UNIVERSITY OF TORONTO

FORMAL OPENING

OF THE

NEW BUILDING

OF THE

BIOLOGICAL DEPARTMENT

DECEMBER 19, 1889.

THE ADDRESSES delivered by SIR DANIEL WILSON, President of the University; HON. G. W. ROSS, Minister of Education; PROFESSOR OSLER, of Johns Hopkins University; PROFESSOR WELCH, also of Johns Hopkins University; PROFESSOR MINOT, of Harvard Medical School; PROFESSOR VAUGHAN, of the University of Michigan; and PROFESSOR R. RAMSAY WRIGHT, of the University of Toronto.

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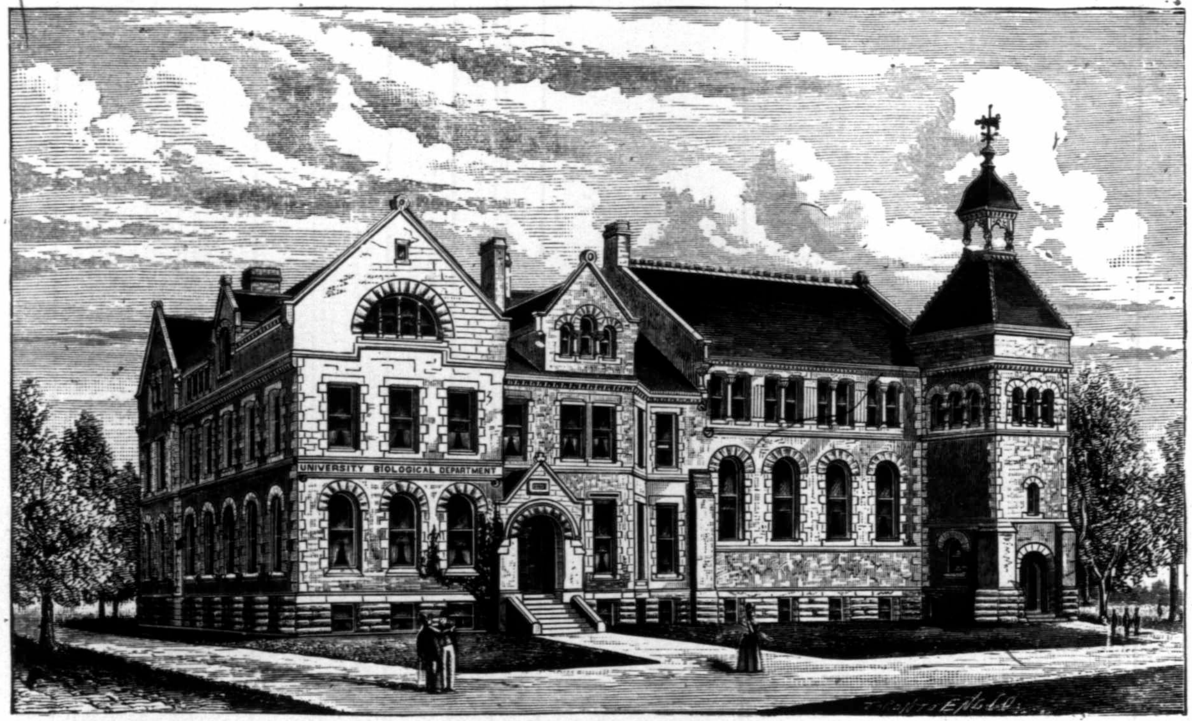


THE NEW BIOLOGICAL DEPARTMENT
UNIVERSITY OF TORONTO.

THE

NEW BUILDING

OF THE

Biological Department, University of Toronto.

FORMAL OPENING

DECEMBER 19, 1889.

ADDRESSES BY THE PRESIDENT OF THE UNIVERSITY, THE HON. THE MINISTER OF EDUCATION, AND PROFS. OSLER, WELCH, MINOT, VAUGHAN, AND WRIGHT.

SIR DANIEL WILSON, who was received with applause, said,—It is my pleasant duty to-day to welcome those who join with us in the public opening of these Biological Buildings. It is a very important step, I feel assured, in the history of the advancement of science in our Province and Dominion. It is an index of our share and sympathy in the progress that peculiarly marks the century that is now hastening to its last decade. From the age of the Renaissance this progress has been gradually achieving successive triumphs. That great change which is known familiarly as the renaissance, or new birth, was unquestionably a revolt against mediæval thought, and the grand claim of absolute freedom of research into all truths, of the right to accept of every manifestation of truth that science may reveal to us. Copernicus Kepler, Galileo, and other great names, have been succeeded by those of men who have advanced step by step into the higher mysteries of science; and last of all we have had in our own day a great thinker in the department of biology, one who has revolutionized thought, and prepared the way for an entirely new advance in the research for truth. I feel nevertheless bound, for myself, to affirm that I cannot accept the doctrine of evolution in so far as it assumes, under certain teachers, that mind and thought, intellect, reason, and all upon which our moral sense and the conception of a future life are based, can be conceived of as a mere production of evolution. Nevertheless as students of science, we are bound to sit humbly at the feet of truth. Whatever truths are disclosed to us in the triumphs of science, however for the time being they may seem irreconcilable with other truths, we need have no hesitation in the assurance that one truth cannot conflict with another.

I rejoice in the ample provision that is now in progress for all the departments of science in connection with this University. These buildings furnish somewhat adequate accommodation for the biological and physiological sections of university training; and I welcome the recent addition to our faculty of one who is a specialist in psychology. I have only to add that already contracts have been accepted for a further extension of these buildings; and when the entire plan is carried out it will furnish accommodation for the other branches of science which we recognize as playing an important part in our Faculty of Arts. It is, therefore, with peculiar satisfaction that I now perform the pleasing duty of proclaiming the building dedicated by the University to the use of the biological department of science, open, and devoted to all the special purposes for which it has been constructed.

Hon. G. W. Ross said that when he was asked to attend the opening exercises of this department of university work he expected that he would not be called upon to take any part but to have the unalloyed pleasure of listening to the other speakers and witnessing the enthusiasm of the students. He could only say at the outset that he was delighted to notice the onward progress of the University of Toronto, and the enlarged facilities which were being provided from time to time in the various departments of thought germane to every well-equipped university. He need not indicate the steps of progress taken within the past few years. They were all familiar with that progress. They had in this building, just declared open, clear evidence that the Senate of the University of Toronto, that those concerned in its success, are determined that at least on the side of the natural sciences, they shall not be behind any other university on this continent. He was glad to hear from the President that the intention is to prosecute the good work further. Last session authority was given the trustees for $60,000 for the promotion and completion of this department, and he supposed next session further authority would be asked to bring within a convenient centre or within convenient access of each other, all the departments in which the students of natural science were interested. He was pleased to hear from Prof. Wright that the classes here were among the largest in any department of university work. Everybody knew the enthusiasm with which Prof. Wright entered upon his work. He welcomed Prof. Osler, who was a graduate of the University of Toronto. He was one of their own people, a Canadian by birth and education, and he supposed he went to America either by choice or by necessity. Probably by choice. They were proud of Prof. Osler, first because he was a Canadian, second because he had been a successful Canadian, and third because he was a distinguished Canadian. He congratulated the President upon the evidence of expansion of the University, and he congratulated the vice-chancellor for the devotion which he had shown in every department of university work.

Sir Daniel Wilson congratulated Prof. Ramsay Wright on his admirably equipped building and alluded in comlimentary terms to his ability for teaching. The president then called on Prof. Wright to deliver his opening address.

THE PATHOGENIC SPOROZOA.

BY RAMSAY WRIGHT, M.A., B.SC.,
Professor of Biology, University of Toronto.

In the course of some introductory remarks, Prof. Wright spoke of the stimulus to the various branches of biological study which he was confident would be given by the erection of the commodious and well-equipped building devoted to his department. He referred to the constant interest shown by the University authorities, and especially by Vice-Chancellor Mulock, in the progress of the work, and expressed the hope that the progress already made would lead to a symmetrical development of all the divisions of biological science in the University. Addressing an audience largely composed of practitioners of medicine, he referred to the circumstance that the youngest of the branches of special study in biology—that of bacteriology—is that which at present has the greatest interest for them. He had selected for discussion to-day, however, the biology of certain low forms of animal life—the Sporozoa—which, he said, were destined to attract the close attention of pathologists within the next few years.

The Sporozoa are a group of low forms of animal life, belonging to the sub-kingdom Protozoa, which, in consequence of the universal adoption of a parasitic mode of life, present certain peculiarities of structure and reproduction which mark them off quite sharply from the rest of the sub-kingdom. The structural peculiarities consist chiefly in the absence of any specialized organs for locomotion or the ingestion of food, while the reproductive peculiarities consist in the formation of large numbers of characteristic spores. It is to these that the group owes its class name, Sporozoa, given to it by Leuckart, who in addition to his invaluable services in familiarising us with the structure and life-history of the higher parasites, has made most important contributions to our knowledge of these lower forms. All of them are unicellular animals, which may occasionally be so large as to be visible to the naked eye, but are often—especially those interesting in human pathology—quite microscopic. Four orders are distinguished, (1) Gregarinidia, (2) Sarcosporidia, (3) Myxosporidia, (4) Microsporidia; these may be shortly characterized before dealing with the forms of special interest to the medical practitioner.

1. The first Order, that of the Gregarinidia, is best known as furnishing the minute vermiform intestinal parasites of insects and other invertebrates. The unicellular nature is obvious in those which are known as *Monocystidea* (Fig. 1a), but masked in the *Polycystidea*, in which the cell shows a tendency towards sub-division into different regions. In all, however, the structure is substantially the same, the protoplasm surrounding the nucleus admitting of the recognition of two regions, the granular endoplasma and the hyaline ectoplasma, the latter the seat of the contractions which lead to the vermiform movements of the body. The cuticle through which the nourishment is absorbed, is frequently provided with an apparatus of attachment (Fig. 1b), but this may be of a temporary character, being discarded before the Gregarine enters into conjugation (Fig. 1c) The result of such conjugation is the fusion of the two cells within a single cyst, and is the general precursor in the intestinal Gregarines of sporulation, which consists in the segmentation of the protoplasmic mass from the periphery inwards (Fig. 1d) into globular clumps of protoplasm, each of which eventually gives rise to a spore with a resistent shell of characteristic form (Fig. 1e and f); such spores, from a fancied resemblance in form to the minute hard-shelled diatoms, used to be called *Pseudonavicellæ*. The spore-cases are voided through the intestine of the host, and the spores escape either through the rupture of the cyst or by special ducts, and are protected by their hard shells till they reach favourable conditions for further development. This consists in the segmentation of the contents of each spore into two or more sickle-shaped or crescentic germs (Fig. 1g), which are

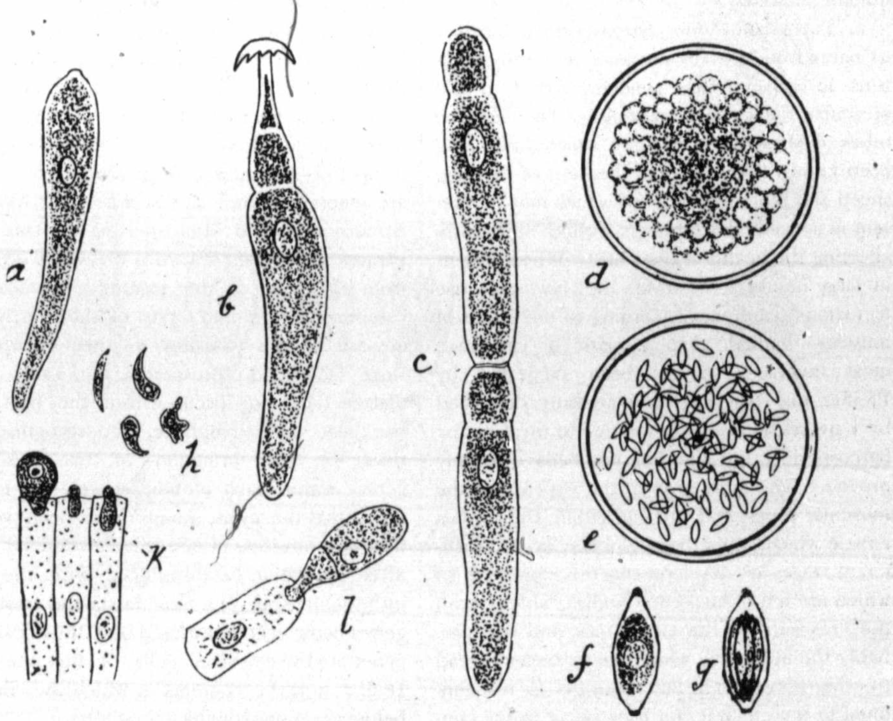


FIG. 1. DIAGRAM OF THE LIFE-HISTORY OF A GREGARINID.

a, A Monocystid form; b, a Polycystid form; c, two individuals of the latter, which have cast off their epimerites, are in conjugation; d, the resulting cyst containing the combined protoplasm of the two cells undergoing segmentation into spores; e, cyst containing the spores, each now encased in its hard shell (pseudonavicella stage); f and g, such spores enlarged, the contents segmented into crescentic germs; h, amœboid movement of the crescents; k, penetration of these into intestinal epithelial cells of insect; l, attainment of adult gregarina-form by same, while still adhering to epithelial cell by epimerite.

capable of change of form, and probably in most cases of active penetration into the intestinal epithelial cells of a new host (Fig. 1h), which cells they leave after having attained the adult form (Fig. 1k). The above is a sketch of the life-history of a typical intestinal Gregarine from an insect; to the same order, however, there also belong forms, which unlike the preceding have a long intracellular life, and a short free life, and it will be necessary to return specially to these as they are the forms most interesting in human pathology.

2. The second order, Sarcosporidia, receives its name from the circumstance that the organisms in question are generally found in the muscular tissues of vertebrates. They are the tubes of Miescher or Rainey, which have long been known (Fig 2a) from the flesh of the hog, sheep and other animals, but which may be present in considerable numbers without apparently affecting the health of their host. When present in large numbers, however, they may give rise to various symptoms, according to the group of muscles—lumbar, diaphragmatic or cardiac—most involved. It has been suggested by Pfeiffer that the acute Polymyositis described by Unverricht and others is due to invasion by Sarcosporidia, but this has not been definitely proved. The tubes grow at the expense of the muscular fibres, and present within the porous cuticle which limits them, globular cysts in different stages of development, the ripe ones of which are full of crescentic bodies, which recall the crescents of the Gregarines, and are probably the means by which the parasites spread to other fibres. The Sarcosporidia are not confined to muscle-fibre, for they occur in the connective-tissue of the œsophagus of the sheep, forming there tumours of considerable size, which may entail various pathological consequences.

3. The Myxosporidia in their adult condition have the least regularity of form of any of the Sporozoa (Fig. 2 b.) They are found on the skin and mucous membranes of aquatic vertebrates, and like the last group are generally observed to be full of spores. These are unlike those of preceding groups, in that they are provided with projectile threads (Fig. 2 b & c) possibly a provision for attachment to a new host.

4. The Microsporidia, finally, include extremely minute Sporozoa, the spores of which (Fig 2 d) are so small that they have been taken for bacteria. They occur as parasites of the tissue elements of insects, and in the form of the pebrine of the silk-worm have led to enormous losses in silk-culture in Europe. M. de Quatrefages calculated that in the first thirteen years after the outbreak of pebrine, France lost two hundred million dollars from the ravages of this sporozoon. They are not confined to any particular kind of cell but invade and destroy all without exception.

We must now return to those forms which belong to the first order, but which differ from the type described, in that their life is chiefly an intracellular parasitic life, a short free or wandering stage, however, permitting the young forms to invade new cells or new hosts. They are generally known as Coccidia, and like the Sarcosporidia and Microsporidia are true cell-parasites. The best known is *Coccidium oviforme* from the liver of the rabbit. It occurs in caseous nodules and cysts of the liver, which are full of the parasites in their encapsuled stage (so called psorosperms, Fig. 2 e.) Sporulation does not occur within the host, but has been studied outside, and recognised to result in the formation of two crescentic germs within each of four spores. It is supposed that the cysts, which have been voided from the intestine of one infected animal, may after sporulation be introduced with the food into the intestine of a new host, the crescentic germs being eventually freed and thus ready to penetrate the epithelial cells of the bile-ducts (Fig. 2, e 5) the contents of which they devour before again undergoing encystation.

Several cases in which man has been attacked by the same parasite are recorded—a particularly interesting one is that described by Gubler, who diagnosed hydatid tumours of the liver. The patient died, and some twenty cysts full of coccidia were found, one six inches in diameter! There is little doubt but that cysts of this nature, full of caseous material, have often been misinterpreted in the past, and closer attention in the future may establish that such psorospermosis of the liver is not so rare as has been supposed.

A large number of similar forms are known in other vertebrates and invertebrates attacking the cells of the intestinal tract and its appendages. One of the most interesting recently described is the *Karyophagus salamandræ* of Steiphaus (fig. 2f), which invades the nuclei of the intestinal epithelium of the salamander, and only becomes free within the cell after all the nuclear matter has been devoured.

A similar nuclear parasite is asserted by Podwyssozki to occur in certain diseases of the liver in man, and a detailed description of these is promised shortly. The parasites, which he proposes to call *Karyophagus hominis*, first produce a hypertrophy of the invaded nuclei of the liver-cells, then distort them, and, after encystation and sporulation, finally cause the pigmentary atrophy and disappearance of the whole cells. Such destruction of the liver-cells as well as the irritating effect on the intra and inter-lobular connective tissue caused by the presence of the coccidia may lead to cirrhosis and icterus. Podwyssozki calls attention to the ease with which the structures may be confounded with normal elements, expressly stating that they may easily be overlooked by an experienced histologist, and remarks that many of the so-called accessory nuclei, plasmomes, etc., described as normal cell-elements, may really be developmental stages of coccidia. It is obvious that the close cystological studies of the present day have prepared the way for researches into this difficult field of investigation.

In adition to the above described cases in which the epithelium of the digestive tract is

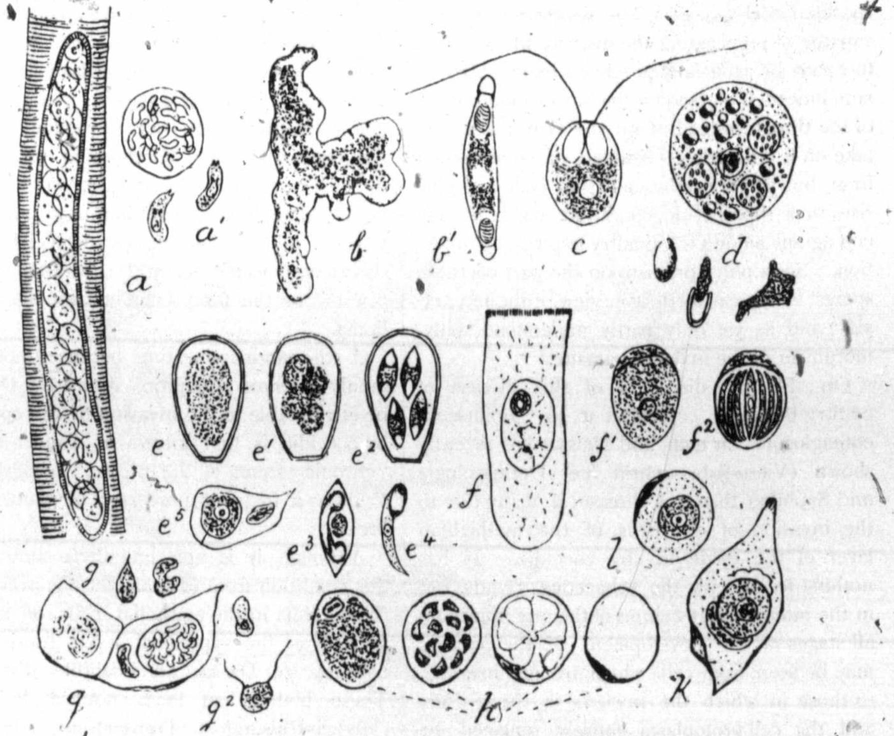


FIG. 2. ILLUSTRATING VARIOUS PATHTGENIC SPOROZOA.

a, A voluntary muscle-fibre from the œsophagus of the sheep containing a tube-like Sarcosporid; within the tubes are cysts in different stages of development, the ripe ones (a1) containing numerous crescentic bodies; b, a Myxosporid from the bladder of the pike, (b1), one of its spores with terminal thread-cells: c, a spore from another species with projected threads; d, yolk-cell from the egg of silk-moth infested with microsporid cysts; below is represented one of the oval spores contained in these and the amœboid germs with emerge from such spores; e, *Coccidium oviforme* from the liver of the rabbit in encysted stage; e1, e 2, contents of cysts segmenting into spores, e 3, one of the spores enlarged containing two crescentic germs, e4; e5, epithelial cell from a bile-duct invaded by a young coccidium; f, intestinal epithelial cell from the salamander, the nucleus of which is invaded by a coccidium (*Karyophagus* of Steinhaus), f1, a similar nucleus almost entirely replaced by the invading coccidium; f2, the coccidium undergoing direct division into segments; g, epithelial cells from the mouth of the pigeon, after Pfeiffer, with coccidia in different stages of development, one encysted with contained crescents; g1, crescents showing amœboid movements; g 2, adopting "flagellate" form on mucous membrane; h, four epidermal cells from *molluscum contagiosum* after Neisser, to the left is a cell, h1, with the contained coccidium in its protoplasmic phase, h2, segmentation into angular refractive bodies follows, which eventually enlarge so as to crowd upon each other, h3, their outlines disappearing and the surrounding cell cornifying give rise to the characteristic "molluscum corpuscle," h4; k, epidermal cell from *psorospermosis follicularis* (keratosis follicularis), after Darier, in which a coccidium pushes aside and distorts the nucleus; l, epithelial cell from Paget's disease "chronic eczema of the nipple" after Butlin, the contained coccidium interpreted by him as an instance of endogenous cell-formation.

attacked by coccidia, instances are not wanting where it is the epidermal cells of the skin which are invaded. Pfeiffer has given us a detailed account of the forms which cause a contagious skin disease in poultry, and which were originally described by Bollinger in 1873. The cells are invaded by the coccidia and the nuclei thrust aside as the parasite grows and proceeds to sporulation (Fig. 2 g). The spores are at once capable of propagating the disease, which therefore may be artificially produced by inoculation, and, indeed, if planted on the mucous membrane of the throat, instead of on the skin, the spores take on a "flagellate" instead of an amœboid form, but penetrate the epithelial cells and give rise to a diphtheritic condition which is very contagious among the poultry exposed to infection. Such polymorphism on the part of these spores is of great interest in view of the remarkable, and as yet only partly understood, polymorphism of the malarial parasite.

On the first discovery of this disease of poultry Bollinger compared it to "molluscum contagiosum" in man, and Neisser has recently shown (Vierteljahresschrift fuer Dermatologie und Syphilis) that this disease is really due to the invasion of the cells of the malpighian layer of the epidermis by coccidia. It has nothing to do with the sebaceous glands, but in the interpapillary colums of the rete mucosum all stages of the development of the parasite may be seen, from cells which are just invaded, to those in which the nucleus is thrust aside and the cell-protoplasm entirely replaced by the parasite (Fig. 2h). Sporulation occurs within the cell, 6, 8, or 10 refractive bodies being formed, these increase in size, so as to exercise mutual pressure, and the typical "Molluscum-corpuscle" is arrived at by cornification of the remains of the invaded cell around the coccidium-cyst. The contagious character is thus satisfactorily explained.

Molluscum is, however, not the only human skin-disease which must be attributed to coccidia. Darier has recently established the fact that certain conditions described heretofore as a variety of *acne cornea* or as *keratosis follicularis* are in reality a "psorospermosis follicularis," (Annales de Dermatologie et Syphilis July 1889). In these conditions the lesion exists in the necks of the sebaceous follicles, which are dilated into a cup or funnel shape, the funnel being occupied by a mass of corneous appearance which projects beyond the level of the epidermis in the form of a brownish or greyish crust. This is formed as a result of the irritation of the cells of the neck of the follicle by coccidia which have invaded them (Fig. 2k). Instead of the lesion being limited as described, the sebaceous gland and the hair-follicle being unaffected, vegetations may be developed from the neck of the follicle, and extend into the adjacent corium, giving rise to tumours which were observed chiefly in the inguinal region. Microscopic preparations of such tumours, Darier says, would be infallibly diagnosed as coming from an epithelioma of follicular origin, for the cells dispose themselves round central invaded cells in "nests" of the form characteristic for epithelioma.

A still more interesting, because more commonly observed condition, shown by Darier to be attributable to the invasion of the epidermis by coccidia, is that known as Paget's disease, "chronic eczema of the nipple," recognized by Paget as a frequent precursor of cancer of the breast.

Although it is not difficult to differentiate this condition from eczema, yet the presence of the coccidia in the epithelial cells of the deep as well as the superficial layers furnishes, according to Darier, an infallible distinction. These bodies had been noticed by Butlin (Medico-Chirurgical Transactions, 1877), who described the ducts and acini as full of epithelial cells of this character, supposed by him to be undergoing endogenous cell-formation (Fig. 2 l). Darier shows, however, that these are coccidia, which, when they attain their full size, distend the invaded cell beyond its normal dimensions and (unlike the coccidia of the psorospermosis referred to above) sporulate in sitû.

The conclusion is at once suggested that the cancer which succeeds this condition is simply due to an inward extension through the galactophorous ducts, and Darier does not fail to draw it.

Darier's account of the two pathological conditions referred to above, presented in the Spring of 1889 before the Société Biologique of

Paris, elicited from M. Malassez the statement that in his belief coccidia are a more important factor in disease than has hitherto been admitted, that since 1876 he has regarded certain intracellular bodies met with in the central cells of nests in epithelioma as coccidia, and that four years ago he had showed these to Balbiani—the most distinguished French authority on Sporozoa—who had confirmed him in his belief. M. Albarran followed with a detailed description of these structures from nests, and others extend into the connective tissue.

Many observers have been struck by these globular elements in the centre of the epithelial cell-nests, retaining their protoplasm while the surrounding cells cornify. They have generally been considered as the result of a mucous or colloid degeneration of the central cell, but it is not only in France that these have been interpreted as coccidia. Pfeiffer in one of his papers on the Sporozoa (Zeitschrift fuer Hygiene, III.)

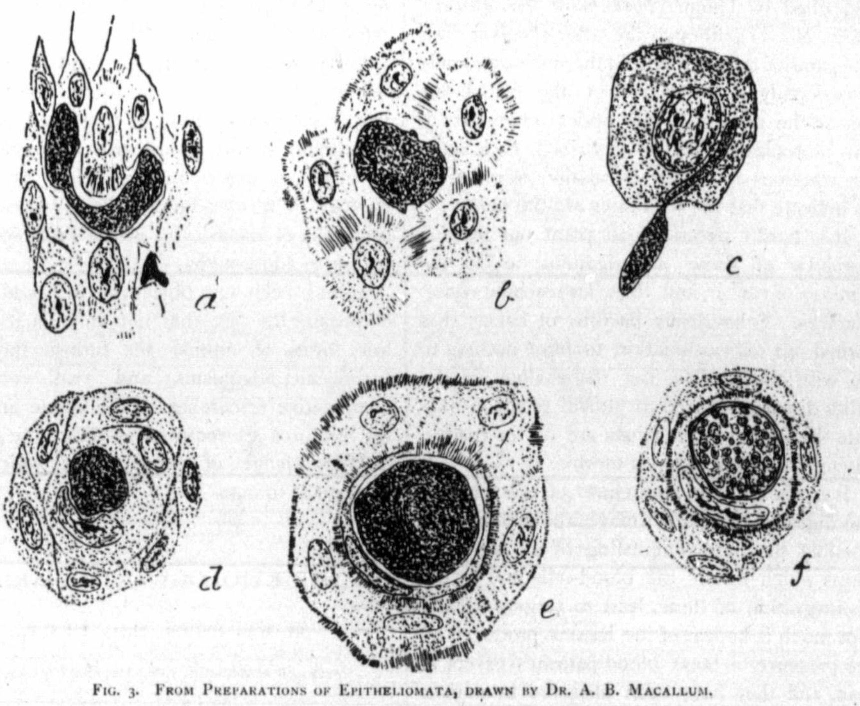


FIG. 3. FROM PREPARATIONS OF EPITHELIOMATA, DRAWN BY DR. A. B. MACALLUM.

a, b, c and e, from preparations made with chromic acid, hæmatoxylin, and eosin; d and f, from preparations made with chromic acid and gold chloride; a, showing a migrating plasmodium, non-nucleated and with granular protoplasm; near letter a is represented a leucocyte; b, showing a plasmodium between the prickle cells and possessing apparently a nuclear body; c, showing a plasmodium entering an epithelial cell; d, plasmodium in an epithelial cell, around which the other epithelial cells are laminated, resulting in a "nest"; the nucleus in the central cell is pushed to one side and partially invaginated by the plasmodium; e, a further stage of d, in which the nucleus and remaining protoplasm of the cell forms merely an envelope for the plasmodium, which is intensely eosinophilous, and which possesses apparently a nuclear vesicle; f, showing an epithelial cell with the nucleus pushed to one side and crescentic in outline, the contained plasmodium surrounded by a doubly-contoured membrane and apparently having undergone sporulation.

two cases of epithelioma. The foreign bodies in the epithelial cells are rounded or oval elements of a faint yellowish-green tinge with granular protoplasm and a central nucleus or entirely homogeneous. Occasionally they are in the form of cysts, and in some individuals six to eight refractive corpuscles of rounded or irregular form are to be seen. Occasionally the invaded cells are surrounded by one or two flattened cells; others occupy the centre of refers to the case of a girl of fifteen, who died of general carcinosis, the growths in the breast and mesentery exhibiting coccidia both in the protoplasmic and sporulating phases. On the other hand, Neisser, in his paper on Molluscum specially contrasts carcinoma with molluscum or epithelioma contagiosum, and adheres to Cohnheim's view of its etiology.

Entirely independently of these observations (which indeed have only been published within the last few months) Dr. A. B. Macallum, who is in charge of the Histological classes in this Institution, showed me four years ago, sporulating cysts in epithelioma, and suggested the parasitic origin of the disease. You will have an opportunity of inspecting these preparations (Fig. 3), as well as others prepared by Dr. Caven, showing the presence of the same bodies in metastatic growths. They are apparently similar structures to those observed by Malassez and Pfeiffer, and probably also to those described by Thoma (*Fortschritte der Medicin*, 1889, No. 11), although the latter observer finds the parasite generally within the nuclei, and only occasionally in a cavity of the cytoplasma beside the nucleus. The optical characters of the protoplasmic bodies described, their staining reactions and their sporulation would seem to indicate that the structures are the same.

It is hardly necessary to point out the importance of these investigations as to the etiology of cancer, and their far-reaching consequences. Scheurlein's bacillus of cancer has turned out on examination to have nothing to do with the disease, but the analogy of the other diseases referred to above, seems to indicate that at last pathologists are on the road to discover the real materies morbi.

It is not only the epithelium of the skin and the digestive tract which may harbour Sporozoa; possibly the most interesting of all are those forms which invade the blood-cells and by the disintegration of these, lead to serious disease. Not much is known of the lesions produced by the presence of these blood-parasites except in man, and they have been observed in animals apparently quite normal. Whether this is the case remains for further investigation, but the observations of Danilewsky show that it is especially in sickly individuals of turtles and birds that the hæmogregarines described by him are to be found.

The earliest known forms of these blood-parasites are the *Drepanidium ranarum* of the frog, which is known in an intracellular crescentic phase, and in a free pha e (Fig. 4 a) and the larger *Trypanosoma* or *Trichomonas*, a flagellate form with an undulating membrane found free in the plasma (Fig. 4 c). A similar Trichomomas is observed in the blood of various fishes, and still another species from apparently healthy rats, while in the blood of mules in India suffering from an epidemic pernicious anæmia—the so-called Surra-disease—entirely similar forms have been found. Whether the flagellate forms are really referable to the group of the Sporozoa remains yet to be determined, but Danilewsky's observations would appear to point out a very considerable polymorphism on the part of these hæmogregarinids, and would seem to support suggestions made that the organisms found in the blood in relapsing fever and pernicious anæmia may also be referable to this remarkable group. The comparative parasitology of the blood is yet in its infancy; there can be no doubt, however, but that a systematic study of the blood in other vertebrates in this regard, will help materially to clear up many obscure points as to the etiology of various human blood-diseases, and especially of malaria, on which Professor Osler is now to address you.

It has been my object in this address to emphasize the fact that not only bacteria, but low forms of animal life furnish important pathogenic organisms, and that continued comparative researches on the whole group of the Sporozoa are required to fill up the gaps in our knowledge of those forms which are pathogenic to man.

THE ETIOLOGY OF MALARIA.

BY WM. OSLER, M.D., F.R.C.P.,

Professor of Medicine, Johns Hopkins University.

During the early triumphs of bacteriology it was confidently anticipated that malaria would turn out to be a bacterial disease, and the *Bacillus malariæ* of Tommasi-Crudelli and Klebs was generally thought to be the looked-for micro-organism. The discovery by Laveran of amœboid bodies in the interior of the blood-cells was at first considered as pointing to phenomena of degeneration of these, and the original descriptions of the organisms seemed rather to indicate a retrograde step in the study of pathogenic micro-organisms. Since then, however, independent and renewed observations by Marchiafava, Celli, Guarneri and Golgi in Italy, by Councilman, James, and myself in

America, and by Vandyke Carter in India, all point to the conclusion that Laveran's organisms are the real cause of the condition, at least that they are peculiar to and diagnostic of the malarial poison.

Laveran's organisms resemble the Sporozoa, which have formed the subject of the preceding address, in their having an active amœboid phase, and a sporulating phase. The latter occurs apparently without encystation, and the resulting spores exhibit either amœboid or flagellate locomotion. Certain resting-stages—the so-called crescents—do not, however, appear to be comparable to the crescentic germs of the coccidia.

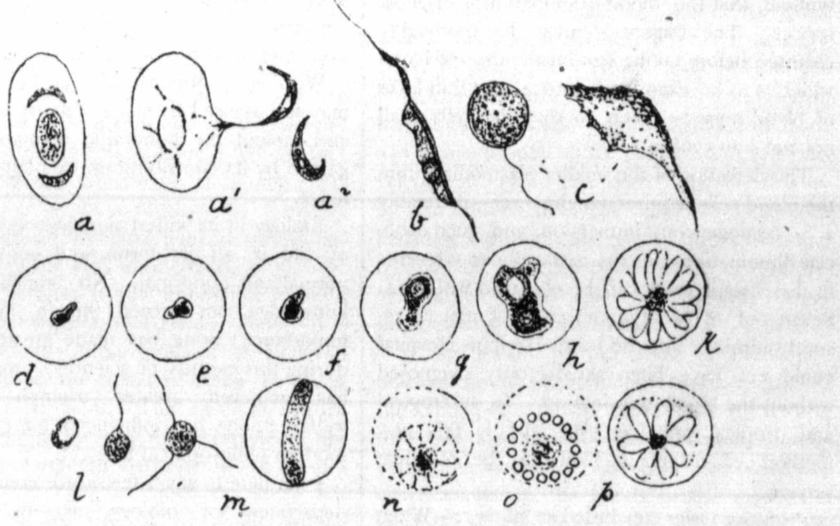


Fig. 4. Various Forms of Blood-Cell Parasites.

a, Red blood-cell of frog containing two crescents of *Crepanidium ranarum*, a 1, a crescent escaping, a 2, a free cresent; b, *Trchomonas* from fish's blood, c, from frog's blood—two phases; d-k, successive phases of development of *Plasmodium malariæ* within human red blood-cells; k, segmentation in the rosette form with central pigment, l, free segments which may be amœdoid or flagellate; n o, plasmodium of tertian, *p*, of quartan ague according to Golgi.

The amœboid bodies, *Plasmodium malariæ*, as they are now called, are to be found within the blood-cells of the acute cases of malaria, and exhibit a different stage of evolution according to the phase of the attack. During the apyrexia the plasmodia are to be recognized as minute, colorless amœboid bodies (Fig. 4) which gradually grow at the expense of the stroma of the red blood-cells, and become more and more loaded with fragments of black-pigment—melanin—the result of the digestion of the hæmoglobin. Eventually the whole of the stroma is devoured the plasmodium assumes a globular form, the pigment generally accumulates at the centre, and the peripheral protoplasm segments into a number of young plasmodia, which are free from pigment and are capable of amœboid, more rarely of flagellate, movement. This segmentation is coincident with the chill. After the attack the resulting small plasmodia may leave the larger vessels to crowd into the capillaries of the spleen, etc., where the central lifeless pigment masses are taken up by the leucocytes, but they are soon found within the blood-cells in the general circulation again. The length of time from the invasion of the blood-cells to the occurrence of segmentation determines the character of the fever, and Golgi believes he has made out specific distinctions between the plasmodium of tertian and quartan fevers (Fig. 4, o, p). The relationship of the intra- and extracellular crescents (Fig. 4, m) of chronic cases to the plasmodium has not yet been satisfactorily made out, but it may be noted that, while quinine at once causes the disappearance of the ordinary plasmodium from the blood, the crescents are on the other hand quite refractory thereto.

Flagellated forms with three or more rapidly moving lashes are to be met with in some cases, especially in the blood from the spleen, and these have been observed to be developed from the free oval or rounded bodies. Nothing so far can be said as to their significance.

We must await the further working out of the life-history of the *plasmodium malariæ* till its zoological position and its causal relationship to the disease can be more thoroughly defined, in the meantime it is necessary to call attention to its great importance in diagnosis. Little difficulty is experienced in recognizing the ordinary cases of intermittent fever; it is in the chronic and anomalous cases which sometimes simulate typhoid, that the blood-examination is of most service. The finger-tip must be thoroughly cleansed before taking from it the drop of blood which is to be examined, and a very thin layer of blood must be taken so that the cells shall not run into rouleaux.

The detection of the smaller plasmodia within the blood-cells requires a high power—preferably a $\frac{1}{12}$ homogeneous immersion, and good artificial illumination, but the extracellular crescents in the chronic cases can be observed with a $\frac{1}{6}$. Seven out of twenty-four cases of malaria recently admitted into the Johns Hopkins Hospital could not have been satisfactorily diagnosed without the blood-examination. In subtropical and tropical practice especially is this new method of diagnosis likely to be of great service.

Professor Osler concluded as follows:—When I look back a few years and think of the appliances and arrangements which we had then in Toronto, and when I go over this building and see the beautiful arrangements, the elaborate apparatus, the splendid appliances for teaching, I feel that it is possible for one to live through a renaissance, similar perhaps in kind, less important in degree, than that to which the president referred in his opening remarks. As most of you know, I have continued to take an interest in the School in which I received my early instructions, and I continue to take a deep interest in everything relating to the profession in this my native Province. Though I am away a considerable part of the time, yet I am able to make repeated visits, and it is always a source of the greatest pleasure to meet my old teachers and my colleagues and my friends.

PATHOLOGY IN ITS RELATIONS TO GENERAL BIOLOGY.

BY WILLIAM H. WELCH, M.D.,

Professor of Pathology, Johns Hopkins University, Baltimore.

I esteem it a privilege to assist at the formal opening of this Biological Laboratory and to be able to extend to this University, and to this City, congratulations for the possession of a laboratory so admirably constructed and equipped and inaugurated with the assurance of an activity so fruitful and well directed. The existence in this place of such a laboratory is not a matter of local pride alone. It may safely be predicted that its influence will be felt throughout this country, and indeed wherever interest in the biological sciences is found.

With such opportunities as here exist, we may feel assured that this country will increase and expand the honorable reputation already gained by its contributions to biological knowledge.

Biology in its widest significance is the study of life in all its forms and activities, both normal and abnormal. No branch of human knowledge can exceed this in interest and importance; none has made greater advances during this century of scientific progress; none has achieved greater triumph for human welfare; none has influenced more profoundly modern philosophical thought.

I am here to say a few words concerning one department of biology, namely, pathology, particularly in its relations to general biology.

Pathology is the study of life in its abnormal forms and activities. The relations of pathology to practical medicine are necessarily so essential and intimate, that the broader conception of this science as a part of biology is in danger of being lost from view. I deem it, however, important for the scientific status and advancement of pathology to keep in mind and to emphasize its relations to general biology, not less than those to practical medicine.

In so doing, it is not intended to detract in any degree from the practical value of pathology and its applications to the diagnosis and treatment of disease. When we consider that pathology embraces the investigation of the causes of disease, of the anatomical changes produced by disease in the organs and tissues of the body, and of the alterations in function resulting from disease, it is plain that pathology must constitute the scientific basis of practical medicine. This is not the less true because the prevention and cure of disease have not kept pace with the advances in our knowledge of the nature and causes of disease, and of necessity can not do so. Preventive and curative medicine, however, is constantly making beneficient application of pathological discoveries, and the most intelligent and efficient management of disease is becoming more and more that which is founded upon the most accurate knowledge of its nature and causes.

Inasmuch as the general public naturally interests itself but little in any side of medicine other than the treatment of disease, there is not sufficient general appreciation of the immense progress in the science and art of medicine of to-day as contrasted with that of a half century ago. The history of medicine is in large part the history of schools of doctrine. Stately superstructures of sweeping generalizations and attempted explanations were erected only to be overthrown because it was impossible to build upon a firm foundation of facts. To-day it is our conviction that these fundamental facts can be discovered in no other way than by observation and experiment. The adoption of this, the only scientific method of investigation, has with the aid of modern instruments and devices not only greatly enriched medical science, but it has overthrown the era in which, among scientific physicians, exclusive schools of doctrine can prevail. The scientific physician, no more than the scientific chemist, can yield adherence to any exclusive dogma. To the one as to the other no way which leads to truth is debarred.

By way of illustration of the achievements of modern pathology, permit me to contrast for a moment with the imperfect, meagre, and confusing information of former times, the fulness of our present knowledge concerning that disease, which of all diseases is the greatest scourge of the human race. Tuberculosis causes the death of not less than one-seventh, and, in some form or other and at some period, affects probably one-third of mankind. But a few years ago, not only was the specific cause of tuberculosis unknown, but there was no general appreciation of the fundamental fact that this is one of the infectious diseases. The knowledge of the frequency and wide distribution of tuberculous disease in other parts of the body than in the lungs is an acquisition of modern pathology. The pathological anatomy of tuberculosis, which not long ago was one of the most confusing chapters in pathology, has been made clear. The unity of all the processes now known to be tuberculous, can be established on an anatomical as well as on an etiological basis. The greatest addition to our knowledge of tuberculosis, and in fact one of the greatest achievements of modern science, is the discovery of the specific living germ which causes tuberculosis. We are now enabled to study both within and without the body, the form and the properties of this germ, the conditions which are favorable and those whi h are hostile to its preservation and development. Who can doubt that all this increased knowledge of the most devastating of maladies is destined to help in prevention and treatment? Sanitarians convinced of the preventability of tuberculosis have already begun the warfare against its spread.

If one seeks an illustration of immediate practical results of the modern investigations of the living germs which cause disease, let him turn his attention to the revolution thereby wrought in surgical procedures. The possibility which is now in the hands of the surgeon of keeping wounds free from all external infection, is a boon to humanity not less than the introduction of vaccination.

It would be pleasant to follow still further the practical benefits resulting from pathological discoveries, but it is not my intention on this occasion to dwell upon the applications of pathology to practical medicine. I have said enough to remove any misapprehension as to my belief that pathology should be made to serve the ultimate aim of medical education, the prevention and cure of disease. This science must ever hold a foremost place in any proper scheme of medical education.

This occasion is an appropriate one to emphasize especially those scientific aspects of pathology which give it an important position among the biological sciences.

In the first place I claim that pathology as a science, quite independently of any practical or useful applications whatever, is as legitimate and worthy an object of pursuit as any of the natural sciences. In and for itself alone it deserves to be studied. Its methods are those of observation and experiment as in other biological sciences. Its subject matter is any living thing which deviates from the normal condition. It is not less interesting and important to learn the nature and causes of abnormalities in form and function than it is to become familiar with the normal, and when this knowledge may aid in the prevention and relief of suffering, added dignity and interest are imparted to the study.

As there comes a line where the distinction between the normal and the abnormal is shadowy and uncertain, so the separation between normal and pathological biology is not sharp. The province of the one encroaches at many points upon that of the other. Mutual aid is to be derived from a closer union between normal and pathological biology. The pathologist should not be content with methods of research less perfect than those employed in normal biology. He should not rest satisfied with results which stop at the mere description and classification of morbid processes. To be able to give a name to some pathological lesion, and to make it fit into some accepted scheme of classification, should not be the sole aim of pathological study. Pathological processes should be studied with the aim of elucidating their real nature, development and causes, their mutual relations and their dependence upon underlying laws. The purely descriptive phase of development of any natural science can be only temporary and unsatisfactory. The more a pathologist is imbued with the spirit of modern biology, the less content will he be to stop at this descriptive phase.

In the next place it can be justly claimed that the study of pathology as a science without immediate reference to practical results is in reality the method which is most likely to yield these results as well as to bear fruit in other directions. Experience has shown that the most important discoveries in science, come not from those who make utility their guiding principle, but from the investigators of truth for its own sake, wherever and however they can attain it. It is short sighted to fail to see that the surest way to advance pathology, even in its relations to practical medicine, is to cultivate it as a science from all points of view. It is impossible to foresee what may be the practical application to-morrow of any pathological fact discovered in the laboratory, no matter how remote from practical bearing it may seem to-day.

The experiments upon animals and other investigations which have led to the present accuracy in the localized diagnosis of lesions of the central nervous system, and have rendered possible the surgical treatment of many of these lesions we owe in large part to physiologists and pathologists who had little thought of the practical applications of the results of their researches. The instrument and methods which have enabled ophthalmology to attain such perfection in diagnosis and treatment rest upon researches in physiological optics belonging to the domain of pure science. It could not have been anticipated by those who began the study of the microscopic organisms which cause fermentations and infectious diseases, that their study would lead to a revolution in surgical treatment, and would open prospects which it would now be hazardous to specify as to the prevention and cure of infectious diseases. Did time permit, and were it necessary, much more evidence of similar character could be brought forward to show that those who work in laboratories, it may be without a thought as to the practical utility of their investigations, are no less genuine contributors to the science and art of medicine, than those who study diseases by the bedside.

As has already been mentioned, pathology has to do with abnormalities, not in man alone, but in all living things, both animal and vegetable. The points of contact between animal and vegetable pathology are more numerous than might at first glance appear. The student of animal pathology can draw many instructive lessons from such subjects as the behavior of wounds and the parasitic affections in plants. We are most of us probably inclined to think too much of the separation between the pathology of man and that of the lower animals. While there is a wide distinction in the dignity of the object of study, yet from a scientific point of view this separation is of little account.

Pathological investigations of diseases of animals constitute no less genuine and valuable contributions to pathology in general, than do similar investigations of human diseases. The advancement of recent years in the education and aims of those who devote themselves to animal pathology, will serve to bring into closer relations the students of human and those of comparative medicine.

It may be useful for us to consider briefly some of the relations and points of contact between human and comparative pathology.

In the first place there are many diseases which are common to man and to animals. These can often be studied to greater advantage upon animals in which many conditions can be controlled, which are beyond our control in man. In animals every stage of development of the disease can be studied, and in general, fresher material can be obtained. We can modify in various ways external and internal conditions so as to reach a clearer comprehension of the morbid processes. Moreover the same disease may present interesting pathological peculiarities in different species of animals, so that the study of its occurrence in a single species, affords most incomplete knowledge. For instance, the pathologist whose sole knowedge of such a disease as tuberculosis is derived from the study of the disease as it occurs in man, has a far less complete understanding of this affection, than one who is also familiar with the striking peculiarities of this affection in cattle, swine, fowls, and other animals.

Especial importance attaches, of course, to the study of such diseases as are communicable from animals to man, as for instance, anthrax, glanders, tuberculosis, many entozoic affections, etc., and in general these are the animal diseases which have received the most attention from the students of human pathology.

One of the most important departments of comparative pathology is experimental pathology, the value of which to human pathology has long been recognized. To make of experimental pathology a distinct speciality and to endow it with a separate professorship as is done in some foreign universities, does not seem to me to be in the direction of the most fruitful and healthy development. The experimental method is the handmaid of pathology in all its branches, and is the only means of solving many important problems. The experimental production of diseases in the lower animals affords an insight to be gained in no other way as to the causes, development, lesions and functional manifestations of many diseases. Experience, however, has shown that grave errors are likely to be committed by experimental pathologists who have no knowledge of the natural diseases and conditions of the animals used for experimentation. How often, for example, have those studying the question of experimental tuberculosis, mistaken for genuine tubercles nodules produced by parasitic entozoa and to what misleading conclusions have such incorrect observations led.

There are as many general pathological processes which can be studied to better advantage in animals than in man. Such subjects as inflammation, œdema, thrombosis, embolism, and infection have been elucidated in large part by observations made on animals. Due caution is of course to be exercised in applying such observations directly to human beings.

Inasmuch as it is rarely possible for us to produce artificially all of the conditions which cause natural diseases, and as our very method of experimentation is in itself often a perturbating factor, it is no less important to study animal diseases resulting from natural causes, than it is to study the same diseases experimentally produced. Of course there are many diseases which have not yet been opened to the experimental method of investigation.

Questions of etiology and of pathogenesis are among those which have received and are destined still further to receive the greatest illumination from studies of comparative pathology. At present, probably no subject engages the attention of pathologists to a greater degree than the microscopic organisms which cause infection. If we had been confined to human beings in the study of infectious diseases, our knowledge in this direction would have been only a small fraction of what it is at present. In no single instance could the complete chain of proof required to demonstrate the causation of an infectious disease by a specific micro-organism, have been furnished. The far-reaching principle of preventive vaccination or inoculation would not be k own.

A most important and promising field of pathological study, at present only partly cultivated, is found in the infectious diseases of animals and of plants, not only on account of the great economic interests often involved, but also as a means of widening and deepening our conceptions as to the causes, development, prevention and treatment of infectious diseases in general. Any pathologist who is at all familiar with the remarkable and peculiar conditions under which the so-called Texas Cattle Fever of the United States develops and spreads, will realize that the complete elucidation of all the etiological factors of this disease not only would contribute to the solution of a great economic question, but also would open fresh points of view in our conceptions of infectious agents and their properties. When we consider the many conditions which it is in our power to control in studying animal diseases, and above all the possibility of submitting to an experimental crucial test our conclusions, it is clear that the study of natural and artificial infections, as well as of many other diseases in animals, is calculated to advance in the highest degree the science of pathology. It is not a small thing that questions which were once considered to be wholly transcendental, as for instance the doctrine of immunity against infectious diseases have been brought within the working domain of experimental pathology.

Nor is it in the causation of infectious diseases alone that the comparative study of human and of animal diseases is destined to advance etiology. It is reasonable to expect that this comparative study will help to clear up many factors, at present obscure, in the causation of human diseases, including the influence of social conditions.

But let us take a broader view of comparative pathology than that which considers abnormalities only in man and in animals related to man in structure and function. I believe that many problems and facts in human pathology await for their complete elucidation the same application of the comparative method of study which has made of normal anatomy virtually a new science. What a barren mass of apparently unrelated facts is human anatomy when studied without reference to comparative anatomy and embryology! If knowledge is the understanding of the real nature of a thing, and how it came to be as it is, then there is no knowledge of human anatomy without the aid of comparative anatomy and embryology. How difficult and unmeaning is the old method of studying the anatomy of the human brain and how fascinating does the anatomy of this organ appear in the light of development!

A light similiar in kind, if not equal in intensity, will be shed upon human pathology by a fuller insight into comparative pathology. We possess at present scarcely the rudiments of a comparative general pathology, but how useful and significant is even our fragmentary knowledge of this subject. The charm and impressiveness with which Metschnikoff has developed and presented the phagocytic doctrine is due largely to illustrations drawn from comparative pathology. It is impressive to see pictured in living forms from the lowest up to the highest, the combat with invading micro-organisms of infection. While the phagocytic doctrine can not be accepted in its entirety, it is interesting to observe that it received its origin and its chief support from observations made upon the lower forms of life, rather than from those on man and the higher animals.

The interesting and important discoveries concerning the curious parasitic organisms associated with malaria may seem to the student of human pathology anomalous and without analogy, but in Prof. Wright's admirable address to-day upon the sporozoa, we have had presented to us not only the life history of the class of organisms to which the malarial parasites probably belong, but also many examples of similiar parasitic affections of lower animals. We may expect still further information concerning this interesting group of infectious micro-organisms from researches in comparative pathology.

Take for instance one of the most disputed and still unsettled problems in pathology, the conditions which cause multiplication of the fixed cells of the body, a question which is intimately associated with the still broader one of the response of cells to the action of external stimuli. Can it be doubted that if we were acquainted with the behavior of cells in all types of living things from the unicellular organism upward, under the influence of such stimuli as cause inflammation in human beings, under the influence of losses of substance and under various other conditions, we should have a much clearer comprehension of one of the fundamental and most common pathological processes in man?

The interesting studies of heredity by Weissman and others, pertain in part to pathology and also illustrate brilliantly the value of the comparative method of research.

The application of embryology to the explanation of congenital malformations is familiar and has long been an acquisition of human pathology. More recent is the endeavor to refer the origin of the genuine tumors to anomalies in fœtal development. It is probable that experimental and comparative pathology also will shed much light upon the still obscure question as to the origin of tumors.

A large mass of observed pathological facts we must now accept without adequate explanation. It is often the fundamental and common morbid processes which are most obscure. For many of these we may hope to find satisfactory explanation in the results which the comparative study of pathology will afford. At present nothing is to be gained by attempting to generalize from scanty and incomplete observations in comparative pathology. We must first accumulate a store-house of facts. We need investigators who shall study pathological conditions not in man alone or in the higher animals alone, but also in the simpler forms of plant and animal life. Something has been done in this direction, more indeed than is generally utilized in human pathology, but much more remains to be done. Conditions and processes which are difficult to comprehend in animals of complex organization often become clear in organisms of simple structure. Our pathological concepts are now derived almost wholly from observations made upon highly complex forms of life. I believe it to be no illusion to anticipate in thought, a time when all forms and kinds of living matter will be included in the domain of pathology, and when pathological laws will be derived from results of investigations which begin with unicellular organisms and which end with man. By the adoption of this comparative method of study, pathology will in reality acquire greater simplicity and deeper significance than it now possesses.

As the student of normal biology does not attempt to cultivate equally the whole field belonging to his subject, so the pathologist can not be expected to cover in his investigations the whole domain of pathology as thus broadly outlined. There will be special workers in various departments. As in normal biology, so in pathological biology, from the combined labors of all there will be constructed a science broader, richer and fuller of meaning than that which we now possess. The ideas which I have endeavored to present, although necessarily in a brief and cursory manner, concerning pathology in its relations to general biology, are naturally suggested by the opening of this biological laboratory. Permit me in conclusion to say that it is in a medical school in intimate and organic connection with a university where such laboratories exist, that the highest cultivation of pathology as a science is to be expected. Here is the favorable atmosphere, here the stimulus of allied sciences, and here the most enlightened appreciation and encouragement.

THE USE OF THE MICROSCOPE AND THE VALUE OF EMBRYOLOGY.

BY CHARLES S. MINOT, M.D.,

Professor of Embryology, Harvard Medical School, Boston.

Mr. President and Gentlemen—It has been said that the noblest study of man is man. There are many who believe it; but we who are gathered here to-day remember the purpose of our gathering, and know that the noble study of man is but a part, and that not even the greater part, of the nobler and vaster science of biology, the new birth among you and fair hopes of which we celebrate. Much has been told you by the able and distinguished savants who have preceded me of the stirring interests of biological science, and of the manifold bearings it has upon our thoughts, our philosophy, and also upon the practical exigencies of our daily life. But were I to tell you, even in mere catalogue form, of the manifold ways they have left unmentioned in which biology touches upon our affairs, I should occupy a far longer stretch of time than even your Canadian courtesy would have the patience to endure.

I must, therefore, select some small portion, and of that speak briefly. I choose, as is common wisdom, from that part of the extensive domain of biology with which I am best acquainted through my own studies. I ask you to permit me to address you a few words concerning the use of the microscope and the value of embryology.

The first microscopes, such as those used by Malpighi, were curiously simple—a small piece of wood with an upright at each end; in each upright, a hole; in one hole the lens was fastened, in the other the preparation; a separate microscope for every preparation. These simple instruments were sent about—many of you have doubtless seen them—and entertained court ladies and others who cared for the newest curiosity. The modern microscope is a creation of this century, and began its development with the invention of achromatic lenses by Amici. Since his time the construction of the compound microscope has made great advances, not only in the build of the stands, but more especially in the lenses. We have only to note the introduction of water immersion; later, of oil immersion, objectives; and the recent invention of the wonderful apochromatic lenses, by which the capacity of the microscope is, I am tempted to say, almost doubled.

The reason why the microscope—why improvements in it are so important to the biologist is, that the size of the elements with which he has to deal is different from that in other departments of science. It is only in the organic world that the explorer finds the microscopic structure to be his most important guide. It is true that the microscope is of great utility in other departments of science. I do not overlook its applications in physics. I do not forget what it can reveal to the retrographer examining rock sections; but still I assert that it is only in biology that the microscope is the supreme instrument of research. Now, the proper use of this precious implement is an art difficult to acquire, but invaluable to the biological possessor of it. It demands not only an acquaintance with the elaborate methods of preparing the tissues, hardening, sectioning, staining, and so forth, but also the acquisition of a peculiar experience of the eye, and habit of the hand, which can be gained only by industrious and well-directed practice, and, besides all this, it demands the cultivation of the geometrical faculty of the mind. With the microscope we can see only one plane, and we have to build up our plastic conception by combining the views we get in various planes into a mental image corresponding with the actual structure, somewhat as the mechanical engineer makes out the form of a machine from the elevation and plan. This mental process is much harder to carry out than one might believe who had had no experience in trying to drill students into the habit of it. In this building there is, to an unusual degree, provision made for microscopical work, as I see by the broad windows open to the best light, and by the general laboratory arrangements. In all this, I believe we have to acknowledge the wisdom of Prof. Ramsay Wright. I congratulate you in having at the head of your biological department one who thus recognizes the real needs of the student, and makes good provision to satisfy them. You all know the immense usefulness of the microscope, not only in medical science, but also in medical practice, as a clinical resource. The time is near when every physician will know, as a matter of course, how to use the microscope in his professional work. What your students learn in this building will tell through years to come.

The field of biology known as embryology has great significance both to the pure investigator and to the practical medical man. It explains structure. As we follow back an organism to earlier and yet earlier stages, we see what is secondary disappear, and what is essential remain, and it is from the embryo that we have the fundamental plan of the body. He, therefore, who wishes his anatomy to be something better than a stupid system of mnemonics, must betake himself to embryology to obtain an intelligent comprehension of the body. Again come the practical applications. Let me instance a few. The so-called germ-layers govern the pathological changes; each of the three layers of the embryo has its specific morbid anatomy, and, with certain limitations, we may say that a disease proper to one germ-layer does not trespass upon the tissues belonging to the others. The laws of reproduction, too, it is indispensable for the physician to know; these we must study in a broad way, and, in fact, the laws of reproduction have been discovered for the most part, not from the study of man, but of the lower animals. We can hardly exaggerate the necessity of the physician's knowing the structure of the uterus and its functional changes. Concerning the uterus we have, indeed, much to learn still. It is only recently that we have discovered that pregnancy induces an extensive destruction of maternal tissue, the mucous lining of the uterus undergoing degenerative changes such as we have been accustomed to think of as exclusively pathological. In a short time the epithelium of the pregnant uterus is destroyed and the glands break down. These appearances have been noted in the so-called uterine moulds, and have been usually considered as evidence of disease, but we now know that they are normal appearances of pregnancy. So with the canalized fibrine of the chorion of the ovum; that, too, is a normal condition of pregnancy. In these instances we have microscopic pictures which we have hitherto associated with the presence of disease, but which are really healthy growths. May we not expect that embryological research, in elucidating these changes, will lend a helping hand to her sister, pathology, who always has, and always must lag a little behind the knowledge of normal structure? To the physician embryology has to offer the key to many malformations of harelip, cleft palate, a foramen between the cardiac ventricles, congenital umbilical hernia, hermaphroditism and pseudohermaphroditism, and a long array of other arrests of development. Indeed, embryology ought to form a part of every medical curriculum, and I am glad that you include it in your plan. May our colleges in the States imitate your example!

Embryology requires to be studied broadly, and by the comparative method. Only by so doing can a just estimate of the facts be secured. Confine your studies to the development of man, and you will never understand it. Give the mind range and opportunity, and it will soon pick out by comparisons drawn between various species that which is essential and significant. It is from such studies that we have been brought lately to deep problems. We see now in the course of development that the early embryonic cells have a large nucleus with very little protoplasm, and that the older cells show a great increase in the amount of protoplasm in proportion to the nucleus. You are all familiar with the famous apothegm which designates protoplasm as the physical basis of life, but in the light of what I have just said, it might be as well defined as the physical basis of advancing decrepitude. Again, we observe that it is only in the simpler tissues that there is much possibility of growth. As the tissues become more highly differentiated, they lose their power of growth. You all know that the cells of the spleen, of the skin, and of other simple tissues, multiply in the adult, but in the highly specialized nervous system we never find any cell divisions. Now this loss of reproductive power, coincident with specialization of structure, may prove to be but the beginning of that final loss we call death. If this be true, then death is a penalty we pay for having a high organization. We pass beyond the present bounds of science, but hope and hypothesis ever lead us, and who dares to say where the bounds of discovery are set in biology? Is not this very building a monumental assertion that we have not reached them yet?

The reason why I allude to these things is largely a personal one. Prof. Wright I have known for many years, and I have often had occasion to wish for his counsel or for his advice, because I have always found that he is one of those minds which naturally take themselves to the consideration of the larger problems of biology. These general questions and these complications of knowledge, which lead us to meditate upon the farthest reaching problems, will receive at his hand a larger share of consideration than they would get from many others of the biologists of the world. I congratulate you all most heartily upon the possession of this beautiful building. We have in the United States, unfortunately, scarcely any building equal to this; none, I think, superior to it for the purpose for which it is designed. Even my own University of Harvard, one of the richest and oldest in the States, has not anything I would call better than this. I thank you all for your most hospitable welcome. I had the pleasure of being here some ten years in the official capacity of examiner. I notice there is a certain difference between that time and now. I was then not welcomed with the applause which you have generously given me to-day.

THE NECESSITY OF ENCOURAGING SCIENTIFIC WORK.

BY VICTOR C. VAUGHAN, M.D.,

Professor of Bacteriology in the University of Michigan.

Science is knowledge; art is the application of knowledge. Science consists of facts; art utilizes these facts. Science investigates; art adapts. Science is the foundation; art is the superstructure. Science is the mariner who sails out over the seas of ignorance, and discovers fair islands and broad continents of truth; art is the immigrant who comes later, and tills the soil, and builds the cities.

We are fond of saying that this is a practical age. By this we mean that our knowledge is utilized for some purpose. We are prone to speak lightly of those who may give their time and attention to the pursuit of knowledge for its own sake. But we should remember that we must possess knowledge before we can apply it. Science must always precede art. Convert all of your investigators, who are the discoverers of knowledge, into adapters of knowledge, and you will arrest the world's progress. Without a Franklin and a Faraday, there could have been neither a Morse nor an Edison. What would have been the condition of applied chemistry to-day, had not the Priestlys and Scheeles of 100 years ago worked and plodded? At that time the study of chemistry was pursued as a pure science, and its devotees were regarded as but little better than fanatics. To-day a hundred arts make practical applications of the discoveries of chemistry. The industries founded upon the researches of the humble chemist now feed and clothe millions, and enrich thousands. It has been stated that the commercial value of the discovery of the aniline dyes alone has repaid Germany a thousand-fold for all the money which that Government, as liberal as it has been in this direction, has invested in its numerous and well-equipped chemical laboratories. There is scarcely an honorable trade or profession which is not indebted to a greater or less degree for its position and efficiency to the labors of the scientific chemists of the past. Without a knowledge of the chemistry of metals none of our vehicles of transportation, from the dainty baby cart to the great ironclad of war, from the cheap dray of the poor man to the elegant private car of the rich man, could have been constructed. Without these labors, which are said to have been begun by Tubal Cain, the world to-day, instead of being occupied for the most part by great nations, would have remained a wilderness, with its solitude broken only by the cry of wild beast and savage man. No great cities, indeed, not even a hamlet, could have been built. There would be no commerce, no learning, no religion.

Yon must not understand from what I have said that chemistry is the only science which has benefited mankind. I have simply taken it as an illustration, and I do not know that it has any claim to first rank. Rob us of the knowledge which constitutes any of our great sciences and we are affected seriously, physically, intellectually, and morally. A wise nation will foster the sciences, for upon these depends its prosperity. Germany has been pre-eminently wise on this point. It has built and equipped universities as no other nation has done. It has filled Strasburg with soldiers and has walled and entrenched the quaint old city with the magazines of war, but the most impregnable fortress raised by the confederation in Alsace is the great university, to which many of the wisest and most learned men of the empire have been called, and the intelligent citizen who is still French in his patriotism, will tell you that his city has more cause of self-congratulation than it had before '72, and he will point with pride to the stately university buildings which are but the outward manifestation of the genius and intellect which labor within.

Now, good neighbors of Ontario, I am happy to be with you, and do rejoice with you in this dedication of these handsome and well-equipped rooms to the holy cause of science. I can assure you that the ability and learning of the director of this department, Prof. Wright, are well-known and highly appreciated by his colaborers in the United States, and many of us have long regretted that you have not earlier supplied him with improved facilities for his work.

Let us briefly inquire into some of the scientific problems, the solution of which will demand the time, attention, and energy of this department. A simple enumeration of all these questions would require more time than I have at my disposal; therefore, I will dwell only upon those in which I am most interested.

All living things consist of individual parts, which the histologist calls cells. Some of the lowest forms of life are simple, free cells, and we say that they are unicellular. This simple cell must perform all the vital functions. It must digest, absorb, and excrete. Its range of function is necessarily limited. As we ascend the scale of organized life, we find a multiplication and differentiation of cells. In man certain cells have for their sole function the elaboration of the digestive juices, others are employed in the separation of effete and poisonous matters from the blood and their elimination from the system; some are devoted exclusively to the reception of impressions from the external world, some convey these impressions to the central nervous system, and others are more directly concerned in the intellectual processes. Health is maintained by the proper and correlated activity of these various groups of cells.

Within the past 15 years it has been clearly demonstrated that the introduction of some of the lower forms of vegetable life, called bacteria, into the body of man and other animals produces disease. The study of these micro-organisms has brought into existence and developed the science of bacteriology. A large amount of information has already been accumulated in this field of scientific work, and the art of the preservation of health, hygiene, and the art of restoration to health, medicine has made valuable practical applications of these scientific facts. One of the objects of these laboratories and lecture-rooms is to make the young student acquainted with what is already known in the science of bacteriology. But there are many problems in bacteriology which remain unsolved, and to this your most earnest attention will be given.

The study of bacteriology, so far, has been nearly altogether morphological. I say this in no spirit of criticism. Indeed, I recognize the fact that it could not have been otherwise. The study of form naturally and necessarily precedes the study of functions. The ornithologist, on finding a new species of bird, first studies its size, its general formation, the colour of its plumage, the shape of its beak, the spread of its wing, etc. It is only later, and after more extensive observation, that he can tell you about its habits, how it builds its nest, what it feeds on, what birds are its enemies, etc. And it would probably require still more extensive observation before he can tell you what effect altered environments would have on the bird, whether or not it would thrive in a different climate, with only unaccustomed food to feed upon, and with new foes to encounter. Therefore, I repeat that I am not offering a criticism when I state that the study of bacteriology has been largely morphological. But I am sure that all will agree with me that these enemies to man's health and happiness, for such we can pronounce the pathogenic germs, should be studied from every possible standpoint. Suppose that we knew nothing about the yeast plant save its morphology, the size and method of development of the cells, we would know but little. The fact that yeast produces carbolic acid gas and alcohol is certainly equally important with a knowledge of its morphology.

The chemical study of bacteria offers a fruitful field for the investigator. What chemical alterations do they cause in the various media in which they grow? What fermentations do they induce? Why is it that altered environment so materially affects the virulence of some of them? Why is it that the bacillus of anthrax is so invariably fatal with certain animals, while others are wholly immune against the same germ? The theory of the action of phagocytes would at best be only a partial explanation of some of these questions. Granting that an army of these, the natural defenders of the domain of the body, turn out to do battle with the invader, with what weapons do they fight? If they digest the bacillus what digestive ferment do they form? How do they destroy those germs which are found lying dead in the intercellular spaces in a case of anthrax in a man?

There are two factors which enter into the causation of infectious disease. First, there must be susceptibility in certain cells of the body; secondly, the inciting cause is the specific micro-organism. Indeed, we might say that the primary cause lies in the tissue itself. Then there is the ever interesting subject of immunity against disease secured by the use of sterilized culture of the various specific micro-organisms. Is such immunity, which has already been obtained in a number of diseases, due to a true vaccination, or is it simply due to the establishment of a tolerance for a poison? How long will the immunity thus secured continue?

But I must not dwell too long on a single word. Should this laboratory be the means of solving a single one of the problems which I have mentioned, the money, time, and energy given to it will have been profitably applied, but there are other questions which will take up a large share of the time spent by professors and students within these walls.

The study of food and drink by the bacteriologist has only been begun. In many of the infectious diseases the specific poison finds its way into the body through the mouth. We are told by those who have investigated the subject that the chief source of infection with cholera in India is by means of the drinking water. The water is collected during the rainy season in tanks. These tanks not only serve the inhabitants for water-supply, but are also used as laundry and bath tubs. We are shocked at these statements, but how many cities in America discharge their sewerage into bodies of water from which they or neighboring cities take their drinking water supply? More than 500 people die annually in Ontario from typhoid fever, more than 5,000 are sick during the same time, and it is certain that the majority of these receive the poison which causes the disease with the water which they drink?

The probability of seriously affecting the health by eating food which has partially undergone putrefactive changes multiplies every year with the increased consumption of canned and otherwise preserved food.

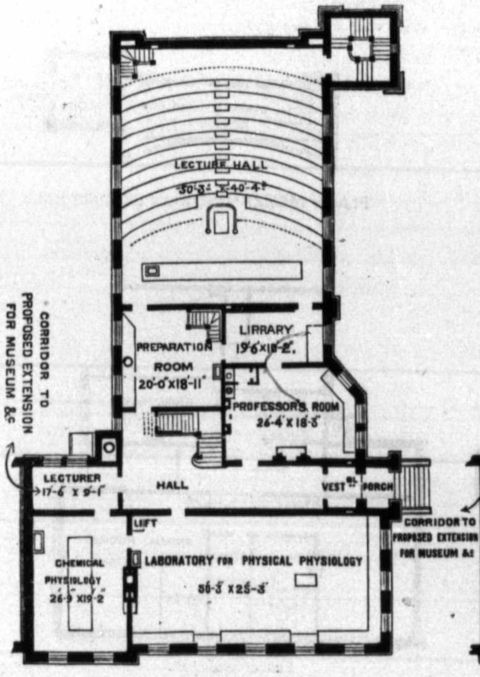
But I must conclude, and in doing so, let me say that no one need fear that too much time will be given to theoretical or abstract science.

Every important scientific discovery in the past has sooner or later found its practical application, and always to the benefit of man. What could have been more unpromising of practical results than the discovery of micro-organisms in the blood of an animal sick with anthrax by Pollemler in 1849. When this observer reported that he had seen minute forms of life in the blood, some said that the objects which he had seen were bits of fibrine, others that they were not real at all but due to defects in the glass, while still others hinted very strongly that the defects were to be found in the observer's brain; but truth prevailed, and from that observation or discovery as a starting point, the science of bacteriology has been developed to its present importance, and by virtue of the facts forming this science the spread of infectious diseases has been limited as it could not have been done in the past. It was owing to knowledge founded upon that discovery that Asiatic cholera was arrested in New York harbor in 1888, and prevented from spreading through the United States and Canada.

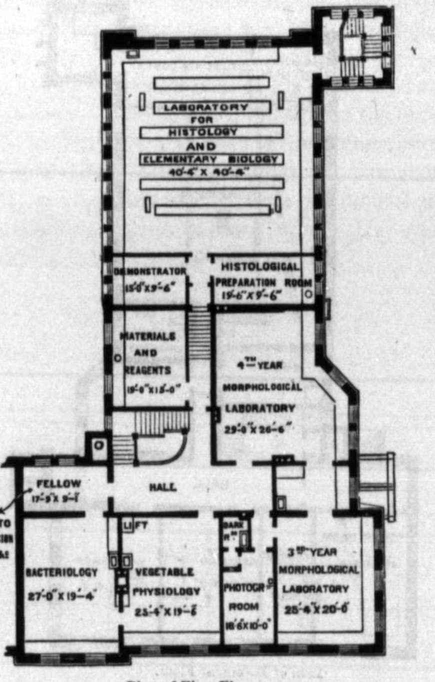
DESCRIPTION OF THE NEW BUILDING OF THE BIOLOGICAL DEPARTMENT OF THE UNIVERSITY OF TORONTO.

The Biological building is situated on the west side of the crescent in the Queen's Park, on the site of the old brick building which served, for so many years, as a home for the Toronto School of Medicine, and is therefore associated with the student days of many readers of the PRACTITIONER. Within recent years it has been occupied by the students as a gymnasium and place of meeting of the College Societies, and has been known as Moss Hall. The new building is a substantial structure in the Scottish Norman style, harmonizing with the University itself, but simple and unpretentious in character. The materials used are brown and grey Credit Valley stone for the basement and general face of the walling, and brown stone for the dressings. The principal feature of the eastern elevation is the lecture hall, which is at the north end of the building, with a staircase tower and bell turret at its north-east corner. This staircase is exclusively for the use of students, and gives access to the waiting-rooms, lecture hall, and large laboratory over it, without the necessity for passing through the main building. The principal entrance is through an arched porch on the east front, and opens on the main corridor running east and west, from which the main staircase rises. Opening on this corridor on the north side is the professor's private laboratory, communicating through the preparation room, and a small library with the lecture hall.

This is a very handsome room, seated for 250 students, but having floor space which is available for many extra seats, as was apparent on the opening day. The seats are comfortable theatre-chairs, each being provided with a folding tablet for note-taking. The staging on which the seats are fixed is arranged on an



Plan of Ground Floor.



Plan of First Floor.

"acoustic curve," the height of the steps increasing as they recede from the front, with the result that the occupants of the back seats can see over the heads of those in front of them. On the south wall of the lecture room are various devices for illustrating lectures, a fixed blackboard has a movable one suspended in front of it, and at either side are diagram frames running on guiding wires, which may be raised and lowered at pleasure. In front of the blackboards a plaster disc of 8 feet diameter can be pulled down. The disc was cast upon a plate glass surface with the finest plaster. So as to afford a suitable surface for receiving the images of microscopic preparations projected by the Zeiss projection microscope. It is also employed for receiving ordinary lantern projections. A brick column independent of the floor rises from the room below, and prevents any vibration of the projection instrument. At present there is no electric light in the building, but the gases for lime light are stored in clinders in the basement, and the water pressure can be turned on to these in the lecture room. The room can be darkened rapidly by drawing down painted shades, which run behind strips attached to the window-casings. Advantage is taken of the space under the staging of the lecture hall to form a ladies' waiting-room, which is entered from the tower staircase, but has also a private stair up to the lecture hall for the exclusive use of the lady students.

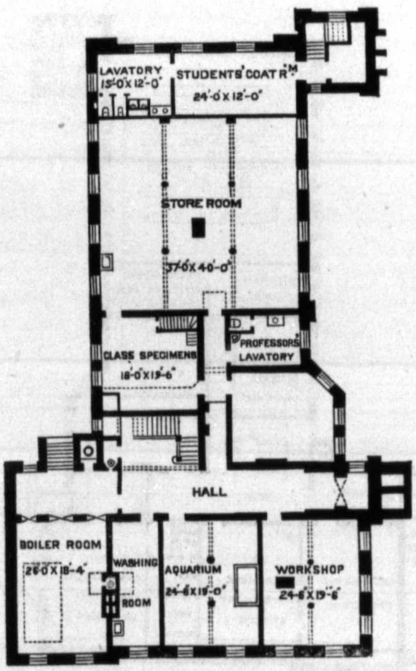
On the south side of the main corridor are the laboratories for physical and chemical physiology, in charge of Dr. A. B. Macallum, whose private room is at the end of the corridor. The large physiological laboratory can be darkened in the same way as the lecture room. It also has an independent brick column for galvano metric work, as well as stone and wooden benches suspended on the east and south walls for supporting other instruments which require to be free from vibration.

The first floor contains the laboratory for histology and elementary biology, arranged for one hundred students working simultaneously, when the tables in the centre are occupied, but generally only used for classes of forty, engaged in microscopical work. The walls are occupied by lockers, in which the students keep their histological reagents, etc.

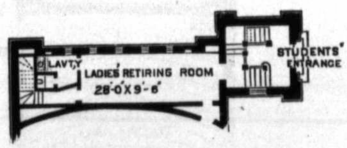
Attached to this large laboratory are a private room for the use of the demonstrators, and a histological preparation room, in which the material is prepared and stored for the classes in histology and elementary biology.

These rooms over the lecture-hall communicate with the rooms over the front of the building by means of a flight of steps. The latter rooms are chiefly used by the senior students of the Arts Faculty, and include special morphological laboratories for third and fourth year students, with a small common room between them in which there are facilities for imbedding, injecting, etc. Each laboratory contains a large case with specimens and models illustrating the prescribed work for each class. A full set of Ziegler's models, illustrating the development of the vertebrates, *e.g.*, occupies the greater part of the case in the fourth year room.

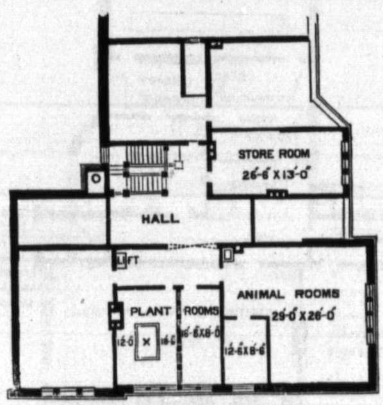
There are also on this floor two rooms devoted to vegetable physiology and bacteriology, at present under the charge of Mr. J. J. Mackenzie, Fellow in Biology. A photographic room, with separate dark room, both finished in dead black throughout, have been specially arranged for photomicrographic work. There is a second floor over the southern portion of the building which contains besides several rooms for other purposes, two plant rooms, so arranged that a different temperature can be maintained in each. The whole of the front and roof are of glass, and face the south so as to get the sun all day. The floors are of concrete, supported by iron beams and brick arches, and are impenetrable to water, while the walls are finished in cement, so that the hose can be used in these rooms and in the adjoining animal rooms as in an ordinary greenhouse. The basement contains the aquarium, workshops, storerooms for various



Plan of Basement Floor.



PLAN OF MEZZANINE UNDER LECTURE HALL



Plan of Second Floor.

puposes, lavatory accommodation, and the heating apparatus. The heating is by steam, mostly by direct radiation, but the indirect system is also used to a certain extent for purposes of ventilation. Stacks of steam radiators are enclosed in boxes under the basement ceiling, into which cold, fresh air is brought from the outside, warmed, and delivered to the rooms above through tin tubes and registers. The foul air is extracted into a duct which is led to the base of the main chimney shaft, which is about sixty-five feet high, and up which it passes. This consists of a brick shaft of about four feet square, and inside, it is the smoke pipe from the boiler, the waste heat from which warms the air in the shaft. This is supplemented by a large coil of steam pipes placed at the bottom of the shaft, so that a steady upward current is maintained at all times. The heating apparatus in the lecture-hall and some other rooms is controlled by the Johnston electric heat-regulating apparatus. By means of a thermostat placed in the room and an electric wire, a compressed air apparatus is made to act upon the valves of the radiators, opening or closing them as the temperature of the room falls or rises. By this means the temperature is so regulated that at the end of a lecture it is found not to have varied more than one degree from what it was at the beginning. The difference which the use of this system makes to their comfort is appreciated both by professors and students. The compressed air for this purpose is obtained by an air pump actuated by the water pressure and connected with it by a pressure-reducing valve, so that the pump stops when the pressure in the cylinder attains twelve or thirteen pounds, and works again when the pressure falls below this point. The compressed air is also available for use at other places for blast or for injecting purposes. The plumbing throughout the building is of the best and most modern description. The building, including fittings, has cost about $55,000, and was erected from the designs and under the superintendence of the University architect, Mr. David B. Dick.