Culture Tested Daily for Acidity.

After one day's incubation ...	2.28	per cent. lactic acid, B.P.
" two days' "	2.58	" " "
" three " "	3.48	" " "
" four " "	4.56	" " "
" five " "	4.56	" " "

It was assumed that acid production, or bacterial activity, terminated as a result of the lactose (milk sugar) contained in the milk having all become converted into lactic acid. To ascertain if the addition of lactose would accelerate acid production, two cultures were made, (a) containing two tablets in 100 c.cm. of milk, (b) containing two tablets in 100 c.cm. of milk, with the addition of 4 grams of lactose; after seven days' incubation at 100° F., the amount of lactic acid produced in (a) and (b) was found to be identical—namely, 3.12 per cent. in each sample. It therefore appears that the addition of milk sugar was unnecessary.

Another question was, Does the curd or the whey contain the greater proportion of acid? A sample of soured milk was examined, in which no separation of casein had occurred; it was afterwards heated in a flask or a water bath for a few minutes, until coagulation had taken place, for a sufficient quantity of whey to be obtained, and the estimation of the acid in both instances was found to correspond exactly.

EFFECT OF TEMPERATURE.

With a view of ascertaining the optimum temperature for the lactic acid organism, a sample of milk treated with the bacillus of Massol was divided into three parts, and the following results were obtained in the same length of time:

Temperature.	Amount of Lactic Acid B.P.
80-90° F. ...	1.44 per cent.
90-100° F. ...	1.68 "
100-110° F. ...	2.28 "

These results were practically confirmed by tests with the tablets which I had prepared; one tablet in half a pint of milk gave—

Incubated below—	Lactic Acid B.P.
100° F. ...	0.12 per cent.
105° F. ...	0.26 "
110° F. ...	0.72 "

I consider the disappointments which have been expressed in the preparation of sour milk are due (1) to employing insufficient bacterial substance, (2) to inefficient temperature. Some popular forms of apparatus on the market are heated by means of a night-light, and the temperature produced with night-lights from the same box has been found to vary 15° F. To obtain the best results a moist culture is recommended and cultivating for at least four hours between 105° and 110° F., the growth of adventitious organisms is thereby inhibited, and an amount of lactic acid quickly produced to retard their subsequent development.

NOTE.—It was found that the milk heated for ten hours at 105° F. gave a reaction to phenolphthalein, which corresponded to 0.048 of lactic acid B.P., and this amount has been deducted in the results above recorded.

AN international Medico-Psychological and Psycho-Therapeutical Association was recently founded at Salzburg on the initiative of Professor Forel, Dr. Oskar Vogt, and Dr. L. Frank, and other well-known neurologists. The president is Professor Raymond, of Paris; the vice-presidents, Professor Forel and Dr. Oskar Vogt, of Berlin.

THE Royal Dental Hospital of London being burdened with a mortgage of £42,086 appeals for donations and subscriptions to maintain the hospital in its present state of efficiency, for which a sum of £3,000 a year is required, in addition to £2,759, a compulsory yearly payment for the redemption of the mortgage. The number of operations performed in 1908 were 109,659, and of these anaesthetic cases numbered 50,050. The secretary is Mr. J. Francis Pink.

LEUCOPLAKIC VULVITIS AND ITS RELATION TO KRAUROSIS VULVAE AND CARCINOMA VULVAE.

BY

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THE occurrence in the tongue of a peculiar type of inflammation, leading on to a leucoplakic condition of the mucous membrane and terminating in carcinoma, has long been known.

It was first described in 1869 in the *Transactions of the Clinical Society* by John Whittaker Hulke, the Council of the Royal Medical and Chirurgical Society having refused to publish his paper some four years previously. Sir Henry Morris described the second case, and also was the first to call attention to the frequency with which a similar type of inflammation preceded carcinoma of the vulva, and operated upon several patients with the combined disease. Both of these eminent surgeons were acting members of the Middlesex Hospital surgical staff, a matter of great interest to the authors of this paper.

It is remarkable that a clinical observation of such importance should have attracted so little attention, especially by gynaecologists, and that the only two English writers who have subsequently drawn attention to the subject, namely Bland-Sutton and Butlin, should both be general surgeons.

The relation borne by leucoplakic vulvitis to carcinoma is closer than that of any other pathological lesion with the exception of the entirely modern x-ray dermatitis. In 1885 Breisky drew the attention of gynaecologists to a disease which he named "kraurosis vulvae." His description led to much confusion, for whilst he undoubtedly described a till then unrecognized condition, subsequent writers on the subject down to the present time, as can be seen from the textbooks, appear to have confused the conditions of leucoplakic vulvitis and kraurosis vulvae, and to have considered them different phases of one and the same disease.

In this paper, then, we shall proceed to show that leucoplakic vulvitis and kraurosis vulvae are two distinct diseases, and we shall then pass on to consider the relation borne by the former to carcinoma of the vulva.

*[LEUCOPLAKIC VULVITIS.]**[Definition.]*

Leucoplakic vulvitis is to be defined as a chronic inflammatory condition of unknown origin characterized in its early stages by marked hyperaemia and cellular activity, and in its later phases by marked epithelial hypertrophy and a thickened, sclerosed, and retracted condition of the subepithelial tissue.

[Distribution.]

Its distribution varies with its severity and time of incidence. In a well-marked case the whole of the vulva may be implicated with the exception of the vestibule and orifice of the urethra, which are never affected; and not only may the labia majora, minora, anterior and posterior commissures and the clitoris suffer, but the disease may even spread laterally to the folds of the thighs and posteriorly over the perineum and skin surrounding the anus.

[Signs.]

Clinically, leucoplakic vulvitis may be divided into four stages, according to the macroscopical features which it presents. In the first stage the parts affected have a reddened, swollen, and excoriated appearance, and their surface is dry.

In the second stage, whilst the labia minora decrease in size and may even become mere ridges, there is a sub-epithelial thickening, so that the parts can be said to have undergone "retraction with thickening." The colour of the affected area now changes from red to white of a

semi-opaque character. This opacity becomes intensified in patches at first and later on over the whole of the diseased surface; from the white appearance resulting the disease obtained its name of leucoplakia of the vulva.

In the third stage, where the disease is most marked, cracks and ulcers may make their appearance, the ulcers giving rise to a slight discharge, and bleed sometimes when touched. At this stage carcinoma quite commonly becomes engrafted on some portion of the diseased area, and as a rule it commences in the ulcer or fissure. If the patient escapes the incidence of carcinoma a fourth and final stage supervenes, in which the vulval surface is smooth, shiny, and white, and the labia minora and clitoris practically disappear, owing to the contraction of the subepithelial tissues, and the disease becomes quiescent.

Symptoms.

The striking and often the only symptom of leucoplakic vulvitis is pruritus, which is peculiarly intense in the first and second stages. In the third stage the pruritus is more or less masked by the pain and acute sensitiveness due to the exposure of the nerve endings in the floor of the ulcer or crack. In the fourth stage the symptoms disappear and the patient ceases to complain. If carcinoma supervenes at the third stage the ulcers become very painful and

over a certain subsurface area, so that a definite zone of de-elasticized and hyaline looking tissue intervenes between the epithelium and the normal tissues deep down (Fig. 2).

That many or all of the lymphocytes seen in the microscopic field are produced in the diseased area is proved: (1) By the absence of these cells in the cross sections of blood vessels, and (2) by the appearance at this stage of definite new lymph nodes (Fig. 2) in the subepithelial tissue, which contain germinal areas showing karyokinesis, and are not normally present there. The appearance of these new lymph nodes is very interesting, because they are commonly found in the neighbourhood of carcinoma, to which disease the condition under discussion bears, as already stated, a very close relation.

The origin of the plasma cells is undoubtedly local. They appear to be developed from certain elongated nuclei found in resting connective tissue. The large hyaline fixed tissue cells proliferate both mitotically and amitotically from similar cells normally found in the part, and the same may be said of endothelial cells. One of us has lately discussed fully the origin of these various groups of inflammatory cells.¹

The epithelium at this stage is markedly hypertrophied, and many karyokinetic figures can be seen in it. The

Fig. 1.—Earliest stage of leucoplakic vulvitis. Surface desquamation of epithelium and diffuse subepithelial lymphocytosis.

tender, bleed easily on being touched, become hard and indurated in spite of local treatment, and enlarge fairly rapidly.

Pathology.

The pathology of leucoplakic vulvitis may be conveniently divided into stages. Such a division, however, bears no reference to duration, but is governed solely by the histological features which the diseased tissue presents. It is necessary to emphasize this, because different parts of the diseased area may be respectively in different pathological stages at the same time.

From a study of a great number of sections obtained from 24 cases operated upon by us, it has been possible to construct an account of the full gamut of histological changes which characterize the disease from its initiation to its subsidence.

In the first stage the epithelium is swollen and the individual cells less firmly attached to one another, so that the desquamation of the superficial cells is excessive. The subepithelial tissue is abnormally vascular and is crowded with lymphocytes, some of which have intercalated themselves between the cells of the basal layers of the epithelium. Few or no polynuclear leucocytes are to be seen, and the fixed tissue cells of the part have not proliferated (Fig. 1).

In the next stage the type of the subepithelial tissue cell proliferation begins to alter. Lymphocytes are still conspicuous objects, but besides these are groups of plasma cells and an increased number of large hyaline fixed connective tissue cells normal to the part. The sustentacular elements become altered, the white fibres become de-collagenized and more hyaline in appearance, whilst the elastic fibres have in many places completely disappeared

Fig. 2.—Second stage of leucoplakic vulvitis. A hyaline zone of the elasticized tissue underlies the epidermis; beyond this area are shown the elastic fibres (stained darkly) which are normally found in the connective tissue. The interpapillary epithelial processes are elongated. A new lymph node is seen embedded amongst the elastic fibres at A.

hypertrophy is chiefly of the basal layers, and the interpapillary processes of the epithelium are much elongated. The surface cells, on the other hand, still show a tendency to early desquamation, which reaches its maximum in the numerous shallow ulcers and fissures that beset the diseased area. At these points so great has been the shedding of the superficial epithelium that the apices of the elongated papillae of the corium almost reach the surface. It is also noteworthy that the inflammatory cells already described, and particularly the lymphocytes, tend to aggregate around the tips of the interpapillary epithelial processes.

In the third stage the cellularity of the subepithelial tissue begins to give place to fibrosis. Many of the inflammatory cells disappear, collections of lymphocytes and plasma cells are still scattered over the field. A re-deposit of collagen occurs around the fibroglia fibres of the fixed tissue cells, which in the preceding stage have been greatly increased in number, so that the tissue from being unduly rarefied now becomes denser than normal. The hypertrophy of the epithelium is still maintained, but the growth tendency now appears to be directed upwards, resulting in the formation of a dense mass of keratinized squames, whilst the interpapillary downgrowths are disappearing, so that the epithelium rests on the sclerosed subepithelial tissue more as a flat sheet. There is a total absence of yellow elastic tissue in the sclerosed subsurface zone (Fig. 3).

In the final stage the sclerosis of the subepithelial tissue is complete. Very few cells are to be seen under

the epidermis. Such as are present are of the fixed connective tissue type. The subepithelial zone of de-elasticized tissue is of less depth, but denser. The epithelium, probably starved by the increasing fibrosis going on underneath it, becomes thinner, whilst the cells show an early tendency to keratinization (Fig. 4).

Clinically at this stage the disease is quiescent. The surface of the vulva is smooth and shiny white in appearance, and the elevations of the labia minora and clitoris have become flattened down almost to disappearance owing to the contraction of the subepithelial tissue. Pruritus has ceased, and the patient ceases to complain.

KRAUROSIS VULVAE.

We have now to contrast leucoplakic vulvitis with kraurosis vulvae. Since Breisky's original paper the most perfect clinical description of this latter disease is that of Thiberge,² with whose conclusion we are in complete agreement. Kraurosis vulvae consists of an atrophic condition of the vulva, associated clinically with stenosis of the vaginal orifice, and pathologically with certain changes in the dermis.

Distribution.

The labia minora, vestibule, orifice of the urethra, and that of the vagina are always affected, the hood of the

Fig. 3.—Third stage of leucoplakic vulvitis. The superficial epithelial cells have undergone extensive hypertrophy and keratinization. The interpapillary epithelial processes are atrophying, owing to the subepithelial fibrosis which has taken place. A new lymph node is seen at A.

clitoris sometimes. The skin on the outer surface of the labia majora between the labia majora and folds of the thigh covering the perineum and surrounding the anus is never affected.

Signs.

Kraurosis vulvae may be divided into two stages. In the first, the muco-cutaneous surface is red, glistening, and shiny, whilst dotted over it here and there, but more particularly on the hymeneal remains round the vaginal orifice, may be seen isolated patches, varying in size from that of a pin's head to half a split pea, and in colour from that of a bright red to a dull purple. In addition, a caruncular condition of the urethral orifice is very often present.

In the second or final stage the muco-cutaneous surface becomes pale yellow and glistening, "recalling the colour as well as the aspect of the surface of a fatty liver, particularly that of a goose such as we see exposed for sale in a provision shop." The muco-cutaneous surface is perfectly smooth, all the ridges having become obliterated. The vaginal orifice has contracted so that perhaps only with difficulty can a digital examination be made, the labia minora and clitoris disappear, the mons veneris atrophies, and the pubic hair becomes brittle and breaks off or falls out. In this disease, though marked shrinkage occurs in the mucous membrane, yet in contradistinction to leucoplakic vulvitis, owing to the absence of epithelial

and subepithelial hypertrophy, the condition may be termed one of retraction with thinning.

Symptoms.

The principal symptoms complained of are those of soreness and pain, together with dysuria and dyspareunia. It is very worthy of notice that whereas in most textbooks pruritus is stated to be one of the constant symptoms of kraurosis vulvae, it is in reality one of the rarest; and that whereas dyspareunia as a symptom is only lightly touched upon, it is in reality the trouble mostly complained of. At least this has been our experience, which also corresponds with that of Thiberge, who remarks in his masterly essay on the subject, "the functional symptoms of kraurosis vulvae are of an exclusively mechanical order."

In the first stage of the disease the parts are extremely sensitive, the passage of urine gives pain, and coitus, for the same reason, is hardly endured or is impossible altogether.

In the second stage the soreness may entirely disappear, but, owing to the retraction of the vaginal orifice, dyspareunia becomes common to both parties.

Pathology.

The microscopical appearances of kraurosis vulvae are quite unlike those of leucoplakia. The epithelium is everywhere thinner than normal, and the papillae and

Fig. 4.—Final stage of leucoplakic vulvitis. The epithelium is thinner than normal; early keratinization of the surface cells is occurring. The subepithelial tissue is diffusely sclerotic.

interpapillary processes are atrophic and in places have altogether disappeared. The subepithelial connective tissue exhibits marked cellularity but of a patchy kind. In the areas of a section which correspond to the red patches seen in the surface of the mucous membrane a very large, in places even massive, proliferation of plasma cells is seen immediately under a thinned and flattened epithelial layer. Surrounding the plasma cell proliferation or partly mixed with it both lymphocytes and polymorphonuclear lymphocytes are seen. The lymphocytes are the more deeply placed, and as the surface is approached the polymorphonuclear leucocytes become increasingly predominant. In the rest of the section simple thinning of the epithelium is manifest with a certain number of polymorphonuclear leucocytes, lymphocytes, and plasma cells in the connective tissue which underlies it. One of the most striking features, perhaps, is the intercalation of polymorphonuclear leucocytes between the epithelial cells. When stained for elastic tissue the sections show that this is present in all parts, save where massive accumulations of plasma cells have occurred. A comparison of these histological appearances with those described as occurring in leucoplakic vulvitis will show that the pathology of the two diseases is quite different (Fig. 5).

Etiology.

Various causes have been assigned to kraurosis vulvae, such as leucorrhoea, syphilis, sexual abuse, age, and operations upon the genital organs necessitating the removal of the ovaries.

Jayle's classification is as follows:

1. Leucoplakia or white kraurosis (simple, syphilitic).
2. Inflammatory or red kraurosis (follicular or vascular).
3. Senile kraurosis.
4. Post-operative kraurosis.

In our experience only the last two factors have any part in the etiology. In the light of our investigations, this classification must be considerably modified. White kraurosis is undoubtedly a misnomer for leucoplakic vulvitis. Red kraurosis is the first stage of the changes we have described under the heading of this disease. The terms senile and post-operative kraurosis are merely an indication of the cause, and have no place in a classification founded on pathology.

Whilst the changes producing kraurosis vulvae are undoubtedly in a large measure inflammatory, yet there is another factor in its production which is of signal importance. The cases may be divided into three groups:

1. Those in young women associated with sterility.
2. Those occurring at or after the menopause.
3. Those occurring after operations involving the removal of both ovaries.

It would appear, therefore, that deficiency or absence of some ovarian factor in the economy of the organism plays a large part in the causation of the disease. We know of no instance in which kraurosis vulvae has been associated with carcinoma of the vulva, and the disease has in our

Fig. 5.—Kraurosis vulvae. The subepithelial tissue is the seat of a massive plasma cell proliferation, over the surface of which the epithelium is reduced to the thickness of a few cells. Many polynuclear leucocytes are present in the subepithelial tissue and intercalated between the epidermal cells.

opinion no relation to it, in this way markedly differing from leucoplakic vulvitis, which, as we will now proceed to show, is very closely connected with cancer in this situation.

RELATIONSHIP BETWEEN LEUCOPLAKIC VULVITIS AND CARCINOMA OF THE VULVA.

The following statistics deal with 58 cases of carcinoma of the vulva and 19 of leucoplakic vulvitis that have been admitted to the Middlesex Hospital and Chelsea Hospital for Women during the last ten years.

Age.

The average for carcinoma was 59; that for leucoplakia 51. The oldest patient with carcinoma was 81, and the youngest 40; the oldest with leucoplakia was 70, the youngest 26.

Civil State.

In carcinoma 58.6 per cent. were married women, 25.8 widows, and 15.6 single women; whilst in leucoplakic vulvitis 63.2 were married, 21 widows, and 15.7 single.

Parity.

In the carcinomatous cases 48.2 per cent. were sterile, and in leucoplakia 47.5. Of those women who were not sterile, the average number of pregnancies in both diseases was seven.

Pruritus and Leucorrhoea.

Of the carcinomatous patients, 36 per cent. complained of pruritus, and 13 per cent. of leucorrhoea; whilst 63 per cent. of the patients suffering from leucoplakic vulvitis complained of pruritus, but none of leucorrhoea.

Etiology.

As we have already indicated, leucoplakic vulvitis is in our opinion an antecedent condition and the cause of carcinoma of the vulva.

What is the cause of leucoplakia is a much more difficult question to decide; it has really never been determined. It cannot be due to a leucorrhoea, because in the first place the age does not correspond with the commonest period for leucorrhoeal discharges; secondly, the disease never attacks the vagina, which canal should certainly be affected if this was the cause; and, lastly, in our experience of leucoplakic vulvitis leucorrhoea has been absent. When one comes to consider the civil state of the patients it is seen that 84.4 per cent. of carcinomatous cases and 84.2 of the leucoplakic are or have been married; whilst with respect to parity both conditions are very similar, about 48 per cent. of the women being sterile, and of those who were not 7 was the average number of pregnancies in each.

Lastly, we see that the average age for both diseases is over 50.

Leucoplakic vulvitis is evidently due to some damage to or interference with the resisting power of the surface epithelium of the labia, and although coition as a cause of this cannot be insisted upon in every case, it seems to be one

Fig. 6.—The earliest stage of the squamous cell carcinoma of the vulva. It begins as an increasing hypertrophy of the interpapillary epithelial processes, whereby they penetrate more and more deeply into an underlying connective tissue which is already crowded with plasma and other inflammatory cells, and from which all elastic fibres have previously disappeared. A, Thickened epithelium, with large interpapillary processes. B, Subepithelial zone, the seat of diffuse rarefaction, due to inflammatory cell proliferation and disappearance of collagen and elastin. C, Normal tissue, with elastic fibres. (Camera lucida drawing.)

of the chief causes when it is remembered that 84 per cent. of the patients at least have been subjected to coition, that the age of incidence corresponds fairly closely to the limit of the most active period of this function, whilst the question of parity is of no assistance, since practically the parous and sterile women are in equal numbers. In none of our cases was there any history or signs of antecedent syphilis.*

PATHOLOGY OF CARCINOMA OF THE VULVA.

In any case of carcinoma of the vulva we have operated upon and in every case we have seen, leucoplakic vulvitis has been present.

It has been shown that in leucoplakic vulvitis the maximum hypertrophy of the interpapillary epithelial processes occurs in the second stage—that is, that in which the cellularity and rarefaction of the subepithelial tissues are also at their maximum. It is in this stage that the supervention of carcinoma is to be feared. It begins over a variable area as an increasing hypertrophy of the interpapillary epithelial processes, whereby they penetrate more and more deeply into the underlying connective tissue. The connective tissue papillae are more than correspondingly elongated, so that they reach much higher than normal, but they are thin and compressed. (Fig. 6.)

It would appear that the growth energy of the epithelial cells becomes confined to those deep down in the inter-

* Sections stained for the spirochaete of syphilis gave negative results.

papillar processes, while the more superficial cells, on the contrary, are of feeble vitality, loosely attached to one another, and actually desquamate before keratinization can occur. Thus the elongated papillar processes of the corium eventually reach the free surface, which now bleeds readily from punctate points corresponding to their apices. The condition may be likened to an area of skin after a Thiersch graft has been removed. This absence of keratinization and early desquamation of the surface cells of a squamous celled carcinoma is very striking, and contrasts markedly with the condition found in a papilloma.

The epithelial downgrowths, which are at first simply the enlarged pre-existing interpapillar processes of the epidermis, later become branched and tortuous.

This development of squamous-celled carcinoma from hypertrophied pre-existent interpapillar processes has been shown by one of us to be a constant feature of the disease, wherever its site; for even in positions such as the vaginal cervix, in which normally no papillae or interpapillar processes exist, a series of such are always formed previous to the onset of squamous cell carcinoma there as a result of the chronic cervicitis which is its invariable antecedent. The formation of interpapillar downgrowths of epithelium would appear to be an adaptation to relieve lateral growth tension, for it is certain that in all conditions of hypertrophy of the lower strata of an epidermis

phases of carcinoma of the vulva, in which the epithelial ingrowth is only as yet foreshadowed, the connective tissue cell proliferation around this area is already typical of that seen in the developed disease.

The disappearance of elastic tissue in the area of a beginning carcinoma is very striking. On the other hand, there is evidence to show that an excess of these fibres probably acts as a check to epithelial ingrowth. In certain very chronic types of leucoplakia in which the subepithelial changes never reach a high degree of cellularity, a great excess of elastic tissue may be found. In the later phases of this condition considerable epithelial hypertrophy occurs, but without those long interpapillar downgrowths which are the first indications of approaching malignancy (Fig. 7).

Further, the more benign papillomatous type of carcinoma of the vulva shows less destruction of elastic tissue than the more malignant ulcerative form. Dense sclerosis of the white fibrous elements also probably checks epithelial ingrowth, and as this progresses in the later stages of leucoplakic vulvitis the tendency to carcinoma becomes increasingly diminished.

Of the cellular elements in the connective tissue, the plasma cells are those which most characterize the second stage of leucoplakic vulvitis, and these are also the predominant tissue cells in carcinoma of the vulva. They bear this relation to the initiation of epithelial ingrowth—

Fig. 7.—Very chronic type of leucoplakic vulvitis, with excess of elastic tissue in the connective tissue. The epithelium is hypertrophic, but the interpapillar epithelial processes are smaller than normal.

they either appear *de novo* (cf. chronic cervicitis), or if normally existent become much exaggerated (cf. the skin). Further, it would appear that so long as the growth energy of the epithelial cells is evenly distributed along the length of the epidermis enormous hypertrophy may take place without malignancy. But that when the growth energy becomes concentrated at a series of points corresponding to each interpapillar process, a want of co-ordination is established which at once makes the condition dangerous.

The relation between the malignant epithelial ingrowth and the altered state of the subepithelial tissues is an important subject.

We have in leucoplakic vulvitis two sets of phenomena going on simultaneously—namely, those in the epithelium and those in the connective tissue. In both of them an accession of cellular energy takes place which then declines and finally gives place to a state of cellular activity and reproduction much below the normal. But a study of the earliest stages of the disease shows that the activity of the connective tissue cells is that first awakened, the growth of the epithelial cells initially being actually inhibited.

Thus it comes about that a profoundly altered state of the subepithelial tissue anticipates the occurrence of epithelial hypertrophy.

Further, it would appear that a condition of rarefaction and cellularity of the subepithelial tissue is an important factor influencing epithelial ingrowth. For in the earliest

Fig. 8.—Portion of a nodule of carcinoma that occurred on a recurrent patch of leucoplakic vulvitis, left after imperfect primary excision. The tissue on the right is carcinomatous; that on the left leucoplakic.

namely, that they are largely responsible for the decollagenization of the subepithelial tissue which occurs in the antecedent leucoplakic vulvitis.

Though changes in the adjoining connective tissue bear some very close relation to the cause of epithelial ingrowth, yet, malignancy having been established, the further spread of the tumour is independent of such assistance. For one of us has shown that the condition of the connective tissues surrounding an advanced inrunner of carcinoma cells is one of passivity, and that the same is true of the tissue surrounding permeated lymphatics* and metastatic growths, excepting those in lymphatic glands, which are an exception to this rule.

Multiple Carcinomata of the Vulva.

Multiple carcinomata are more frequently met with in the vulva than any of the other common sites of this disease. This occurrence has been interpreted by some as an evidence of autoinoculation.

The cases that have been interpreted in the manner mentioned may be divided into two classes: Pseudo-multiple growths and true multiple growths.

(a) *Pseudo-multiple Growths*.—Many growths which at first sight appear to be double are in reality bridle-shaped, a thin tract of carcinomatous tissue uniting them across the middle line, usually just under the clitoris. When a

* This fact concerning lymphatic channels permeated by carcinoma was first stated by Sampson Handley, Hunterian Lecture, Royal College of Surgeons, 1906.

growth crosses the middle line it rarely does so directly by way of the vestibule. This is due to the fact that the vestibula mucosa usually escapes the antecedent vulvitis—that is to say, it is not in a precarcinomatous state. Ribbert stated, and we confirm his view, that the surface spread of a carcinoma is at first by successive carcinomatous conversion of the epithelium covering the precarcinomatous area. When this is exhausted further growth continues by division of the cells already formed, but there is no conversion of normal epithelium into carcinoma, the former simply undergoing a pressure destruction owing to the infiltration of the subepithelial tissues by the cells of the growth.

(b) *True Multiple Growths.*—We have seen four such. In three out of the four they occupied the same side of the vulva, and in none of them do we think that there was any reason to believe that they arose by autoinoculation. In all of them the vulva was leucoplakic, and the double growths were separate by a tract of mucosa that showed the typical changes belonging to that condition. Each separate growth was an entity to itself, starting in its own set of hypertrophic interpapillar processes, and in three of the cases contact between the two tumours was from their position impossible. Moreover, there was no microscopical evidence of any new element having been introduced either from the surface or from the subcutaneous tissue.

Such multiple growths, therefore, should neither be attributed to autoinoculation from the surface nor to metastatic deposit via the subcutaneous tissue. Microscopically it is quite common to find dual, treble, or even quadruple points of beginning carcinoma. In fact, seeing that every downgrowth begins as a hypertrophic interpapillar epithelial process, the growth may be said always to begin at multiple points.

The rarity of multiple primary growths of the vulva, in spite of the large precarcinomatous area existent, suggests the possibility that the epithelial ingrowth at the point of the carcinoma may act as a safety valve to the increased lateral growth tension that undoubtedly exists throughout the leucoplakic epidermis, and relieves the latter of its tendency to ingrowth.

Local Recurrences of the Growth.

There are two types of local recurrence. The first is that in which the original growth has been inefficiently removed, and recurrence takes place in the scar a short time afterwards. We have met with none such. The second is of a different nature, and we have met with examples of this after excision of the vulva. It is due to a separate cancer originating almost from a portion of the precarcinomatous area that has escaped removal. It is here to be noted that unless the lines of incision on removal of the vulva for leucoplakic vulvitis are so planned as entirely to be without the diseased area, the leucoplakic condition returns in the scar.

These recrudescences in a portion of leucoplakic epithelium left behind at the original operation are in no way to be confounded with secondary metastatic nodules. Such nodules are subepidermic in origin, whilst the recrudescence is obviously arising from a certain group of hypertrophied interpapillar processes belonging to an area the whole of which is leucoplakic and precarcinomatous (Fig. 8).

Glandular Metastases.

Glandular involvement occurs late as compared with squamous-celled carcinoma in other sites. The inner set of horizontal inguinal glands are those first affected on one or both sides. When affected they rapidly enlarge, and subsequently often break down. Sections cut from them at this period may fail to demonstrate the nature of the change, so complete is the destruction of the cells that has taken place.

All enlarged glands are not, however, carcinomatous. It has been shown by one of us¹ that lymphatic glands prior to their invasion by carcinoma cells are enlarged by a plasma cell proliferation affecting the trabecular elements together with a great hypertrophy of the germinal areas and an increase in number of the lymphocytes derived from them. Glands thus affected may attain a large size, mimicking true carcinomatous enlargement so closely that microscopical investigation is alone competent to decide its nature.

TREATMENT.

We have tried a large number of remedies for the pruritus in leucoplakic vulvitis, and have found that most of them have failed to give relief. We have had the greatest success with zymocide lotion, resinol ointment, and the x rays. In view, therefore, of our pathological findings, we advise that the affected area should be excised in all cases where these fail, and since we have shown that a permanent change of character has taken place in all the epithelial cells over the affected area, the excision should be a wide one lest the disease recur again in the scar, which has happened to us in two of our cases.

The treatment for kraurosis vulvae is to dissect out the painful parts complained of and enlarge the vulval orifice. In carcinoma the inguinal glands on both sides should be removed, whether enlarged or not.

REFERENCES.

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A NEW COLOUR-PERCEPTION SPECTROMETER.

By F. W. EDRIDGE-GREEN, M.D., F.R.C.S.

THE instrument here described is a spectrometer so arranged as to make it possible to expose to view in the eyepiece the portion of a spectrum between any two desired wave-lengths. It consists (Fig. 1) of the usual

Fig. 1.

parts of a prism spectroscopie—that is, a collimator with adjustable slit, prism, and telescope with eyepiece—of the following dimensions:

Focal length of collimator and telescope object glasses = $7\frac{1}{2}$ in. (180 mm.). Clear aperture of collimator and telescope object glasses = $\frac{3}{4}$ in. (22 mm.). Slit 7 mm., effective length of jaw, with wedge for reducing the effective length of the slit, protective cap, comparison prism, and screw adjustment for the slit with divided head (see Fig. 2). The prism is of flint glass, 1.65 refractive index for D. Eyepiece, Ramsden form, focusing on to the shutters described below.

Fig. 2 (0.6× actual size).

In the focal plane of the telescope are two adjustable shutters with vertical edges, the shutters being carried by levers which rotate about centres near the object glass of