, and many other reagents, produce discoloration of the red globules, the hæmo globin becoming dissolved in the plasma. What is left of the corpuscles is called the *stroma.* The re-

ticulated structure of this stroma has been described by Elsberg and others. Brücke experimented with boracic acid on the blood of Triton, and these experiments were repeated by Stricker and Lancaster, who found similar results with tannic acid. These indicate a double nature in the red globules, a body, or reticulated stroma (œcoid), which is porous, non-contractile, soft, and transparent, and a retractile mass (zooid), containing hæmoglobin. Chloroform changes the zooid into oval ghosts; and further chloroform produces evanescent globules.

4. *Number.* Various methods of counting the blood corpuscles under the microscope have been used, the field of view being divided into squares of known capacity. It is estimated that in a cubic millimeter (about $\frac{1}{25}$ inch) there are 5,000,000 red globules, having a surface of 643 square millimeters.

5. *Structure.* The old opinion of a vesicle with outer membrane and contents is generally abandoned, and histologists consider the red globules to be semi-solid bioplasmic masses of complex structure. Klein, Flemming, and others have referred to a reticulum, and my own observations have convinced me that their structure varies greatly, as might be supposed from their functions as embryonic, adult, or effete masses. In a solution of potassium bichromate, said by Rollet and Elsberg to be neutral in its action, and a magnifying power of 1,000 to 2,000 diameters with the best lenses, the variations in the same field of view are quite striking. Fig. 4, Pl. 3. Some of the discs have a central nucleus and concentric rings, while others are irregular or globular, with numerous projections. After a few hours many become reticulated, as in Elsberg's figures. A large number of them show protuberances from the stroma, which are jelly-like and amœboid, and afterwards break up into fibers and granules, which simulate bacteria or micrococci. It may be that some microbes, so called, are but minute particles of degraded blood discs, or other forms of elementary living matter. This was the original germ theory of Dr. Beale, who considered their rapid multiplication to be in proportion to their degradation. This view will account for some forms of sepsis of autogenetic origin.

V. HÆMATOBLASTS.

In addition to the white and red corpuscles of blood, some histologists describe certain pale circular and oval discs in fresh blood, of small size, under the term hæmatoblasts, or blood plates. According to Ranvier, these seem to be centers of coagulation, as crystals of salt in a solution of the same salt act as centers of crystallization. The name hæmatoblasts was given by Hayem, who considered them intermediate forms in the development of red corpuscles.

VI. BLOOD CRYSTALS.

The chemical constitution of the blood has been an object of much research, especially with the spectroscope. So delicate is this mode of analysis that old blood stains on iron, wood, or linen, may be demonstrated by the chemist for the purpose of jurisprudence, by the absorption lines of hæmoglobin, consisting of two large dark bands to the right of the sodium line (Frahenhofer's line D) being observed in the spectrum. But the best test of the presence of blood is finding hæmin crystals under the microscope. This will, however, be no discrimination between human and animal blood. A drop of blood is dried upon a slide, a small quantity is then scraped off and placed upon another slide, and a small quantity of sodium chloride added. To this add a few drops of glacial acetic acid, put on a cover glass and warm the slide over a spirit lamp until air bubbles appear. The hæmin crystals are in the form of rhombic plates, varying in color from bright yellow to dark brown. Old blood stains on clothing, etc., should be cut out and boiled in glacial acetic acid with a little sodium chloride. After evaporation the crystals are deposited. The hæmin which crystallizes in this way is the hydrochlorate of hæmatin. Hæmatin is the coloring matter of the blood, which forms spontaneously in effusions of blood within the tissues and in blood kept for a long time in vessels. It is always amorphous and of a deep red color. Hæmatin, sometimes called hæmatosine, united with globulin—a substance resembling casein—forms hæmoglobin, the most important constituent of the blood discs. It used to be called hæmato globulin, and hæmato crystal-

lin. It is a crystallizable albuminous substance, and always exists in the body loosely combined with oxygen. On this account it is termed oxy-hæmoglobin, to distinguish it from the same substance deprived of oxygen by reducing agents. Oxy-hæmoglobin crystallizes sometimes spontaneously, but more or less readily with various reagents, or after putrefaction or freezing. In man and most animals the crystals are prisms or rhombic plates of blood-red color. In the guinea pig they are tetrahedric, and in the squirrel hexagonal. Fig. 5, Pl. 3. In old hemorrhagic spots and effusions oxy-hæmoglobin is changed into hæmatoidine, which also yields small rhombic crystals. This substance is considered identical with bilrubin, the coloring matter of the bile. Hæmatoidine differs from hæmatine by containing one part less of iron and one more of water. Hæmatine contains 7 per cent of iron, and as in an average body there are about 100 grammes of hæmatin, the quantity of iron in the whole mass of blood is about seven or eight grammes.

It is an interesting chemical fact that the red globules contain different salts from those of the plasma. They have principally phosphates and salts of potash, while the fluid contains chiefly carbonates and salts of soda. Kuss infers from this that potash salts are more useful than soda when we wish to increase the number of red globules.

VII. ORIGIN OF THE BLOOD CORPUSCLES.

We consider the white corpuscles as elementary or embryonic particles of bioplasm produced by rapid multiplication in the lymphatic glands or in proliferating endothelium in the serous cavities. Some histologists think the red globules to be produced by the transformation of the white ones, and Recklinghausen, Kolliker, etc., describe all the transitional forms. Others contend that they differ so much as to point to a different origin. Malassez considers the red globules the product of invisible nuclei from certain marrow cells, and Hayem claims that they are produced by hæmatoblasts.

The lymphatic system, including the spleen, lymphatic glands and red bone marrow, and perhaps, also, the thymus,

thyroid and supra-renal glands, is chiefly concerned in blood formation. The red bone marrow was first pointed out by Neuman as a place where red globules were formed, and subsequent research confirmed his observations. The giant cells of the marrow (myeloplaxes), as well as of the spleen, liver and lymph glands of the fœtus, have been seen to have a part in blood formation. Ranvier has described such cells in the omentum of young rabbits, and Heitzman in ossifying cartilage. It has even been proposed to call the giant cell angioblast. In fine, we may regard any particles of bioplasm swept into the circulation as leucocytes, or white blood cells, and chemical or structural changes transform them into red ones, while many of the latter may have an independent origin.

VIII. PATHOLOGICAL CHANGES IN BLOOD VESSELS.

I. Lymphatics.

1. *Inflammation* of the lymphatics is termed *lymphangitis.* It is generally secondary to some inflammation of the tissues, and may extend beyond the original affection, as from a wound in the hand to the lymphatics and glands of the axilla. Red and painful streaks may go from the wound to the nearest lymphatic glands. In lymphangitis the contents of the vessels are more abundant and richer in cells. The fluid is often purulent or fibrinous, while the endothelium is swollen and disintegrated.

2. *Occlusion* of lymphatics, or lymphangiectasis, is from inflammatory engorgement, pressure from without, or the presence of parasites or tumor elements.

3. *Lymphatic tumors*, or lymphangiomata, and other vascular new growths will be described hereafter. It must be remembered that the lymph channels afford the most ready means of propagating new growths, such as carcinoma and epithelioma.

II. Arteries and veins.

1. *Inflammation* in arteries is termed *arteritis*, and of veins *phlebitis.* It may be purulent or hyperplastic. In syphilitic arteritis the inner and outer coats are usually more thickened than the middle one. Tuberculous inflammation of the

vessel wall is quite common, tuberculous patches appearing and disintegrating the wall, producing hemorrhage if in an artery, or in a vein admitting bacilli and products of degeneration into the blood.

2. *Sclerosis* is a local thickening of the inner coat of an artery, generally in patches or plaques. The white or yellowish patches are called atheromatous patches and the eroded spots atheromatous ulcers. The whole process is known as *atheroma*. There is often a calcification of the affected spots. Atheroma may result from chronic endarteritis or degeneration. It produces serious obstruction to the circulation and may end in obliterating the artery.

3. *Aneurism* is local dilatation of an artery involving all its coats. The inner and outer middle coats may atrophy, leaving the outer as the only covering. It is generally caused by atheroma or sclerosis, although an embolism may also cause a sac, as in some vessels in the brain, or there may be a hernial protrusion of the inner coats through a weak place in the sheath.

4. *Arterial hæmatoma* is the term given to a mass of coagulated blood from a ruptured aneurism. The rent may be closed by cohering leucocytes, and the part formed into a bulging sac, the interior of which communicates with the lumen of the vessel, while the exterior is formed by fibrin and the clots resulting from the hemorrhage. Such a sac is called *false aneurism*, distinguished from the true by the coats of the vessel forming no part of its wall. If the blood from the rupture strips the outer from the middle coat it is termed a *dissecting aneurism*.

5. *Capillary dilatation*, when general, is termed *capillary ectasis;* when more local, *capillary aneurism*. The first is the result of chronic congestion; the latter may be congenital, as in nævus, or the result of morbid change in the tissue around the capillaries.

6. *Venous dilatations* are known as *phlebectases*, or *varices*, and usually occur from mechanical obstruction. Venous sacculations or sinuses on the hemorrhoidal veins surrounding the anus form hemorrhoids, and dilatation of the veins of the

spermatic cord forms varicocele. Varicose ulcers are apt to form by inflammation of varicose patches of skin, and thrombi in dilated veins may calcify into phleboliths.

7. *Varicose aneurism* occurs from the adhesion of a true aneurism to a vein, resulting in absorption of the walls, and a communication between the vessels. Occasionally, as from a wound, we may have a connection between an artery and a vein without an aneurismal sac. This is termed an *aneurismal varix.*

IX. PATHOLGICAL CHANGES IN BLOOD.

1. Variation in amount.

1. *Plethora*, or increase, may be produced artifically by injection in animals, but is only temporary. The rapid destruction of red corpuscles and excretion of water by the kidneys soon brings back a normal condition. Some doubt if real plethora exists in man, since excessive food does not increase the number of corpuscles, but produces fat. Yet a difference in individuals is perceptible, and we term a florid stout person plethoric.

2. *Oligæmia*, or decrease, occurs after hemorrhage, but is rapidly relieved by the absorption of fluid from the lymphatics.

2. *Variation in elements.*

1. *Hydræmia*, or excess of water in blood. Not uncommon temporarily after drinking much fluid, but rapidly removed by kidneys and skin. In chronic nephritis it becomes permanent from interference with the secretion. The water is also excessive in anæmia and when there is decrease in albumen.

2. *Hypalbuminosis* and *hyperalbuminosis* designate reduction and increase in albumen. Chronic diarrhea and albuminurea leave the blood deficient in albumen, while the loss of the watery element in cholera, and excess of food, produce a relative increase.

3. *Anæmia* or *oligocythæmia* refers to diminished number of red globules. It may occur after hemorrhage and in many chronic or wasting diseases. Chlorosis is a disease in young women, chiefly due to poverty of red corpuscles or oxygen carriers, and manifested by paleness, fatigue, and debility.

The loss of blood necessary to produce death varies according to age, nutrition, etc. The loss of one pound generally produces syncope, and of four to six pounds usually causes death. In newborn children the loss of a few ounces is dangerous. In pernicious anæmia the only pathological change is progressive and extreme diminution in the number of red corpuscles. In some cases the number of red globules is reduced to 500,000 per cubic millimeter. Several forms of apparatus for counting the corpuscles have been devised. That of Zeiss, after Thoma, is simply an eye-piece micrometer divided into squares, with a device for mixing the blood with a 3 per cent solution of chloride of sodium, in the proportion of 99 parts to 1 of blood. The area of the squares being known, it is easy to calculate the number.

4. *Leucæmia* or *leucocythæmia* is an increase in the number of white corpuscles, with a decrease of red ones, so that from the normal standard of 1 to about 300 red globules they may be 1 in 20, or even less. There is usually hyperplasia, or increased size, of the lymph apparatus, either spleen, lymph glands, or bone marrow, singly or combined. Mild cases may be transitory, as in pregnancy and many diseases. The white cells in leucæmic blood are of different sizes, and on this account some have tried to locate their origin, but unsatisfactorily. Occasionally in this disease needle-like octohedral crystals, called Charot's crystals, are found in the blood. Erlich has recently shown a difference in white blood cells in their power of absorbing eosin. He terms such as absorb it, *eosinophilous* cells, and considers them multiplied in disease of the blood-making organs, while ordinary white cells are alone increased in acute cases of leucocytosis.

5. *Poikilocytosis.* Under this name is described the irregular forms of blood discs occurring in debilitating diseases, especially in progressive pernicious anæmia. A large number of minute cells have given rise to the term *microcythæmia*, and abnormally large cells to macrocythæmia. Such terms are unnecessary. In the account given of the structure of red corpuscles the presence of cells of various sizes and irregular forms was referred to in normal blood. As some blood cells

are embryonic or constructive, and others carriers of effete matters, it is but natural that they should exhibit different forms and act differently with reagents. The normal process of disintegration of the red corpuscles may be exaggerated by various morbid influences. They rapidly crumble into fragments under high temperature, or from the action of chlorate of potass, pyrogallic acid, sulphuric acid, certain poisonous mushrooms, and the venom of some serpents.

3. Variation in substances held in solution.

1. *Thrombi and emboli.* When coagulation occurs in the vessels during life the process is called *thrombosis*, and the coagulum a *thrombus*. A fragment of a thrombus carried by the blood until it is arrested in a smaller vessel is an *embolus*. The formation of a thrombus may be seen in the web of a frog's foot under the microscope by injuring the vessel mechanically or chemically. Thrombi formed during life are distinguished from *post-mortem* clots by their greater firmness and consistency.

According to Schmidt's views, now generally adopted, fibrin does not exist in solution in the blood, but results from the interaction of two substances, *fibrinogen*, which is held in solution in the plasma, and *fibrinoplastin*, or paraglobulin which, together with a third material or ferment, is held in the white corpuscle. On the death of white corpuscles the fibrinoplastin and ferment are set free, and, by their action upon fibrinogen, produce fibrin.

Coagulation within the blood vessels during life is prevented by the motion of the blood, but chiefly by the integrity of the endothelial lining. If the latter be destroyed, or the motion retarded or stopped, the blood coagulates. When an artery is tied coagulation occurs up to the first branch, and the thrombus thus formed is red, since it contains all the elements of blood, but when the lining endothelium is injured, the white corpuscles adhere to the eroded spot, and by their death produce fibrin, called the pale or parietal thrombus. This may occur in the heart, an artery, vein, or capillary, or in the lymphatic vessels. A portion of such thrombus may be

washed into the general circulation, or detached portions of diseased valves, etc., may be carried into the blood and produce embolism in the arteries, capillaries, or some branch of the portal vein. This is invariably followed by partial or complete suspension of function in the part thus deprived of nutrition.

Mechanical thrombi and emboli do not necessarily produce pyæmia or septicæmia, only as they become foci for septic poison. They may be organized into new connective tissue in the place where they lie, or fatty degeneration may begin in the center and form a pap-like mass, ending in lactification and absorption.

2. *Altered hæmoglobin.* Hæmoglobin readily unites with various gases. With oxygen it forms oxyhæmoglobin and gives the bright red color of arterial blood. With a small proportion of carbon dioxide it produces the dark red color of venous blood, and with a larger amount, as in death from suffocation, a nearly black color. Combined with carbon oxide, as in inhalation of burning charcoal fumes, and some kinds of illuminating gas, the blood becomes a bright cherry red and there is absence of post-mortem coagulation.

Diminution of hæmoglobin, as in leucæmia, produces a pale red blood. Sometimes, after severe burns and certain poisons, as well as in septicæmia, the hæmoglobin is dissolved out of the red corpuscles and is held in solution by the serum. This state is known as *hæmoglobinæmia.* When it produces a flow of nearly black urine it is *hæmoglobinuria.*

4. Presence of abnormal elements.

1. *Melanæmia.* After severe or long continued malarial intermittents, the blood may contain granules of black, brown, or yellow pigment, probably the result of destroyed red globules. The granules may be free in the plasma, or inclosed in round or spindle-shaped cells of various sizes. Some of these cells have amæboid motion. Occasionally they appear cylindrical, and more or less fractured. Melanæmia is generally accompanied by decrease of red corpuscles (oligocythæmia) and temporary increase of white globules (leucocytosis).

There can be little doubt of the destruction of the red globules by the malarial poison. Some suppose them to be destroyed in the spleen or liver, and others in the vessels, and regard their deposit in the spleen and other organs as secondary.

2. *Gluchæmia*, also called *mellitæmia*, and from its effect upon the kidneys *glycosuria* and *diabetes*. It refers to the presence of sugar in the blood, stimulating the urinary secretion, which also contains grape sugar. Various methods of testing the urine for sugar have been proposed. The readiest are the fermentation test, and Fehling's solution. A few drops of the latter boiled with suspected urine will throw down a red deposit of oxide of copper if sugar be present. Sometimes *inosite*, or muscle sugar, is found in diabetic urine. This does not reduce Fehling's solution but changes it to a green color.

3. *Acetonæmia*. The coma which occurs in the latter stages of diabetes is considered to be due to the action upon the nervous system of a substance called *acetone*, a derivative of acetic acid. This condition is called acetonæmia. Acetone is found in the blood in other diseases besides diabetes.

4. *Cholæmia* is the presence of bile in the blood. This is generally from reabsorption caused by mechanical obstruction to its flow into the intestines. The biliary coloring matter colors nearly all the fluids and tissues yellow, producing icturus or jaundice. Bile in the blood dissolves the red globules and sets free the hæmoglobin.

There is another form of jaundice, sometimes called hæmatogenous or blood icturus, which is produced by the transformation of the blood pigment of destroyed red globules into bile pigment. Some regard the icturus of phosphorus poisoning, etc., as produced in this way.

5. *Uræmia* is the retention in the blood of matter which is usually excreted by the kidneys. Some refer to the condition as lithæmia, but whether urates or lithates are found actually in the blood is uncertain. As albuminuria generally precedes uræmic coma the urine should be tested for albumen, by boiling and nitric acid. It has been suggested that in uræmia the urea is changed into carbonate of ammonia, since the injection of that substance into the blood produces similar symptons.

Uræmia may occur from any disease of the kidneys which obstructs the secretion of urine.

6. *Ammonœmia.* Retention of urine and septic inflammation of the bladder may lead to urinary decomposition and the formation of ammonia, which passes into the blood, exhibiting its presence by fever, vomiting, strong ammoniacal breath, and chronic catarrh of the intestines.

7. *Hydrothionœmia*, or sulphuretted hydrogen in the blood, produces its poisonous effects of general collapse, and the urine gives to acetate of lead paper the reaction of the gas.

8. *Chylœmia*, or molecules of fat in blood, may occur after a meal of fatty materials. In larger drops—lipæmia—fat may be found in diabetic blood, and after injuries.

9. *Accidental products.* Air, fatty degenerated epithelial cells, bits of detached valves of the heart, emboli or portions of thombi, and calcareous plates from the aorta, may also be found in the blood.

10. *Parasites* are living organisms inhabiting other living organisms from which they derive their nutriment.

a. Plants. 1. The schizomycetes or bacteria play the most important part in pathology. Many are innocuous, but others, by their great multiplication, or by abstracting nutriment or oxygen from the tissues, or by the irritation of their poisonous products, cause many forms of disease, both of structure and function. As the serum of the blood is an excellent germicide, bacteria are rarely found in it, although they or their spores may be conveyed by the blood vessels or lymphatics to internal organs, where they multiply. The details of bacteriology form an extensive study, but our present purpose will be served by reference to the principal forms of pathogenic bacteria. The microscopic forms or appearance are by no means sufficient to distinguish disease-producing species from those which are innocent. For this purpose it is necessary to cultivate the bacteria on artificial media, and reproduce the disease by injecting the culture into another animal. Such procedure involves great care and skill in laboratory experiments. It is generally necessary to stain the specimen and examine with oil-immersion lenses in connection with an achromatic or Abbe

condenser. The staining is done by spreading a layer of the blood, sputum, etc., between two thin covers, separating the covers, and passing them rapidly through the flame to coagulate the albumen. They are then stained with some of the aniline dyes and the excess of stain removed by water or alcohol. Sometimes a contrast stain of some other color is used. Some kinds of bacteria are more difficult to demonstrate than others, and tissue sections more difficult than fluids. The details of technology must be referred to the intermediate course.

Bacteria was a term formerly appropriated to bacilli, but is now used generically. They may be classed according to form into *micrococci*, *bacilli*, and *spirilla*. The micrococci are spherical or oval. They may occur singly or in groups. Chains of cocci are called *streptococci*, those forming irregular clusters *staphylococci*, double ones are *diplococci*, and groups of four, *tetragoni*. Sometimes groups of four, sixteen, etc., are seen resembling packets bound with cords at right angles; these are termed *sarcinæ*. The bacilli are rod shaped, and sometimes occur in chains called *leptothrix*. Some bacilli are constricted in the middle, or dumb-bell shaped, and others are rods with parallel sides and rounded, square, or concave ends. Bacilli which are curved on the long axis are called *commas*, or *commabacilli*, and a chain of them forms a *spirobacterium* or *spirillum*. Fig. 6, Pl. 3.

Pathogenic cocci. 1. The cocci of pus. (1) Staphylococcus pyogenes aureus. (2) Staphylococcus pyogenes salivarius (3) Streptococcus pyogenes. (4) Streptococcus septo-pyæmicus. (5) Streptococcus salivarius septicus. (6) Streptococcus pyogenes malignus. (7) Streptococcus articularum. (8) Micrococcus pyogenes tenuis. (9) Micrococcus gonorrhæa—gonococcus. This is a diplococcus, sometimes in groups of four. (10) Micrococcus subflavus. (11) M. tetragenus. (12) M. Pasteuri (found in saliva of healthy persons, produces septicæmia in rabbits).

Pathogenic bacilli. (1) Bacillus anthracis. (2) B. ædematis maligni. (3) B. of symptomatic anthrax-rauschbrand. (4) B. typhic abdominalis. (5) B. pneumoniæ-pneumococcus. (6) B. tuberculosis (considered the origin of tuberculo-

sis, including lupus). (7) B. lepræ. (8) B. mallei (of glanders). (9) B. murisepticus. (10) B. diphtheriæ. (11) B. of syphilis. (12) B. of chicken cholera. (13) B. of diphtheria in pigeons. (14) B. tetani. (15) B. of swine plague.

The spiro bacteria. (1) Spirillum choleræ asiaticæ-comma-bacillus. (2) Spirillum of Finkler and Prior, and Sp. tyrogenum. (These greatly resemble S. choleræ, but are not as pathogenic.) (3) Sp. obermeieri (these are long spiral threads, found in blood during the fever of remittents).

b. Animal parasites in blood. (1) Protozoa. Of this class of unicellular animals, the malarial parasite—*Plasmodium malariæ* of Laveran—has attracted attention. Various shapes are described, both intra-corpuscular and extra-corpuscular, but some writers hold that they are but changed blood corpuscles. Some of the forms described are flagellated, and quite motile. Flagellated protozoa are found sometimes in the blood of healthy rats, hamsters, and fishes (Hæmatomonas or Trichomonas), as well as in blood of horses and camels affected by a disease called in India *Surra.*

2. *Vermes.* (1) The filaria sanguinis hominis, a microscopic worm found in warm countries like India, sometimes occurs in the blood and urine of patients having chyluria and hæmaturia. It produces lymph obstruction and local inflammations. It is thought to spread by the agency of mosquitoes. (2) Distomum hæmatobium. In certain cases of tropical dysentery in Egypt, Bilharz found this parasite in the portal vein. It is a trematode worm, and its eggs collect in the bladder and intestine, producing inflammation and hemorrhage.

Trichinæ, and the embryos of cysticerci and echinococci, are rarely found in blood.

11. *Ptomaines and leucomaines.*

Ptomaines are alkaloids resulting from the putrefaction of albuminoid substances, as bacteria, etc. Leucomaines are similar substances resulting from albuminoid decomposition during life. Ptomaines are termed post-mortem alkaloids. The poisonous effects of certain articles of food when in incipient putrefaction first attracted attention to this subject, and

many experiments have been made in order to isolate the chemical constituents of decomposing nitrogenous substances, as in poisonous sausage or cheese.

Selmi, in 1872, read a paper before the Academy of Sciences at Bologna, describing experiments which enabled him to identify and characterize the ptomaines of cadaveric matter, and since then there have been important contributions to medical literature respecting it.

The following is a list of the more important ptomaines and leucomaines:—

1. *Cadaveric alkaloids*, or ptomaines formed during putrefaction of muscles and viscera of mammals. (1) *Choline*, obtained from ox bile in 1849. It is not poisonous, save in large doses, when it acts like muscardine. After seven days it is decomposed into other substances. (2) *Neuridine*, a base which appears three days after death. (3) Other bases, called *cadaveric putrescine* and *saprine* are also non-poisonous. (4) Among the poisonous alkaloids we find *mygdalein*, *neurine*, *mydine*, *mydatoxine*, *methylquanidine*.

2. *Ptomaines from putrid fish*, as *muscarine*, identical with the alkaloid from the fungus agaricus muscarius and *gadinine*

3. *Ptomaines from cheese. Tyrotoxicon.*

4. *Ptomaines from poisonous mussels*, as *mytilotoxine*, and the non-poisonous *betaine* or *oxyneurine*.

5. *Leucomaines* produced in the normal living body. *Creatinine*, which with others produces uræmic poisoning. *Salamandrine* from the poisonous secretion of the salamander. (Some think serpent poison due to some alkaloid.) *Xanthocreatine*, *adenine*, etc.

6. *Peptic alkaloids.* A solution of peptone, produced by the action of pepsin on albuminoids, produces symptoms of poisoning when injected into the circulation. This led to the thought that cadaveric poison might be due to peptone, and Brieger has separated from peptone, made by the action of pepsin on fresh fibrin, a poisonous substance called *peptotoxine*.

7. *Pathogenic ptomaines.* The ptomaine of Asiatic cholera is said to have been isolated by Villiers and others, and the ptomaines of typhus and of tetanus by Brieger. The subject is yet in an experimental stage.

12. *Pyæmia and Septicæmia.*

The views of surgeons respecting the febrile and other constitutional disorders following injuries have been greatly modified by the germ theory of disease. Billroth says: "By septicæmia we understand a constitutional, generally acute disease, which is due to the absorption of various putrid substances into the blood, and it is thought that these act as ferments in the blood and spoil it so that it cannot perform its physiological functions." "Pyæmia holds the same relation to simple inflammatory and suppurative fever that septicæmia does to simple primary traumatic fever; it is characterized by intermittent attacks of fever and by the frequency of metastatic abscesses and metastatic diffuse inflammation." Cheyne says: "Septicæmia is a complicated affection, and probably arises under several circumstances. Continued absorption of the poisonous material (leucomaines) from wounds will keep up a feverish state with all the symptoms of septicæmia, and if long continued may end fatally. In other cases the micrococci grow in the tissues of the wound and pour their products, or ptomaines, as they are called, into the blood; here micrococci may be found in the blood, but the essential seat of disease is in the tissues. In a third form micrococci grow in the blood, and, multiplying there, give rise to the symptoms. In a fourth form organisms grow in the blood, but they belong to the class of bacilli. The last two cases correspond to what is found in the lower animals. In them septicæmia is caused by more than one form of organism growing in the blood and giving rise to symptoms and post-mortem appearances which can only be classed together as septicæmia." The results of practical experience combine with microscopical observation to show the advantages of great cleanliness and antiseptic treatment in all surgical cases of importance.

Plate II

Fig 1. Network in Bioplasm – after Heitzman.

Fig 2. Spiral ganglion of nerve from frog's heart.—(Beale)

Fig 3. Neuclear Division.

Fig 4. Ovary. Graafian follicle & ovum.

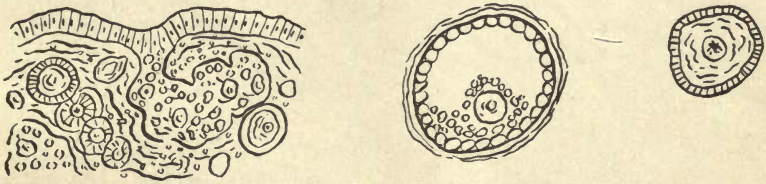


Fig 5. Blastoderm.

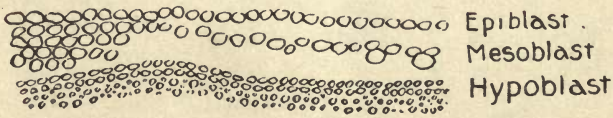
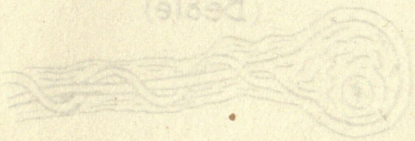


Fig 6. Migration of cells.

Fig 7. Granulation-tissue.

Plate II



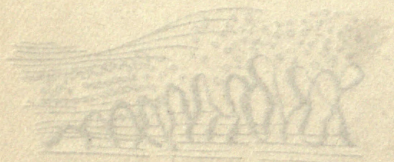


Plate III

Fig 1. Endothelium & germinating cells.

Fig 2. White blood cells or leucocytes.

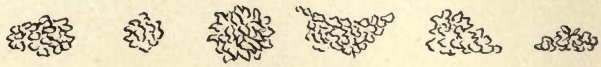


Fig 3. General view of red blood-discs. Man. high-power

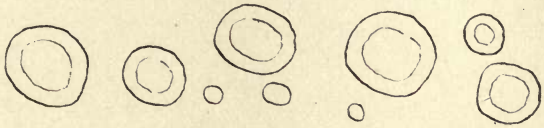


Fig 4. Structure of Red-corpuscles.

Fig 5. Blood crystals.

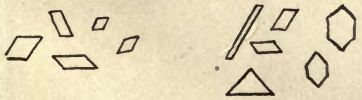
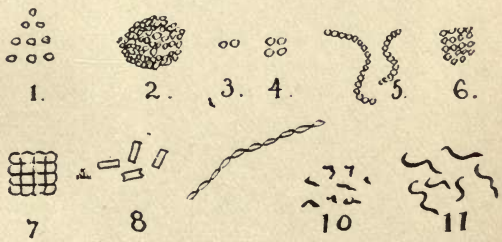


Fig 6. Forms of Bacteria.



1. Micrococci 2. Zoogloea. 3 Diplococci. 4. Tetragoni.
5. Streptococci 6. Staphylococci. 7. Sarcina 8 Bacilli.
9. Leptothrix. 10. Comma bacilli. 11. Spirillum.

(INTERMEDIATE TERM.)

ELEMENTARY TECHNOLOGY.

I. THE SIMPLE MICROSCOPE.

1. Lenses.

Ancient Assyrian lens from Sargon's palace, Nimroud, B. C. 721.

Two ancient glass bosses in British Museum, B. C. 270—controverted.

Pliny speaks of glass globes used as burning glasses—minutely engraved gems—etc. Yet essentially the microscope is modern. Spectacles for old men referred to A. D. 1299. From Malpighi in 1661 to Di Torre 1771, the most ingenious plans were made to construct and use very small lenses. The discoveries of Lewenhœck, Hook, Lieberkuhn, Hewson, etc., were made by patient industry with these, often constructed by themselves. Different kinds of lenses, Fig. 1, Pl. 1.

2. Optical principles.

Optical principles few and simple depend on laws of light *Law* a mode or order of things. Nature of light not needed to be known, but laws.

1. Rays from a luminary go in straight lines.

2. Rays from a rarer to a denser medium are refracted (bent) *towards* a perpendicular, and *vice versa.*

3. The sines of the angles of incidence and of refraction are a constant ratio for each substance (refractive index).

4. The angles of incidence and reflection are equal.

In Fig. 2, Pl. 1, A B is the surface of denser medium, C D the perpendicular, E F refracted ray, G reflected ray, a b sine of angle of incident, a′ b′ sine of angle of refraction.

Indices of Refraction.

From vacuum to air 1.00294
" " " water 1.336
" " " Canada balsam 1.540
" " " Crown glass 1.530
" " " Flint glass 1.6
" " " glycerine 1.475
" " " oil of cloves, etc., 1.535
" " " diamond 2.439

3. Visual angle.

The angle formed by the intersection of the rays from the extreme points of an object. All objects with the same visual angle appear of the same size. Thus, 1, 2, 3, Fig. 3, Pl. 1, although different, appear of the same size because of the same visual angle.

We bring a minute object near the eye to increase the visual angle and get as large an image as possible. The structure of the eye makes a limit to this—variety—yet average standard of distinct vision 10 inches. A convex lens increases the power of the crystalline lens of the eye and enables an object in its focus to be seen at a larger visual angle, or magnified. Comparing focal lengths of lenses with the average standard (10 inch) a lens of 1 inch focus magnifies 10 diameters $\frac{1}{2} = 20$, $\frac{1}{4} = 40$, etc.

4. Faults of lenses.

1. Spherical aberration. Errors due to the spherical surface of a lens.

The axial ray A, Fig. 4, Pl. 1, being perpendicular to the surface of the lens, is not refracted. Rays near the axis, as C C, are slightly bent and focused at c, but lateral rays, as R R, are bent to r, so that the margin of the image formed at c is misty and illy defined. Spherical aberration may be somewhat corrected by intercepting the lateral rays with a stop or a diaphragm, but there is loss of light.

Dr. Woolaston showed that spherical aberration could be nearly removed by combining two plano-convex lenses of focal lengths as 1 to 3 with plane sides to object, this more im-

proved by Holland's Triplet, with a diaphragm in front of upper lens. Further improvement was made by the Steinheil loup (as it is called) and the Brücke lens. The former is an achromatic doublet, and the latter an addition to it of a concave eye lens which magnifies more the further it is drawn from the loup or doublet. Simple microscopes are used as hand lenses, or as dissecting or preparing microscopes.

2. *Chromatic aberration* is due to the unequal refrangibility of the colored rays composing white light. Thus the violet ray V, Fig. 5, Pl. 1, is focused nearer the lens than the red ray R, and the other rays of the spectrum are intermediate. Different sorts of glass vary in the proportion between refractive power and the dispersion of the colored rays, hence it is possible to calculate curves of such ratios as shall overcome chromatic aberration when lenses of different kinds of glass are combined, as in telescopes. Newton's failure, Euler's hint from the eye, Dolland, etc.

Achromatic objectives for the microscope aim to overcome both spherical and chromatic aberration. Generally triplets, often complicate; different formulæ. Wenham's formula connects four convex lenses by one concave of flint glass. This has reduced the price of good lenses.

Opticians usually aim to unite the extreme red and violet rays, but, on account of the irregular proportion of refraction of colored rays by different glass, the best objectives have some imperfection. Professor Abbe and Zeiss, after years of experiment, obtained new glasses and constructed objectives which unite not only the extreme or mean rays, but nearly all in one beam of white light. They are called Apochromatic lenses. Fluorite is also used in their construction.

5. *Effects of cover glass.*

Microscopic objects require a cover glass for preservation and for the safety of the objective, but its use produces aberrations easily seen with high-power objectives. An objective which defines well without a cover will be imperfect if a cover be used.

In Fig. 6, Pl. 1, rays from a luminous point, or object, are

represented as spread out by refraction through the cover glass so that the rays from the object C pass through the edge of the lens B as if the focus was at E, while the more central rays have their apparent focus at D. Hence, with a thick cover glass there must be imperfect definition. For high powers the thinner the cover the better. Optician's sizes known as 1, 2, 3. If there were no cover glass all the rays would diverge from C, and the objective would require to be *Aplanatic* (free from error), or having all the rays brought to the same focus. But since with a cover glass the marginal rays apparently diverge from a nearer focus than the central rays, the objective will only define well when it is what is called *under corrected.* The increased curve of the convex or crown lens renders the flint lens unable to neutralize all the spherical aberration. An opposite condition is termed *over corrected.* A flatter crown lens and a deeper concave flint cause the marginal rays to have a longer focus than the central ones. An aplanatic objective can be made into an under-corrected one by causing the back lenses to approach the front lens. For this purpose a screw collar is provided in the objective which moves the lenses to and fro. It is better it should move the back lenses than the front. Another way of obtaining the same result is to cause the eye piece to vary in distance from the objective by means of a draw tube. Such arrangements are needed in high power work to compensate for thickness of cover glass, and also for varying tube lengths of different opticians.

6. *Dry and immersion objectives.*

An oblique ray from the cover may pass away from the objective, while in water, whose refractive index is higher than air, it is bent towards the lens, as in Fig. 7, Pl. 1. In homogeneous immersion objectives, where oil of cedar, or thickened glycerine, etc., are interposed, still more rays are utilized. This light-grasping power is expressed by the term Numerical Aperture.

7. *Numerical aperture.*

Numerical aperture must not be confounded with the older term, angle of aperture, which merely expresses the relation

of the diameter to the focus of the lens. The larger angle gives better definition of objects in the focal plane, but moderate angles give more penetration, or define to some extent, below the exact plane.

Numerical aperture is a standard of comparison with all kinds of objectives, and gives the light-grasping power of the entire combination. For instance, if a dry objective could take in all the rays of the maximum air angle, or 180°, a water immersion of N A of 96°, or an oil or homogeneous immersion of 82°, would be equivalent.

The unit of N A is the maximum air angle of 180° = N A 1.00.

To illustrate, suppose an objective of 60° air angle (.5 N A) transmits a circle of rays of ¼ inch diameter, then one of 97° (N A .75) will transmit one equal to ⅜ inch diameter, one of 180° = 96° water angle, or 82° oil angle (N A 1.00) will = ½ inch diameter, 180° water angle = N A 1.33, transmits a circle of ⅝ inch diameter, and 180° oil angle (N A 1.52) = ¾ inch diameter.

II. THE COMPOUND MICROSCOPE.

1. *General view.*

In its simplest form the compound microscope consists of two convex lenses, Fig. 8, Pl. 1, A the eye glass or ocular, B the object glass or objective. The rays from an object, O, in the focus of B, form a large but inverted image at a distance on the other side, which is again magnified by A. The magnifying power of a compound microscope may be increased by lengthening the distance between the objective and the eye glass, but since there are limits in practice to this mode, a stronger eye glass may be used with the same length of tube. Since magnification brings every error into prominence, it is also best for increased power to use more powerful and better corrected objectives. On account of the divergence of the rays from the objective, a collecting lens, C, called a field glass, is interposed between A and B. This is usually combined with A and called the eye piece.

The greatest improvements in modern microscopes relate to the objectives, removing spherical and chromatic aberrations, and collecting the greatest possible amount of light rays from the object observed. The various kinds of objectives are termed air lenses, or dry objectives, water immersion systems, and homogeneous immersion systems, the principles of which have been explained. The line of future improvement will be in the more perfect illumination of the object observed.

The German opticians usually distinguish their objectives by letters, the French by numbers, and the English and American by their equivalent focal lengths, or the focal lengths of lenses to which their amplification corresponds.

2. Eye pieces.

The eye piece most generally employed is the Huygenian. It has two plano-convex lenses whose foci are as 1 to 3, with plane sides next the eye and a diaphragm or stop between them. Another form, called the positive or Ramsdem eye piece, is sometimes used. It is similar to the Huygenian, with the flat sides of the lenses outwards.

The Orthoscopic eye piece is useful for low powers, since it gives a large field of view. It has a double convex field lens and an achromatic eye lens, but no diaphragm. The Periscopic has a triplet eye lens and a double convex field lens.

A new eye piece, made by Zeiss and by Powell & Lealand is called the Compensating eye piece and used chiefly with the new apochromatic objectives, but serviceable with ordinary achromatics. They have an eye glass of a single plane lens, and a field lens which is an achromatic triplet. As these are numbered according to amplification, it is easy to know what power you are using. Thus a 1 inch objective=10 diameters. With eye piece 12=120 diameters. Or this eye piece with ¼ inch objective=480 diameter. These numbers refer to the proper length of tube. Sometimes an amplifier consisting of a concave lens (generally achromatic) is used between the eye piece and the objective and may double the power of the eye piece.

3. The mechanism of the microscope.

Mechanical contrivances are for holding the optical parts in proper position and for convenience in manipulation. Many forms in use. Three classes.

First class, made of hard metal so that screws and racks allow more work without "backlash." Most elaborate every way. Not mere expensive luxuries, since the most delicate work requires the best instruments.

Second class, or students' microscopes, have stands of fair workmanship but reduced to great simplicity. May have objectives equal to the first class but adapted to moderate powers and everyday work.

Third class, or educational, are cheap stands and lenses, fit for school and family demonstrations but not for research.

1. The base. Two principal forms, the horseshoe and the tripod. The latter best. Must be firm with the instrument in any position.

2. The arm carrying the body must be free from vibration. English and American microscopes have two forms, the "Ross Model," with end of tube on arm, and the "Jackson," with arm on side of tube. The Powell & Lealand stands have the Ross Model and are good, but a cheap stand on Ross Model is worst of all. Jackson form most used, but the supporting arm is often too short.

3. Inclination of body. French and German students' instruments can only be used perpendicularly. An inclinable body and stage are best.

4. Coarse and fine adjustment. The coarse adjustment is often by rack and pinion. Sliding tubes are fairly efficient if cloth lined. The fine adjustment is by various screw mechanism in different instruments. If attached to the stage it is only useful if well made, and with moderate powers.

5. Telescope body tube is a sliding combination, or draw tube, useful for varying magnifying power and to adjust for different objectives or thickness of cover glass.

6. Stage should be large and firm, yet thin, to allow oblique illumination. Mechanical stages are useful but not necessary.

7. Mirror should be flat on one side and concave on the

other, large and adjustable for oblique light. Some turn over the stage to illuminate opaque objects instead of a condensing lens.

8. Sub-stage is for carrying the Abbe condenser or other illuminating apparatus, the polariscope, etc. It should always have centering screws, and adjustment for focus is desirable. In purchasing a microscope be careful to avoid disappointment. The advice of an expert is of advantage. Good work may be done with patience by inferior instruments but microscopy in the future will depend upon the best glasses and stands. For economy get such a stand as can be added to by degrees. A 1 inch or ¾ objective and a ¼ or 1-5, will suffice for general histological work. For high-power work, like blood structure, bacteriology, etc., a homogeneous immersion ⅛ or 1-20, or an apochromatic of like power with an Abbe condenser, or, better still, with achromatic condenser of wide angle, will be needed. Whatever form of stand is procured, have it of hard brass, with heavy foot, well balanced, no backlash in racks or screws, inclinable, with plane and concave mirrors, with the Society screw for objectives, etc. This latter is quite important.

4. Binocular instruments.

These give a stereoscopic view of objects and are used for the display of fine pictures under low powers. They divide the rays by using a Wenham prism in a small box sliding over the objective. Bausch and Lomb have contrived a swinging prism. The body tubes are made adjustable for different eyes. For high powers binocular eyepieces are made by Zeiss & Tolles, which act well.

III. PREPARING OBJECTS FOR THE MICROSCOPE.

1. *Living tissues.*

Examine in natural fluids or indifferent or neutral fluids, as serum, aqueous humor, amniotic fluid, or dilute albumen. (Dissolve 2 grammes dried sodium chloride in 25 C C of water, add 28 grammes egg albumen, 2.3 C C tinct. iodine and 2 or 3 drops carbolic acid. Mix thoroughly and filter. This is termed iod-albumen.) The moist chamber, the warm stage,

or the electrical stage are all useful in observing living tissues.

2. Hardening tissues.

Hardening tissues which are too soft to be cut or dissected.

Chromic acid in dilute solution of pale lemon color. Small pieces of tissue ½ inch square, in large quantities of solution from two days to two months.

Picric acid. Saturated solution in cold water.

Muller's fluid. Potassium bichromate 2.5 grammes, sodium sulphate 1 gramme, dist. water 100 C C. Very generally useful.

Potass. bichromate. One or 2 per cent solution. For blood corpuscles even 50 per cent.

Alcohol. For rapid hardening. At first weak, then strong, then absolute. Chiefly used to complete hardening after chromic acid, etc.

Chromic acid and alcohol. Chromic acid 1 gramme, water 20 C C, dissolve and add slowly alcohol 180 C C. Useful for delicate tissues, as retina, cochlea, etc.

Osmic acid. 1-10 to 1 per cent solution hardens embryonic and nerve fibers.

Freezing. For quickly hardening and cutting fresh tissues not needed for preservation, or for completing for section partially hardened tissues.

3. Softening hard tissues.

1. Removal of calcareous matter, as from bone or teeth.

Chromic and nitric acid. Chromic acid 1 gramme, water 200 C C. Dissolve and add commercial nitric acid 2 C C. A ½ per cent solution of chromic acid or a strong solution of picric acid may also be used.

2. Softening connective tissues.

Dilute alcohol. One part to 2 of water. Softens white fibrous tissue, as in separating muscle fibers or epithelial cells.

Dilute sulphuric acid 1 to 1000.

Acetic acid and glycerine. One oz. glycerine and 5 drops glacial acetic acid is recommended by Beale for softening white fibrous tissue and tracing nerve fibers with high powers.

4. Mechanical separation of tissue elements.

By dissection with needles, in fluid. By shaking in test tube with fluid. By pressure under cover glass (compressor).

5. Making sections.

For bone, teeth, etc., use fine saw, then cement on slide and file down, hone and polish. For softer tissues extemporaneous sections may be made by scissors curved on the flat, Valentin's knife, razor or scalpel.

The microtome or section cutter is used when accuracy or many specimens are required. Elevate the object by screw or inclined plane, or both. The freezing microtome is sometimes used.

Hand sections. Keep back of knife to operator. Draw obliquely from heel to point razor, (if *vice versa*). Dexterity is gained by practice. Always keep the knife wet with water or alcohol, and manipulate sections with a camel's hair pencil.

Imbedding serves to hold small or brittle specimens for cutting.

1. In pieces of carrot, potato, etc., for hard sections, as of softened bone, or hardened cord.

2. In elder pith. After placing the specimen and binding with thread it may be held fast by placing in water.

3. In paraffine, 5 parts to one of lard. A little clove oil renders it less liable to stick to the knife. Melt in water bath at low temperature. Pour into paper cone or box or microtome well with tissue in center. Tissues must be dry. The sections are to be picked out of the débris.

4. In gum arabic. Solution thick as possible. Gives interstitial as well as internal support. Remove alcohol from tissues by soaking 24 hours in water. Put delicate specimens in gum 6 to 24 hours in paper cone, etc., then place 24 hours in alcohol. Remove paper and imbed in paraffine.

5. In celloidin. Dissolved in equal parts of alcohol and ether. The dried tissue soaked in alcohol and ether for 3 or 4 hours is then put in a thin solution of celloidin for 10 to 12 hours, taken out, and, as the ether evaporates and a film is formed, is covered by layers of thicker solution, and kept in

strong alcohol till needed for section. For the freezing microtome the gum process is best

6. Increasing transparency of tissues.

1. Impregnating with strongly refractive fluids, as glycerine, turpentine, clove oil, Canada balsam or Damar varnish.

2. Partially or completely dissolving some elements of the tissues so as to permit others to be seen. Acetic acid, or caustic potass. or soda for dissolving soft albuminoid elements. Glycerine and caustics for wet preparations, clove oil or turpentine for dry or alcoholic.

7. Staining tissues.

1. The stain may be uniform and be serviceable by rendering very transparent parts more evident.

2. Some parts may be more affected than others and so differentiate elements. Thus the nucleus is most deeply tinged by carmine or magenta, epithelial cement by silver nitrate, and nerve fibrils by gold chloride.

From a large list the following most useful. Best procured in solution from opticians.

Carmine. Beale's weak and strong fluids, or solution of alum carmine.

Picro-carmine. For double stain. Nuclei, etc., red; muscle, epithelium, etc., yellow.

Logwood. Violet.

Magenta. For rapid stain. One gr. to ʒi water and ℥i alcohol.

Nit. silver. ½ per cent solution. Tissue afterwards exposed to light.

Gold chloride. ½ per cent solution. After soaking tissue in it 15 minutes to 2 hours, place it in 1 to 2 per cent acetic or lactic acid and expose to daylight till a gray or violet tint appears.

For staining bacteria various methods are used, as different bacteria stain differently. It is more difficult to stain them in tissue sections than in fluids. Watery solutions of stain must be used and sections cleared up after alcohol with cedar oil or xylol and not with oil of cloves.

Among the many stains proposed for B. tuberculosis, the following from Pittion & Roux is commended by Dallinger: Prepare three solutions. 1. Ten parts fuchsin to 100 parts absolute alcohol. 2. Three parts liquid ammonia to 100 distilled water. 3. Alcohol 50 parts, water 30, nitric acid 20 and aniline green to saturation. Dissolve the green in the alcohol, add the water, and lastly the acid. To 10 parts of sol. 2 add 1 part sol. 1 and heat until vapor appears, then immerse the cover glass with a drop of sputum which has been drawn over another cover and dried quickly by passing through the flame of a spirit lamp. After 1 minute wash with plenty of water, rinse with distilled water and drop on the film side of the cover a little of sol. 3. After about 40 seconds wash well, dry, and mount in xylol balsam.

8. Injection of vessels.

By steady pressure on a syringe or the pipe of pressure bottles so as to uniformly fill the vessels.

1. With substances fluid at ordinary temperature.

a. Aqueous solution of Prussian blue 2 per cent solution. After injecting, the blue may be prevented from diffusing through capillary walls by immersing in 90 per cent alcohol. Mount in damar.

b. Beale's Prussian blue in glycerine and water preserved in acid glycerine.

c. Solution of silver nitrate ½ to 1 per cent for showing cells of vascular wall.

2. Substances solid at ordinary temperature.

a. Carmine and gelatine.

b. Prussian blue and gelatine.

3. Opaque injections. Artists' colors rubbed up in ether, or opaque colors in gelatine.

9. Preservation of specimens.

1. Dry mounting. On a slide with ring covered with thin glass.

2. In Canada balsam or dammar varnish (equal parts dammar resin and gum mastic in benzole). The balsam may be obtained dissolved in chloroform, benzole or xylol. Re-

move water from specimen by alcohol, dilute at first then absolute. Render object transparent by clove oil or turpentine, place it in medium and put on thin cover.

3. Glycerine. For wet preparations. Use glue to cement cover glass.

4. Farrant's solution. Equal parts glycerine, gum and arsenious acid.

5. Glycerine jelly. Gum and glycerine with carbolic acid. Tissues best soaked in dilute alcohol.

10. Mounting.

1. Slips. Standard size 3x1 inch.

2. Cells. Made with rings of glass, vulcanite or cement.

3. Turntable. For cement rings or to cement cover to slide.

4. Thin covers, three sizes, 1, 2 and 3. From 1-50 to 1-250 inch thick.

5. Cements, Canada balsam, dammar, gold size, white zinc cement, asphaltum varnish. The latter most generally useful.

Plate I

Fig 1. Shape of lenses - in section.

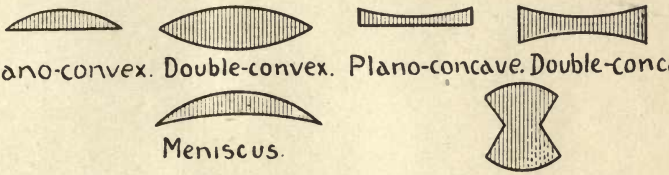
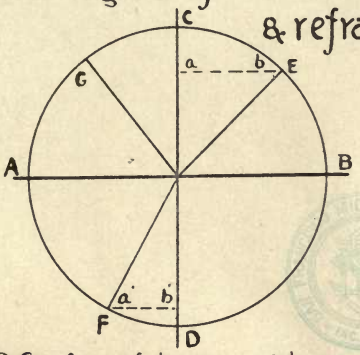


Fig 2. Angles of incidence & refraction.



A B Surface of dense medium.
C. D. Perpendicular. E F. Refracted ray.
E. G. Reflected ray. a b Sine of angle of incidence. a' b' Sine of angle of refraction.

Fig 3. Visual Angle.

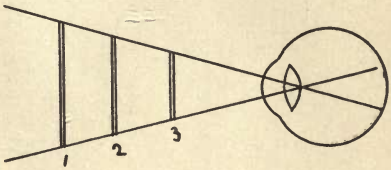


Fig 4. Spherical Aberration.

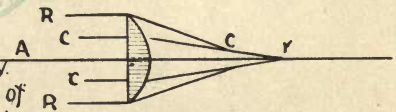


Fig 5. Chromatic Aberration.

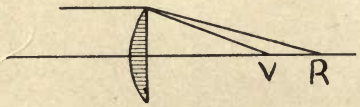


Fig 6. Effects of cover-glass.

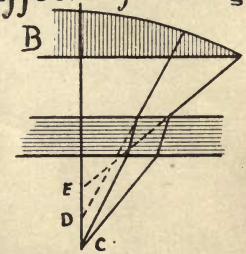


Fig 7. Immersion Objective.

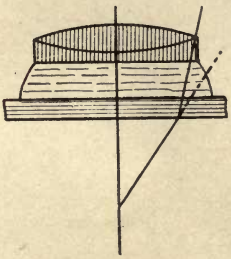
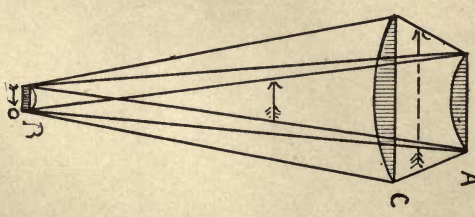
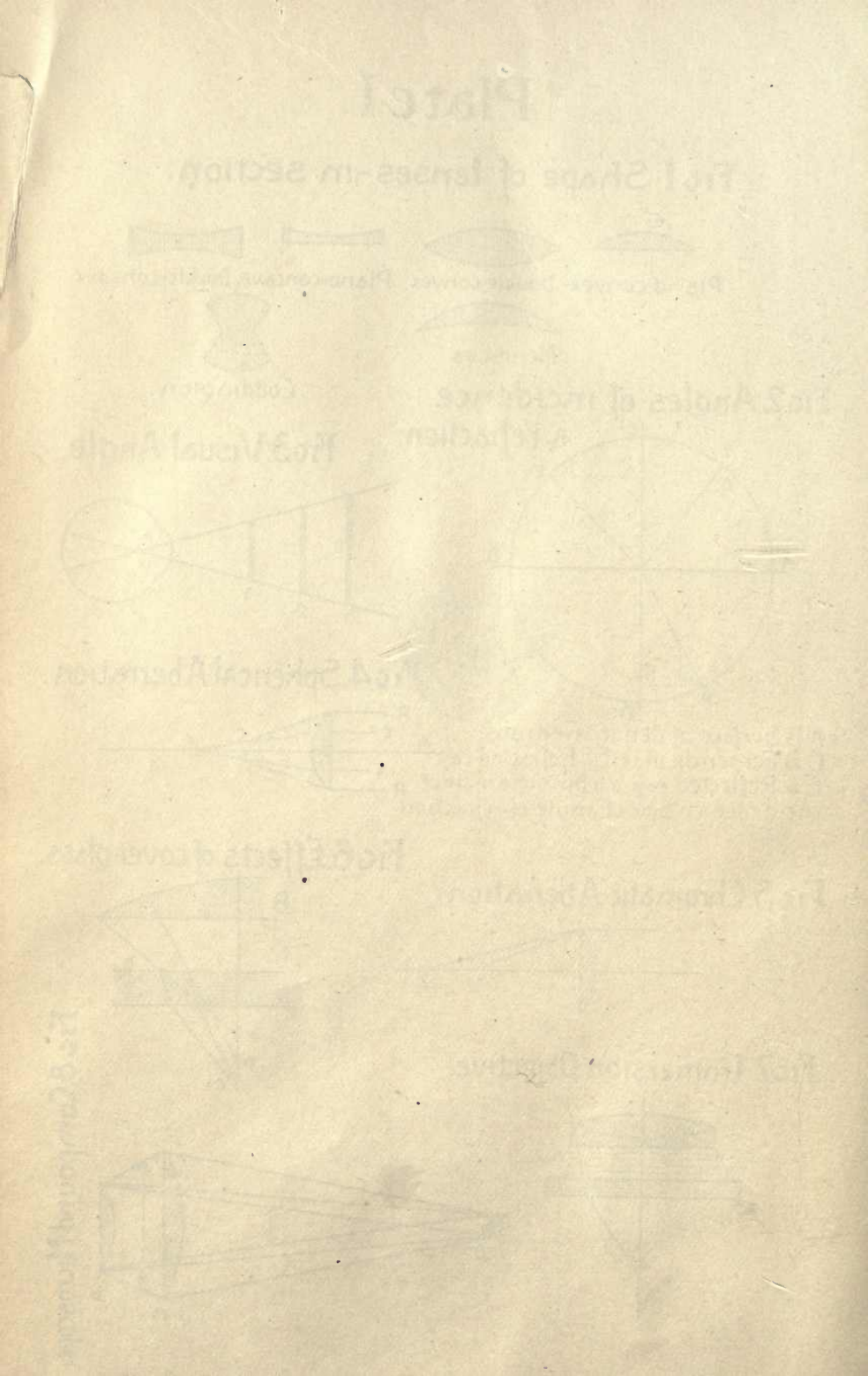


Fig 8. Compound Microscope.





Histology.