in the abdomen by x ray examination and all doubt as to the cause of the patient's condition removed; at all events, it would have indicated the seat of operation, a very important matter, for there is no doubt, I think, that had we not luckily hit upon the right site for the operation and had instead of aiming directly at the appendix at first cut down upon the stomach she would not have survived the further necessary extension of the proceedings. Naturally, in such cases the facilities for x ray examination would only be forthcoming in a minority, but when forthcoming I am sure there is scope for this aid to diagnosis which should be well considered by all practical surgeons. There is still far too strong a tendency to decline the aid of x ray examination

FIG. 5.

Reproduction of an x ray photograph of the appendix removed in Case 6, containing a large concretion (B). An oxalate of lime renal calculus (A) has been included in the photograph in order to show the comparative density of the two structures. (Mr. Mackenzie Davidson.)

because it is unlikely to give positive information, and although it is true that in abdominal work the x ray examination may frequently show nothing very definite it will if made by a competent person invariably show stones in the kidney, ureter, and bladder, caseous tuberculous glands, new growths of bone, not uncommonly concretions in the appendix, sometimes stone in the gall-bladder, and generally tuberculous disease of organs, and of course metallic and bony foreign bodies, as well as in favourable circumstances subdiaphragmatic abscess and other things. Although for the proper appreciation of the situation of some of these the stereoscopic method is indispensable for clinical purposes the mere existence of most of them can be demonstrated by a properly taken ordinary skiagram.

In conclusion, I have no hesitation in saying that in cases of abdominal pain or discomfort, unless the diagnosis is obvious, no examination is complete which does not include the use of the x rays, and that the practitioner is failing in his duty to his patient, especially if an exploratory operation is contemplated, who does not in such cases employ the x rays when they are available unless the delay involved in obtaining the necessary investigator be detrimental to the patient's safety.

THE INVALID CHILDREN'S AID ASSOCIATION.—

The annual meeting of the friends of this association was held on May 13th at Grosvenor House, which was kindly lent for the afternoon by the Duke and Duchess of Westminster. There was a large attendance of ladies and gentlemen interested in this excellent work. Sir Edgar Speyer, Bart., was in the chair and in his opening speech drew attention to the very careful character of the work which is being done, careful both from the medical and social points of view. He pleaded for increased financial support. The meeting was also addressed by the Rev. Father Waggett who justified the care of the suffering on scientific grounds as well as from the natural instincts of sympathy. Among the other speakers were Mr. Andrew Lang, Mr. D'Arcy Power, Mr. E. A. H. Jay, and Mrs. Bouchier (Miss Violet Vanbrugh). The admirable work of the ladies who visit sick children in their own homes was much dwelt upon and Mrs. Bouchier pleaded earnestly for new helpers. Mr. D'Arcy Power pointed out the value of their influence in the eyes of the medical profession. The formal business of the meeting was unanimously carried and the proceedings closed with hearty votes of thanks to the hosts and the speakers.

The Hunterian Lectures

ON

THE CONNECTIVE TISSUE IN CARCINOMA AND IN CERTAIN INFLAMMATORY STATES THAT PRECEDE ITS ONSET.

*Delivered before the Royal College of Surgeons of England on
Feb. 17th, 19th, and 21st, 1908,*

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LECTURE II.¹

Delivered on Feb. 19th.

MR. PRESIDENT AND GENTLEMEN,—Having now reviewed the changes exhibited by the connective tissue in relation to primary carcinoma in general it is necessary to consider these changes as applied to primary carcinoma in particular situations and specially to study certain inflammatory states which clinically so often precede the development of the growth as to warrant them being termed precarcinomatous.

CARCINOMA OF THE VULVA.

The frequency with which the chronic inflammatory condition known as leukoplakia of the vulva passes into carcinoma has been noted by Henry Morris, Bland-Sutton, and others. A clinical investigation of a large number of cases, shortly to be published by Comyns Berkeley, failed to find one example of carcinoma of the vulva in which this condition was not antecedent to the onset of the new growth. I have microscopically studied material from a large number of these cases with the following results. In the early stage of the affection there occurs a marked hyperæmia of the subepithelial tissues and a number of thin-walled blood spaces become apparent. At the same time a connective tissue cell proliferation takes place, at first of lymphocytes only, but later of plasma cells as well. The lymphocytes are aggregated immediately under the epithelial margin and particularly at the tips of the interpapillary processes. Here they are seen intercalating themselves between the epithelial cells in places in such quantity as fairly to break up the epithelial edge and to render the demarcation between connective tissue and epithelium indistinct. (Fig. 6.) Deeper down lymphocytic aggregations are seen. These usually surround small vessels, which, however, only contain polynuclear leucocytes as a rule. Here and there in the connective tissue are seen new lymph nodes with germinal areas similar to those found in the neighbourhood of a carcinoma. (Fig. 7.) There is no evidence of degenerative changes in these lymphocytes, but certain of them exhibit the peculiar black nuclear network to which I have already referred. Plasma cells are seen proliferating in rows along rifts in the fibrous connective tissue. They are situated often at a considerable distance from the epithelial margin, nor do they ever intercalate themselves between the epithelial cells. The fixed connective tissue cells do not show marked changes, though it is probable they, too, are somewhat increased in number. Endothelial proliferation does not occur to any extent and polynuclear leucocytes do not apparently play much or any part in the process.

As a result of the plasma cell and lymphocytic proliferation there occurs at first a marked rarefaction of the connective tissue, due to a disappearance of collagen and elastin. The fibroglia fibres become more apparent and the yellow elastic fibres disappear, so that the thin-walled blood channels in the subepithelial tissue are without an elastic tunic. The epithelium becomes much thickened and keratinisation becomes a marked feature in the more superficial epithelial cells, whereas in the normal vulval epithelium it is almost absent. The subepithelial papillæ are elongated by the connective tissue proliferation, whilst the interpapillary epithelial processes are correspondingly lengthened.

¹ Lecture I. was published in THE LANCET of May 16th, p. 1389.

Thus we have under the thickened epithelium a practically new formation made up of a large number of new tissue cells, together with the de-elasticised and de-collagenised pre-existent elements.

In the older and quiescent stages of leukoplakia of the vulva the cell aggregations disappear and collagen is re-deposited in abnormal amount in the subepidermal tissues, so that we then see a much thickened and extensively

FIG. 6.

A portion of a leukoplakic vulva under high magnification, showing lymphocytic intercalation. A, Epithelial cells. B, Intercalated lymphocytes. C, Lymphocytes and plasma cells in the subepithelial tissue.

keratinised epidermis resting on a peculiarly dense connective tissue, from which, however, all yellow elastic elements are absent. This stage might be regarded as a state of healing but there is no true cure in the sense of a return to the normal, the relation between epithelium and connective tissue having been permanently altered. My

FIG. 7.

Leukoplakia of the vulva, showing the complete disappearance of the elastic tissue under the epithelium and a new lymph node with a well-marked germinal area in the subepithelial connective tissue.

specimens, however, and clinical evidence also, support the view that carcinoma is much less likely to develop in this stage than in the preceding one, and then only when for some reason the tissues have taken on a renewed cellularity.

In the larger number of cases in which carcinoma develops

it would appear to do so in an area which has never attained this resting stage but in which active tissue cell proliferation has gone on up to the beginning of the malignant process. For in my earliest cases, in which the epithelial down-growth is only as yet foreshadowed, the connective tissue cell proliferation around this area is already typical, and clinically, when carcinoma develops in the quiescent stage, it does so in some small fissure or erosion which had refused to heal.

The beginnings of carcinoma are seen over an area of variable extent, large and diffuse, when it starts in the

FIG. 8.

The earliest beginnings of carcinoma of the vulva. A, Down-growing epithelium. B, De-elasticised subepithelial tissue crowded with plasma cells and lymphocytes. C, Unaltered elastic fibres.

earlier stages of leukoplakia, but small and localised when it begins in its later phases. The carcinomatous change begins as a great hypertrophy of the interpapillary processes over a certain area whereby they penetrate more deeply than normal into the underlying connective tissue. The connective tissue papillae are, however, more than correspondingly elongated so that they reach much higher than normal, but they are thinned and compressed. The connective tissue shows a great cell proliferation of the type I have described as occurring both in the earlier stages of leukoplakia and outside the margin of fully developed carcinoma. (Fig. 8.) It is particularly to be noted that the earliest down-growth of the epithelium is into a tissue deficient in yellow elastic fibres and otherwise profoundly altered by the pre-existent inflammatory process. (Fig. 9.) As the growth advances

FIG. 9.

Carcinoma of the vulva superimposed upon an old leukoplakia of the vulva, showing the epithelial down-growth into the altered subepithelial tissue.

the surface epithelial cells do not keratinise completely and become loosened in their attachment to surrounding epithelial cells. Many probably desquamate and eventually the elongated connective tissue papillae reach the free surface. The surface of the growth now bleeds readily, and its condition may be likened to the skin after a Thiersch graft has been removed. Later still the epithelial down-growths which at first are simply the enlarged pre-existing interpapillary processes of the epidermis become branched and tortuous. The surface extension of the growth is at first by successive conversion of these hypertrophied processes into

definite carcinomatous down-growths, and this seems to continue, as Ribbert stated, until the whole "precarcinomatous" area is exhausted. After this my investigations show that the growth continues by division of the cells already formed but that there is no conversion of normal epithelium into carcinoma cells.

All carcinomata of the vulva are raised at their commencement, this elevation being due partly to proliferation of the epithelial cells, partly to the elongation of the papillæ and partly to the connective tissue cell multiplication that is going on under the epidermis. In the papillomatous types this elevation is very marked but the vast bulk of these projecting masses is epithelial, the connective tissue papillæ being extremely elongated and thin and showing signs of pressure atrophy. In my specimens of the papillomatous type of growth there is less evidence of profound changes in the subepithelial connective tissues than in the commoner or ulcerative variety, for though lymphocytes are present in large numbers plasma cells are much scarcer, whilst the elastic tissue has not been destroyed to the same extent. Clinically the prognosis of this form of growth is better than that of the ulcerative form.

CARCINOMA OF THE TONGUE.

From the clinical standpoint most cases of carcinoma of the tongue exhibit well-marked evidence of pre-existent inflammatory changes in the affected organ. In the larger number of these the tongue is definitely leukoplakic. Pathologically all the cases that I have examined have apparently arisen as an epiphenomenon on a condition of chronic inflammation.

In the earlier stages of chronic superficial glossitis the subepithelial connective tissue becomes crowded by a number of lymphocytes, which are especially aggregated at the tips of the interpapillary epithelial processes and are here seen intercalating themselves between the individual epithelial cells. This process of intercalation particularly affects the Malpighian layer. The "basement membrane" is usually intact, the cells having apparently passed through it, but at the points of maximum lymphocytic aggregation the epithelial edge becomes much broken up and the definition between epithelium and connective tissue is obscured. The distribution of these lymphocytic aggregations is, however, unequal, many of the epithelial processes being slightly affected, whilst around others enormous collections have occurred. Deeper down are seen quantities of plasma cells proliferating in rows or masses. As in leukoplakia of

FIG. 10.

Acute leukoplakic inflammation of the tongue, showing the loss of elastic fibres under the epithelium and the proliferation of plasma cells and lymphocytes.

the vulva, these cells do not often occur immediately under the epithelial margin but are situated some slight distance from it. Superficially they are mixed with lymphocytes, but lower down they are "pure." (Fig. 10.) The hyaline connective tissue cells show some evidence of multiplication and the connective tissue papillæ are enlarged and elongated. The apices of these papillæ are usually free of lymphocytes and plasma cells and show the hyaline cells only. Coincidentally with the proliferation of these various types of cell a great rarefaction of the subepithelial connective tissue takes place and the yellow elastic fibres which are present in large quantity in the normal organ disappear, whilst the epithelium

becomes thickened and the keratinisation of the superficial layers is exaggerated. In the older or quiescent stages the hypercellularity disappears, much collagen is deposited, and the subepithelial connective tissue becomes dense and fibrous, but there is no regeneration of the elastic tissue. The papillæ shrink and the epithelium becomes much more of a flat sheet. In the oldest stages it becomes less thickened and the cells undergo early keratinisation. In any of these phases it is apparent that the epithelium is resting on a much altered and largely new subepidermal tissue.

Comparing these changes with those which I have already described as occurring in leukoplakia of the vulva it is seen that they are identical. In the earliest carcinomata of the tongue that I have examined the down-growing epithelial columns are continuous with hypertrophied interpapillary processes and are growing down into a subepidermal tissue already the seat of the changes which I have just described. Surrounding the epithelial masses is a connective tissue cell proliferation identical in quality with that seen in chronic glossitis. The general relations of the connective tissue cells to the epithelial cells and the composition and arrangement of the stroma are similar to that which I have already described in the general survey.

CARCINOMA OF THE LIP.

The relation that carcinoma of the lip bears to chronic irritation is well known. This irritative process is limited to a comparatively small area in most cases. Hence in endeavouring histologically to ascertain the relation borne by the carcinoma to any antecedent inflammatory process very early specimens are alone of value. For in more advanced cases the whole precarcinomatous area is already taken up by the growth and all evidence of pre-existent change is destroyed. In a specimen of the size of a small split pea the following appearances are present. Microscopically the surface is covered by a thick squamous epithelium which at the periphery of the nodule is seen to be sending downwards multiple epithelial processes of large size into the underlying connective tissue. These processes are unbranched and well defined and would not ordinarily be termed carcinomatous though they constitute the earliest changes in the production of malignancy. (Fig. 11.) The

FIG. 11.

Edge of a small carcinoma of the lip. The epithelial processes are growing into a tissue already deficient of elastic fibres and the seat of a large plasma cell and lymphocytic proliferation. To the left is seen a quantity of granular elastin under the non-malignant epidermis.

subepithelial tissue into which they are projecting is practically a mass of plasma cells and lymphocytes. The lymphocytes are aggregated around the tips of the epithelial processes, whilst the plasma cells cover a wider area, at whose periphery many isolated groups are seen, the cells of which, lying in rows or masses, are producing rifts in the connective tissue matrix. The connective tissue lying beyond the area of tissue cell proliferation is seen, when stained by Weigert's method, to be totally deficient in elastic tissue and to be composed of a dense homogeneous collagenous fibrous tissue with a few hyaline connective tissue cells.

lying in it. Such an appearance is the result of a pre-existent inflammatory change corresponding to the quiescent stages of leukoplakia of the vulva or tongue. This de-elasticised area extends beyond the area of plasma cell proliferation for about the same distance as that area itself occupies, and it reaches under the epithelium for some distance beyond the most peripherally placed epithelial down-growth. Under the epithelium beyond this is seen an abnormally large amount of elastic tissue, for the most part granular and ill arranged, whilst the epithelium here is unduly thickened and keratinised. This condition is also due to a chronic irritation, which has never reached an intensity sufficient to produce tissue cell proliferation. Sections taken from the centre of the growth show typical carcinomatous down-growths occurring into a tissue the seat of old inflammatory changes. These down-growths are enlarged and branched interpapillar processes and they are surrounded by a dense mass of plasma cells and lymphocytes. The relatively large area occupied by the tissue cell proliferation is a point to which I shall have occasion to refer later.

CARCINOMA OF THE CERVIX.

Carcinoma of the cervix bears clinically a striking relation to the inflammatory conditions of the cervix consequent to childbirth. Pathological evidence of pre-existent cervicitis and "cervical erosion" is present in all the early cases which I have examined. In the more advanced cases the growth is so extensive that the signs of pre-existent inflammation are not so obvious, but they are to be found nevertheless if search be made for them.

FIG. 12.

The normal epithelium of the vaginal cervix, showing the subepithelial elastic fibre plexus.

It is necessary, then, to describe in detail the pathology of chronic cervicitis and to study particularly the changes seen in cervical erosion. In the earlier phases of this condition the subepithelial tissue underlying the squamous epithelium is infiltrated with lymphocytes. (Figs. 12 and 13.) The same appearances are seen under the columnar

FIG. 13.

Early erosion of the cervix, showing the breaking up of the epithelial layers and the destruction of the elastic fibres coincident with the lymphocytic and plasma cell proliferation.

epithelium of the cervical canal higher up and around the mucous glands there. In these glands are seen polynuclear leucocytes, probably a remnant of the original acuter inflammation which initiated the process. The squamous epithelium over the eroded area is largely broken up, lymphocytes have intercalated themselves between the individual cells, and these latter appear loosened in their attachment to one another so that the superficial cells have desquamated. The surface is therefore irregular and the

epithelium thinner than normal. Immediately underlying the squamous epithelium of the normal cervix is a fine plexus of yellow elastic fibres. In the stage of erosion that I am describing this plexus becomes broken up, apparently as a result of the lymphocytic proliferation, whilst a new layer of tissue deficient of elastic fibres is formed above it. This proliferation is irregular in its distribution, especially at the periphery of the inflammatory area and consequently the elastic plexus is at first destroyed irregularly. The whole cervix is unusually vascular and an abnormal number of thin-walled blood spaces are seen. At a later stage plasma cells begin to appear under the epidermis. They bear the same relation to the lymphocytes and epithelial cells that I have described elsewhere. The elastic plexus now entirely disappears and the loosened epidermal cells become largely detached so that practically only the basal layer remains,

FIG. 14.

Cervical erosion. A later stage, showing hypertrophy of the glands, disappearance of the surface epithelium, and aggregation of plasma cells.

and this is deficient at various points where the exposed highly vascular connective tissue comes to the surface. In cases where the tissue cell proliferation is very profuse these areas become raised as papillary elevations which consist entirely of plasma cells. Coincidentally with these changes under the epithelium is seen a great hypertrophy of the cervical glands, which become characteristically convoluted. They lie in a matrix containing a great number of plasma cells and lymphocytes which are specially aggregated around them. The hyaline tissue cells are also increased in quantity. (Fig. 14.)

FIG. 15.

Chronic cervicitis, showing ingrowth of epithelium at a spot where the elastic fibres have been destroyed by plasma cells and lymphocytic aggregation. Note the layer of de-elasticised tissue intervening between the epithelium and the elastic fibres at A.

It is probable that the cellular condition of the subepithelial tissue favours epithelial ingrowth, and that the loss of the elastic tissue plexus also acts in that direction; for in sections where this plexus is irregularly destroyed it is noticeable that protrusions inwards of the epithelium

correspond to areas of tissue cell proliferation and disappearance of the elastic fibres. (Fig. 15.) Somewhat later the epithelium overlying the area of the erosion (which at first was thinned and irregular) also hypertrophies, and layer upon layer of squamous cells are laid down which show an abnormal tendency to keratinise. Thus the whole area of the erosion becomes covered by a thickened whitish-looking squamous epithelium, exhibiting large interpapillar down-growths, so that the area which was originally covered partly by squamous and partly by columnar epithelium becomes coated with squamous epithelium alone. The ducts of the glands in this area now have to pass through many layers of squamous cells to reach the surface. These cells presently block the ducts and the resulting retention cysts form the so-called "ovules of Naboth." The de-elasticised connective tissue still exhibits many lymphocytes and plasma cells specially marked at the tips of the inter-papillar epithelial processes and around the glands. (Fig. 16.) In the oldest stages the lymphocytes and plasma cells largely disappear and the subepithelial tissue presents a fibrous matrix with a number of oval hyaline connective tissue cells contained in it.

Carcinoma of the cervix may begin either in the thickened squamous epithelium that covers the area of an old erosion or in the hypertrophic cervical glands higher up. In either case the development of malignancy appears to bear some relation

FIG. 16.

A late stage of erosion of the cervix, showing the hypertrophied epithelium, blocked glands, and cellular sub-epithelial tissue.

to the altered conditions that obtain between the epithelium and its underlying connective tissue as a result of long-continued cervicitis.

In squamous cell carcinoma the epithelial down-growths correspond to the large interpapillar epithelial processes that characterise the old erosion. Surrounding them are very large masses of plasma cells together with many lymphocytes. The hyaline fixed tissue cells do not show much evidence of proliferation. The superficial muscular and fibrous elements are rarefied and largely destroyed by the plasma cell proliferation. Underlying the thickened epithelium beyond the margin of the actual growth the same tissue changes are seen in progress and the subepithelial elastic plexus is absent. (Fig. 17.)

In the columnar cell growth similar tissue changes are observed. The malignant glands are invading a tissue rich in plasma cells and lymphocytes. Beyond the area of actual malignancy many hypertrophic glands are seen surrounded by masses of plasma cells. The squamous surface of the cervix shows changes due to old inflammation.

In the case of either form of growth then the tissue changes are those of a chronic cervicitis which has undoubtedly preceded the onset of malignancy.

CARCINOMA OF THE SKIN.

There are a number of conditions which clinically predispose to carcinoma of the skin. It is necessary to consider these conditions separately and I shall now proceed to describe the result of my own observations in this connexion.

Scar tissue.—If a healthy and united wound be examined on the third day after its infliction remarkably little is to be seen. The line of the incision is distinguished by a slight irregularity of the epidermis and by the abrupt break in the elastic fibres. Here and there in the deeper parts are seen collections of fibrin and entangled blood corpuscles. The tissues bounding the wound show very little increase in cellularity. Such as there is is due to large connective tissue cells with hyaline nuclei. These cells are also found entangled in the collections of fibrin. On the sixth day an increased number of large tissue cells are seen and in addition some lymphocytes make their appearance. The elastic tissue appears to have retracted from the wound margins so that when stained by Weigert's method a definite de-elasticised streak of tissue appears. Further, the margins are thickened by a material resembling collagen but staining faintly with methyl violet. On the tenth day there is very little further change. The fibrin deposits have disappeared and the tissues are entirely united across the wound with the

FIG. 17.

Edge of a squamous-celled carcinoma of the cervix, showing the precarcinomatous state of the area not yet malignant.

exception of the elastic fibres which are absent over this area. On the twenty-second day the disappearance of the elastic tissue for some distance around the wound is very marked. Large mononuclear hyaline tissue cells are seen proliferating in groups and a number of new thin-walled blood spaces have formed, in and around which leucocytes are seen. On the fortieth day the scar is definitely raised. Stained by Weigert's method, it is seen that elastic tissue is entirely absent over a large and somewhat wedge-shaped area. In this area are many groups of large hyaline connective tissue cells with a single round or oval nucleus. Besides these there are many lymphocytes and here and there an occasional plasma cell. The epithelium covering this area is somewhat thinned. At the end of four months much the same condition is apparent but there are fewer cells to be seen and the scar is beginning to contract. At the end of a year the scar is depressed. Elastic fibres are absent over a large area. The hypercellularity has almost disappeared and the connective tissue is practically normal in appearance. When stained by Weigert's method, however, the scar area shows up in the section as a pale de-elasticised patch.

In scars the seat of chronic irritation, however, a different appearance obtains. The connective tissue is rich in a number of cell types consisting of lymphocytes, plasma cells, and hyaline tissue cells, arranged in a manner practically identical with that seen in the other chronic inflammatory processes I have described. The epithelium covering these irritated scars is at first thin and ill-formed; at a later period, however, it becomes hypertrophied and thickened. Elastic tissue is absent as in the healthy scar.

Chronic suppurating ulcers.—The granulations forming the free surface of a chronically suppurating ulcer or sinus are microscopically composed of a number of hyaline cells with pale oval nuclei united to one another by delicate processes. These cells stain very poorly and their appearance suggests a low vitality. Intermixed with them are numbers of polynuclear leucocytes so massed at the actual free edge as to almost obscure the paler connective tissue cells. As one passes deeper into the tissues the polynuclear leucocytes decrease

and the hyaline tissue cells become more definite. Lymphocytes begin to make their appearance to the exclusion of the polynuclear leucocytes and deeper in still plasma cells are seen in increasing numbers. As the periphery of the process is approached polynuclear leucocytes disappear altogether from the field of view and the dense cell aggregations consist entirely of lymphocytes and plasma cells lying in a groundwork of hyaline fixed tissue cells. Elastic tissue is totally absent from the whole area under consideration. At the edge of the ulcer the epithelium is undermined for a considerable distance by this tissue cell proliferation and the normal subepithelium elastin is absent. Moreover, the epithelium is greatly hypertrophied and exhibits long and often slightly branched interpapillar processes. Thus both in chronically irritated scars and at the edge of very chronic ulcers a similar condition is eventually arrived at—namely, a much hypertrophied epidermis superimposed on a connective tissue exhibiting a characteristic cell proliferation and a total deficiency of elastic tissue.

Chronic warty conditions.—A certain proportion of carcinomata of the skin begin on a previously warty condition which has existed for some time before the onset of malignant disease. A histological examination of such a specimen exhibits the structure of typical squamous cell carcinoma; but in the outlying portion, not as yet malignant, the epithelium is greatly thickened, the interpapillar processes are long and branched, and there is a corresponding elongation of the papillæ themselves. The subepithelial connective tissue is hypertrophied and unusually dense owing to a great increase in the white fibrous elements. Here and there in this tissue are seen aggregations of lymphocytes and plasma cells, whilst the hyaline connective tissue cells are increased in number. In sections of this warty skin stained by Weigert's method it is seen that the tissues underlying the epidermis for a considerable extent present a complete absence of the elastic tissue which should normally occur there. Microscopically the condition is identical with that of the other inflammatory states clinically predisposing to carcinoma.

Lupus vulgaris.—The frequency with which carcinoma supervenes on old lupus is known. This has been especially frequent since the introduction of x ray treatment. An acute tuberculous lesion of the skin is not characterised by the presence of plasma cells and lymphocytes, the nodule being made up almost entirely of hyaline "endothelioid" cells

FIG. 18.

A normal hair-bulb and sebaceous gland, showing the distribution of the elastic tissue. Weigert's stain.

from which the giant cells appear to be a derivative. In old-standing cases, however, the hyaline tissue cells disappear before an increasingly large quantity of plasma cells and lymphocytes, and the condition of the subepithelial tissue becomes cytologically identical with those of the other precarcinomatous conditions that have been considered. The elastic elements have early disappeared. Finally comes an epithelial hypertrophy on which carcinomatous in-growth may be superimposed.

Rodent ulcer.—Borrmann found evidence of pre-existent tissue changes in every specimen of the very large number of cutaneous carcinomata examined by him. In the specimens of rodent ulcer studied by me I have also found these changes. They consist in a disappearance of the delicate elastic fibres which normally encapsule the hair follicles and sebaceous glands (Fig. 18) and the substitution of a hyaline connective tissue in that situation. There is a similar change in the constitution of the connective tissue immediately adjoining the surface epithelium, but beneath

this zone is found an abnormal quantity of granular elastin, certainly the product of chronic irritation. The connective tissue remote from the actual seat of malignancy exhibits an abnormal number of lymphocytes, whilst local areas of plasma cell proliferation are seen chiefly around the hair follicles. Moreover, the subepithelial tissue is hyperæmic and the epithelial elements, especially those of the sebaceous glands, are hypertrophied. (Fig. 19.)

FIG. 19.

Tissues beyond the edge of a rodent ulcer, showing disappearance of elastic tissue around the hair-bulbs and under the epidermis, with an increased amount in the tissue elsewhere. Weigert's stain.

X ray carcinoma.—Rowntree, in an investigation shortly to be published in the reports of the Cancer Investigation Department of the Middlesex Hospital, has found that in the skin exposed to x rays there is an initial hypertrophy of the epithelial elements which is subsequently followed by atrophy with complete disappearance of the hair bulbs and sebaceous glands. The connective tissue shows changes which particularly affect the elastin. In an advanced case of x ray dermatitis this has completely disappeared in a zone immediately under the epithelium, where it is replaced by an immature connective tissue. In cases where carcinoma is threatening to supervene large numbers of plasma cells and lymphocytes are present.

PROPHYLAXIS IN THE CARE OF CHILDREN IN HOSPITALS.¹

By HENRY KOPLIK, M.D.

THERE is no department of medicine in which greater advances have been made in the last 20 years than in the science of preventive medicine in the management of infants and children from birth to older childhood, and it is for this reason that I have chosen this theme, inasmuch as I know that your daily work is concerned in the pursuit of this very department of medicine and I desire you to know some of my personal work in this field.

The hospital ward designed for the care of children as it existed some 25 years ago, when I was a hospital interne, may not be without interest as compared with what we think it should be to-day. The chief of such a service was a man who had gained a reputation not only as a general clinical all-round practitioner but who had added, according to the light of that day, distinct advances to our knowledge in the diseases of children. He was thus a general man. As you might surmise, in most cases such a man was a very busy man and his skill in handling children was recognised and admitted to be an additional charm to his medical attainments. The ward which such a man would control or the children's hospital under his management was arranged very much like an adult service with the exception that the patients were children. There was nothing about the ward which would strike one as having been intended to house

¹ A paper read before the Society of School Inspectors, New York Board of Health, on Jan. 8th, 1908.