right lung, with typical sputum—the general symptoms and the pulse, temperature, and respiration indicating a rather grave case; and we agreed to continue the treatment on which she had been from the commencement—namely, the administration every fourth hour of three grains of quinine in pill, with the occasional use of a cough mixture. On the seventh day, when we met again, the patient's condition was as follows:—She had passed a restless and almost sleepless night, and had been wandering more or less for the previous twenty-four hours. She could give no assistance in turning herself in bed, owing to prostration. Her skin was moist. The respiration was 50, the pulse 90, and small and weak, and the temperature 102·4°. She had a good deal of cough, and had brought up a considerable quantity of prune juice sputum. We had hesitation in raising her up, but on doing so found the evidences of pneumonia over the entire right back, and some dulness and bronchial breathing over the lower lobe of the left lung. We agreed to continue the beef-tea and brandy, which she had been taking, and to give every eighth hour ten grains of quinine in milk. On the following morning Dr. Cahill found the patient so much better that he directed the dose to be give only twice in the twenty-four hours, and this was continued until we met on the evening of the tenth day, when there was such an improvement that we agreed to discontinue medicine.

In two cases in which quinine had been freely given, violent delirium occurred. Perhaps it was not due to the drug, but I rather think it was, and the circumstance suggests caution in the use of the remedy. In the last of these cases the delirium soon ceased on the substitution for the quinine of bromide of sodium in full doses, after the third dose of which sleep was obtained by the administration of fifteen grains of chloral.

ART. VIII.—*The Changes occurring in the Skin in some forms of Disease.** By HENRY T. BEWLEY, M.B., B.Ch., A.B., Univ. Dubl.; Sch. and ex-Med. Sch.; First Senior Moderator and Large Gold Medallist in Natural Science; Assistant to the Professor of Physiology, and formerly Assistant Demonstrator of Anatomy, Trinity College, Dublin.

WHEN I began to consider in what province of Physiology or Pathology it is possible for one who is but lately qualified, and

* Being the Essay, by "In cute curandâ plus æquo operata Juventus," to which the first triennial award of the Reuben Harvey Memorial Prize was made, July 1, 1885.

who has but little time or material for research at his disposal, to do any work which has any pretension to originality, the first thought that struck me was that which presented itself to Solomon long ago—that there is nothing new under the sun. However, on further consideration, I perceived that, although it is now, thanks to the number and skill of the investigators of medical science, well-nigh impossible to find any field which has not been more or less explored already, still some fields have been much more thoroughly worked than others. Considering these latter, it occurred to me that the Microscopic Anatomy of Skin Diseases was a subject which has been comparatively overlooked and passed by, at any rate in this country. This arises, I think, from two causes—in the first place, it is very difficult to obtain, for microscopic examination, specimens of skins affected with various diseases; and, in the second place, many forms of these diseases do not present any very striking microscopic lesions; and their classification, in contrast with the modern classification of tumours, is made to depend more on their clinical and macroscopic features than on their microscopic lesions. Hence it happens that, at any rate among students, the histology of skin diseases is almost unknown, and fifty could accurately describe the microscopic appearances of a case of croupous pneumonia or of a carcinoma of the stomach, for one who could describe the structure of a vesicle in herpes zoster, or the changes in a skin affected with chronic eczema. Therefore, having been recently in a position in which I was able to obtain specimens of various skin diseases, I resolved to do so, and chose as my subject for the present essay “The Changes occurring in the Skin in several forms of Disease.” At the same time, I am aware that this subject is in several respects an unfavourable, or, at least, a difficult one to work at. In the first place, the microscopic appearances in many skin diseases vary more or less, as regards details, with the intensity or mildness, the acuteness or chronicity, and the recent appearance or long existence of the disease; and, in the second place, in order to be able to assert that any single lesion is normally present in any given form of disease, it is necessary to examine a considerable number of specimens of this disease.

These conditions, necessary for the full description of any pathological process, I have been unable to comply with, having, for the most part, been able to obtain only one specimen of each disease. Therefore, I cannot attempt to give any complete account

of all the various lesions that have been described in the different varieties and stages of those skin diseases of which I have examined single specimens, as, if I were to attempt to do so, I should be obliged to copy largely from the authors who have written on the subject; but I have set before me a less ambitious object, but one which is, I think, more truly original, or, at least, less full of mere copying out of books—namely, to describe as accurately as possible the lesions present in that particular variety and stage of each disease which I have been able to examine.

The books which I have consulted, and which I have found most useful in connection with this work, are—Neumann's *Lehrbuch der Hautkrankheiten*, Vienna, 1880; the two volumes of the *Handbuch der Hautkrankheiten* in v. Ziemssen's *Cyclopædia*, Leipzig, 1884; and Ziegler's *Text-book of Pathological Anatomy*, London, 1884.

As I have only been able to examine specimens of some few out of the large number of skin diseases, I have not attempted to arrange them in any scientific order.

ACNE ROSACEA.

Of this disease there are two varieties:—1. Non-hypertrophic; 2. Hypertrophic. My specimens belong to the latter variety, being sections of a man's nose, which, after having won the first prize at an exhibition of large noses in Vienna, was amputated on account of its excessive size.

The first stage of this disease is characterised by dilatation of the cutaneous blood-vessels; in the second all the tissues of the true skin become hypertrophied. In my sections the connective tissue of the cutis is enormously increased in amount. It is extremely vascular, being permeated in all directions by hypertrophied or newly-formed vessels. In it are contained very many cells—both spindle-shaped connective-tissue cells, scattered everywhere through it, and also small round lymphoid cells, which are here and there collected into masses or foci, which tend to break down in the middle. These inflammatory foci are chiefly to be found in the neighbourhood of the sebaceous glands.

The hairs are small, appearing merely as appendages of the sebaceous glands, which are enormously increased in size, being both wider and extending more deeply into the cutis than they do in their normal state. They are in this case, as in one described by Duhring, divided into lobules by a new growth of connective

tissue. Their openings on the surface are dilated. The sweat glands appear diminished in number.

Papillæ are almost absent in my specimens, the basement membrane lying quite evenly. In a case examined by Dr. Piffard, of New York, the opposite condition was found, "the papillæ being enlarged in length and breadth, and containing round and fusiform cells."

The epidermis appears normal, except that the superficial layers, and even in places some of the stratum spinosum, have a tendency to fall off, which may be owing to the long-continued maceration in oil to which they were exposed.

ECZEMA.

There are so many varieties and stages of this disease, each differing more or less from the others, that, in order to describe in anything like an adequate manner the lesions that occur in it, a large number of sections of different forms of this disease would be necessary. Such a collection I have not been able to obtain, and hence have been able only to examine a few of the numerous forms of eczema.

In a case of chronic papular eczema which I have examined the surface of the skin is irregular, rough, and warty; the horny layer of the epidermis is greatly thickened, so as to present almost the appearance of ichthyosis. The stratum spinosum is also increased in thickness. The fibrous tissue of the cutis and subcutaneous connective tissue is seen in the form of coarse bundles, which are matted together into a very firm and dense network, containing but few connective tissue cells, and resembling somewhat the condition of the connective tissue in a case of elephantiasis Arabum. In several places in my sections the connective tissue network is so dense that it is stained yellow, as the stratum corneum is, instead of pink by the lithia carmine.

The papillæ and superficial part of the cutis are richly infiltrated with lymphoid cells, which are especially numerous along the course of the blood-vessels.

The papillæ are here and there enlarged. In this case there is no abnormal pigmentation to be seen.

In another case which I examined the appearances, though similar, are not so characteristic. The horny layer of the epidermis is not nearly so thick as it was in the last case; in it are seen here and there collections of small black pigment grains.

Numbers of lymphoid cells are seen in the superficial part of the cutis and along the course of the blood-vessels, as in the last specimen; but the network of fibrous tissue, of which the cutis is composed, is not nearly so dense in this section.

In both these specimens the hair-follicles and sweat-glands do not appear to be materially altered.

I have examined portions of skin taken from two patients who were suffering from chronic eczema of the scalp. In one of them the epidermis is considerably thickened and the papillæ enlarged, while in the second they are not much altered. There is some inflammatory infiltration of the cutis with lymphoid cells. In one specimen this infiltration is confined almost entirely to the upper layers of the cutis, and the deeper layers are remarkably dense; in the other the connective tissue network is not so dense, and the infiltration extends down into the subcutaneous areolar tissue. The hairs and the sebaceous and sweat glands appear normal.

I was given two pieces of skin from a case said to be one of eczema impetiginosum. There are, however, in them several small ulcers, with steep, sharply-defined edges, as if a piece had been punched out of the skin. Therefore, I am very doubtful if this case should be classed as one of eczema at all. Perhaps it is one of ecthyma; but it is very difficult to diagnosticate skin diseases by their microscopic characters.

In this case the cutis is infiltrated with many leucocytes. In several places this inflammatory infiltration has become so intense that the tissues have broken down, leaving ulcers with sharply-defined edges, which extend down to the subcutaneous fatty layer, and whose base and edges are composed of ordinary granulation tissue. At the edge of the ulcer the interpapillary processes of the rete Malpighii are much enlarged, extending a considerable distance into the cutis, and in one of these a very perfect epithelial pearl is seen.

Coming to the margin of one of the ulcers the epidermis becomes covered on its surface by a mass of dried secretion and desquamated cells; the stratum spinosum becomes thinned, and its deeper layer infiltrated by some leucocytes; the boundary line between epidermis and cutis becomes indistinct, and the epidermis ceases, the surface becoming covered with granulation tissue.

In the case of another of the ulcers the epidermis at the margin ceases much more abruptly, its cells becoming flattened up to a defined boundary line, where it ceases, and granulation tissue begins.

In a large number of the cells in the stratum spinosum the nuclei are seen to be in a state of vacuolation. The horny layer is very thin or almost absent. The veins in the cutis are enlarged.

HERPES ZOSTER.

The process of formation of the vesicles begins by the formation of vacuoles in the cells of the middle layers of the stratum spinosum. The cells in the neighbourhood at the same time undergo rapid proliferation, and some of them are seen to contain many round, deeply-staining nuclei. The vacuoles increase in size and number, and finally a number of them coalesce, thus forming a cavity of irregular shape. A number of small round cells are at the same time seen in the epidermis, which have, I think, migrated thither from the cutis, as towards the middle of the base of the vesicle the line of demarcation between epidermis and cutis is almost obliterated, and many small cells with deeply-staining nuclei may be traced from the cuticular infiltration up into the epidermis.

The vesicle, therefore, comes to lie in the layers of the stratum spinosum. Many of the cells forming its walls are large and multinucleated, being quite unlike any epidermal cells I have seen in other skin diseases, and forming remarkable objects. These do not lie close to one another, but are separated by the exudation. Among them are many lymphoid cells. The cavity of the vesicle is traversed irregularly by bands composed in part of cells and in part of coagulated fibrin. The cells in these bands are some of larger size, belonging to the stratum spinosum, and some smaller, being leucocytes.

Haight, in his figure of a section of a herpes vesicle—which appears to be the classical woodcut of this disease, as it is copied into all the books I have consulted which give any woodcuts—represents these cells as being all spindle-shaped or stellate, describing a band across the vesicle as being formed entirely of spindle-shaped cells. Such cells I have not been able to see in my sections. I find this network to be composed either of thick bands of round, plump cells held together by a little fibrin, or to be mainly fibrinous, containing a few cells.

In the middle—the oldest—parts of the vesicle the epidermal cells undergo a horny transformation, which is most marked in the roof of the vesicle, but is also found in the cells forming its floor. The nuclei are lost, and the outlines of the individual cells become less distinct.

The cutis corresponding to the bases of the vesicles is infiltrated with leucocytes, which infiltration extends down to the fat of the subcutaneous areolar tissue. It is especially abundant in the neighbourhood of the blood-vessels.

LEPROSY.

The lesions in tubercular leprosy consist in the formation in the cutis and subcutaneous tissue of nodes of granulation tissue. In my sections these nodes extend up to the basement membrane and down to the subcutaneous areolar tissue. They are made up of a number of cells embedded in a fibrous stroma, and contain blood-vessels. The cells are not arranged in so dense masses as in lupus and the more acute forms of inflammation, consequently the fibrous stroma makes up a good part of the node, and to this peculiarity may perhaps be due their permanence and comparatively slight tendency to undergo degenerative changes. The cells in these nodules are of two varieties—small lymphoid cells with deeply-staining nuclei and larger epithelioid cells with larger paler nuclei, in which several nucleoli may be seen. In some of the smaller arteries the internal coat is considerably thickened, and the lumen narrowed thereby. Others, however, of the arteries are not so affected.

Although there are no hairs to be seen in my sections, the unstriped muscular fibres of the skin appear hypertrophied.

The epidermis appears normal; the horny layers are very thin in comparison with the thickness of the stratum spinosum; the nuclei in many cells of the latter are vacuolated.

In one of my sections, which I have stained according to Gram's method—stained first in carmine, then in a solution of gentian violet in anilin water, and removed the excess of staining with a solution of iodine and iodide of potassium in water, and finally with alcohol—the bacillus lepræ may be very clearly seen stained blue, while the surrounding tissues are purple in colour. In the leprous nodules some of the cells are stained purple, while others are stained blue, the latter receiving this colour from the large number of bacilli which they contain. The bacilli may be seen lying, some within the protoplasm of the large cells, and others in the intercellular substance. They are said to measure in length about half the diameter of a human red blood corpuscle.

LUPUS.

Lupus consists in the subepidermal formation of foci of granulation tissue, which consist of small lymphoid and larger epithelioid

cells set in a fibrous network, and containing here and there giant cells. In the neighbourhood of the nodules the skin is diffusely infiltrated with small round cells. The nodules are seen to be permeated by blood-vessels, and there are seen around them some of those "strings of cells following the course of the lymphatics" described by Ziegler.

The papillæ are large, are thickly infiltrated with lymphoid cells, and contain enlarged vascular loops.

The stratum spinosum corresponding to the nodules is much thickened, as it is over the nodules in glanders; growths of the epidermal cells, in the form of branching and interlacing columns, extend for some distance down into the cutis, "reminding one of the cellular growths of epithelioma" (Ziegler). This layer is also permeated by a number of small round cells, which have migrated thither from the cutis. Here and there the epidermis shows a tendency to form pearls. The horny layer is also thickened. Many of the cells in the stratum spinosum contain a vacuole inside their nucleus.

In another specimen of lupus the disease is not in such an advanced condition. Many collections of lymphoid cells are seen in the cutis and subcutaneous tissue, where they chiefly group themselves about the blood-vessels. In some of these foci the cells are much more closely grouped together than in others. Kaposi speaks of these foci as being, at any rate when recent, sharply defined from the surrounding tissue; in my sections they fade off gradually.

GLANDERS.

The cutaneous lesions in glanders consist in the formation in the skin and subcutaneous tissue of inflammatory nodules or foci, which at first view are not unlike those found in lupus. These nodules are pretty sharply defined, and here and there, where the inflammatory process has not gone too far, are seen to be crossed by the remains of hair-follicles, sweat-glands, and blood-vessels.

They are described as consisting of "a delicate vascular stroma, filled throughout by numerous round cells, crowded together in clusters, and presenting the appearance of ordinary pus corpuscles or granulation cells."—Ziegler.

These glanders-nodules are, however, distinguished from other localised inflammatory foci, such as those of lupus, by the great violence of the process, and the extreme rapidity with which the

cells of which they are composed break up and disintegrate, so that even the smallest and most recent nodule is seen to be made up in the middle, not of ordinary granulation tissue, but of a mass of detritus, consisting of broken up and disintegrated cells, nuclei, and granules of all sizes.

The lymphatics in the neighbourhood of the nodules are much enlarged.

In my sections the epidermis is as yet unaffected; the stratum spinosum is, however, considerably increased in thickness in the neighbourhood of the nodules.

CUTANEOUS HORN.

Of these rare structures there appear, from the descriptions given of their histology, to be several varieties.

The horn of which I have cut sections rests on enlarged papillæ. Up to the edge of the horn they are of normal size, but then become enormously long, branching and subdividing many times. About these enlarged papillæ the stratum spinosum is greatly thickened, and upon it a large mass of horny cells is placed. On the top of the horn this layer is arranged in columns, so that the horn ends in a number of bristle-like processes, each of which corresponds to a branch of a papilla. The papillæ are seen extending a long way up into the horn in the form of narrow tubes surrounded by epidermis.

The cutis at the base of the horn is infiltrated with many small round cells, which are rather suspicious of commencing epithelioma—a kind of growth which these horns are very liable to take on.

G. Simon (*Oesterr. Zeitschr. f. prakt. Heilkunde*, 1854) describes another variety of horn, in which he distinguishes cortical and medullary substance, saying “that the tissue is penetrated by many canals, which are held to be blood-vessels cut through, and which are partly coloured red from their contents. The central part of the horn is more compact and less vascular than the outer,” which is the opposite condition to that which I find in my sections.

Lebert (*Ueber Keratose oder die durch Bildung von Hornsubstanz erzeugten Krankheiten*, Breslau, 1864, p. 76) says horns spring from the deeper layers of the epidermis. He describes their structure, when examined in longitudinal sections, as consisting of “a mass of small columns, rods, or palisades lying close one to another, and so intimately united by a connecting substance as to appear blended into a homogeneous mass. The individual columns

have a striped, shreddy appearance, and are made up entirely of epidermal cells arranged one upon another in an imbricated manner."

Neumann (Lehrbuch) says they are hyperplasias, sometimes of the epidermis, sometimes of sebaceous glands, sometimes even of sweat glands.

FIBROMA MOLLUSCUM.

These tumours vary in hardness. Ziegler says "the less firm varieties are rich in small cells, and the fibrillation of the inter-cellular tissue is indistinct; the firmer varieties have fewer cells, and are markedly fibrous; but in no case is the tissue so coarsely fibrous as that of the normal cutis."

The two tumours seen in my sections consist of a mass of finely fibrous tissue, containing many cells, which appear spindle-shaped, with elongated nuclei. The tumours are separated from the surrounding tissue by a very distinct line; this fibrous tissue round them is much coarser, and contains much fewer cells. The fibroma is remarkably rich in blood-vessels, which have thin walls.

The papillæ of that portion of the skin which lies over it are atrophied.

The structure of the softer variety is described by Neumann (Lehrbuch) as consisting of large areolæ, permeated by a fine network of fibrous tissue, from which an albuminous fluid containing numerous cells may be pressed out. The figure which he gives of such a tumour presents an appearance very similar to that of an alveolar sarcoma.

GASSERIAN GANGLION IN A CASE OF PEMPHIGUS OF THE FACE.

The opinion has for some time been held that certain skin diseases are caused by lesions of the nervous system. To this class, besides herpes zoster—whose ætiology seems now better known than that of most forms of skin disease of this class—some cases of pemphigus are thought to belong, and in a few this opinion has been confirmed by microscopic examination. The lesions occur in various parts of the nervous system. In a case of herpes iris (pemphigus?), Jarisch (Sitzungsb. a. k. k. Akad. d. Wissensch., III. Abth. Bd. 81, Mai, 1880) found lesions in the gray matter of the spinal cord in several places in the length of the cord, especially in the anterior cornua. The changes consisted in inflammatory appearances of the ganglion cells, swelling of their processes, and of the fibrillar connective

tissue, where a network with coarse meshes, and bodies looking like drops of myelin were seen, giving the idea of proliferation.

Dejérine and Leloir (*Gaz. d. Hôp.*, 1876, p. 835), again, found lesions in the peripheral nerves in a case of pemphigus. Near fresh vesicles they saw nerves in a state of degeneration—the axis-cylinder had disappeared, the myelin had run together into lumps, the neurilemma was in places varicose, owing to accumulations of myelin. In the neighbourhood of old vesicles the axis-cylinders and myelin of the nerves had disappeared, and only the neurilemma tubes were left; in them the nuclei were increased in number.

I have made sections of a Gasserian ganglion in a case of unilateral pemphigus of the face; in it are seen a number of small hæmorrhages, apparently not very recent; the connective tissue is in parts thickly infiltrated with small round cells, which are especially numerous about the ganglion cells, and about some of the nerve-trunks which come off from the ganglion.

If the lesions in the spinal cord, and in the peripheral nerves in Jarisch's and Dejérine's cases respectively, are to be looked on as the cause of the eruptions of pemphigus, I think there is just as good ground for holding these extravasations and inflammatory infiltrations to be the cause of the eruption in this case, where the disease was confined to the skin, which was supplied by the fifth nerve on the side on which these changes are seen in the ganglion.

[*To be concluded.*]

ART. IX.—*Neurasthenia, Acute and Chronic, and its Importance.*

By J. STRAHAN, M.D.; late Medical Officer, Belfast Dispensary; formerly Resident Surgeon and Resident Physician, Belfast Union Hospitals.

THIS disease, in its almost innumerable forms, is sufficiently common in this country, and sufficiently important to the profession, even as influencing diagnosis and prognosis in many obscure cases, in general practice, to justify much more attention than it has yet received in medical literature. In almost all of our best text-books the subject is never even mentioned, under any head whatever. Indeed, the only common text-book which mentions it is Flint. He indicates, at least, the existence and importance of this disease. In Quain's Dictionary there are two articles, one on spinal neurasthenia, another on spinal irritation, by Drs. Bastian and Brown-Séquard respectively; but these diseases are treated as separate affections, and no indication