

3. On this portion of skin a pitch black tumour subsequently developed. Partly raised and indurated, partly ulcerating and spongy in character.

4. Histologically, therefore, three forms of epithelial newgrowths present themselves, ^{ie.} pigmented and non-pigmented basal cell types the former mixed or in close proximity with keratinising epithelial strands of the cancrioid type.

5. The purely cancrioid parts of the tumour do not contain pigment.

6. The cancrioid ^{vulvar} part of tumour developed a considerable time after the primary anal tumour.

In this connection does the continual macerating effect of the exudate which runs off the primary tumour, play a part in the production of the cancrioid, which appears to have developed subsequently. It is now fairly widely accepted that the type of neoplasm which develops as a result of chronic irritation including tar cancer is of the cancrioid type. The question is a difficult one to answer. There are so many possibilities that beyond making the suggestion one does not feel justified in forming an opinion.

Clinical Observations No. 14772

20.8.26 Angora she-goat, aged. (only stumps of incisors left). Condition fair. The perineum presents a dark red, rounded tumour, hanging by a short stalk from the lower, left, aspect of the anus. It is granulomatous in nature, soft, covered by a moist, sticky exudate, and bleeds very easily when manipulated. Its size roughly is 2.5 c.m. wide, 1.5. c.m. high, 1 c.m. thick. The anus and vulva openings are unaffected, so that defaecation and urination are not interfered with. Just above the vulva the perineal skin shows a pigmented patch (melanosis). On this date the whole of the tumour was excised surgically for histological study. It was found to be attached only to the skin and did not penetrate or involve the underlying

tissues to any extent; the stalk being about 1 c.m. in thickness. The operation wound was treated antiseptically and was completely healed up in 15 days. This animal was then kept without any further interference, being only examined from time to time. In this way it was observed that at times the cheesy matter accumulating beneath the tail would cake into small crusts which, on being scratched off, often left a small bleeding erosion of skin. These, however, healed up repeatedly and never showed a tendency to develop further.

This animal was killed on account of old age and poverty on 27.9.28, i.e. about 25 months after removal of tumour.

Post mortem findings.

Emaciation, anaemia (due evidently to malnutrition). A few specimens of *haemonchus contortus* in stomach. Old encapsulated abscesses in lungs. The post mortem examination otherwise negative. The perineal skin was somewhat roughened and showed small elevations above anus, but otherwise the skin was fairly soft and pliable still.

Histological findings. Specimen No. 6189 & 8481.

Small almond shaped tumour removed surgically on 20.8.26. There is a central core of fibrous tissue continuous at the base of tumour with the corium. It ramifies in fan shaped fashion to form a delicate stroma which supports a closely packed, very uniform mass of epithelial cells. They have large round or oval nuclei with one or more nucleoli, which are rather poor in chromatin. The cytoplasm seems to be absent in most cases, or nearly so. This apparently is due to its very delicate nature. Indeed, it seems that the very finely fibrillar substance often drawn out into shreds and elongated processes of various shapes and in which the above nuclei are more or less embedded, constitutes the protoplasmic part. This in life probably is very delicate and soft, so that it undergoes these changes

during preparation of the sections. This substance is apparently gathered along the stroma in greater amounts, so that the cells lying away are separated by small more or less empty spaces. The stroma has thus the appearance of trellis work, composed mostly of this finely fibrillar substance and tumour cells, amongst which young fibroblasts, round cells, neutrophiles and blood capillaries can be seen. There are also numerous smaller cells with elongated, deeply chromatic nuclei, possibly of endothelial origin. Blood capillaries and smaller vessels are numerous, especially near the surface. In parts small haemorrhages can be seen near surface. These contain brownish pigment like haemosiderin. No melanin could be seen in the whole of this tumour. Mitoses, if at all present, are very rare in the tumour cells. By following up the small amount of epidermis covering the stalk one side, one reaches a point where it merges into the tumour. There is a peculiar elongation of the germinal cells at this point, so that they appear to be loosened and "shelled out" into the tumour parenchyma. There is very little infiltration with inflammatory cells, considering that the whole tumour is covered only by a thin layer of necrotic exudate.

Diagnosis.

200 Musocellular carcinoma. After the death of the animal sections were prepared from various portions of the perineal skin. Particular attention was paid to those parts above anus, which showed small elevations. The epidermis here appears much thinner than usual as if atrophied, in parts being barely 3-4 cells thick. The sebaceous glands in this region are about as numerous as in the normal skin, but show this peculiarity, ^{that} the basal cells appear proliferated to form a dark staining, well defined layer all round the central mass of fatty cells. In one place what appears to have been a sebaceous gland from its circumscribed indented outline causes a slight out-

ward bulge in the epidermis. This round elevated focus between 1-2.5 m.m. in diameter, consists practically of a solid mass of epithelial cells similar to those forming the basal layer of sebaceous glands. See fig. It is situated in the corium, but is not visibly connected with the exterior as it is still covered by intact epidermis. The nuclei of these cells are fairly closely packed together and no fat carrying gland cells are left. Serial sections were prepared from the remaining material and showed that the focus was more or less globular in outline. The structure of this focus certainly has a close resemblance to that seen in the closely packed round cell epithelial tumours such as for instance the one removed previously from this animal and described above, and also 7256A and 7256D.

Comments.

The tumour removed surgically proved, on microscopic examination, to be a straight forward example of a non-pigmented basal cell carcinoma. 25 months later the animal was killed and portions of skin in the same region examined. To the naked eye a few small elevations of skin could be noted. The epidermis was thinner than usual (Senile atrophy?). The elevations were due to small foci of closely packed epithelial cells resembling those seen lining the neighbouring sebaceous glands. It seems possible, therefore, that by a process of proliferation, the basal cells of the sebaceous glands displace the fatty cells.

As growth continues the epidermis becomes pushed out by the enlarging focus and becomes thinner and thinner until it finally ulcerates. The epidermis is in direct contact with the underlying tumour cells at least near the base. The basal layer of the sebaceous gland and that of the epidermis are fundamentally continuous with each other, so that allowing for displacements, the derivation of the

tumour cells from the germinal layer should remain apparent in the young neoplasm.

This appears to be a reasonable explanation of the origin of basal cell carcinoma and one that has already been suggested by various authors.

Clinical observations No. 14773.

Angora she-goat, aged, incisors worn down to gums, condition fair.

6.9.26 On lifting the tail a large newgrowth measuring 5 x 4 c.m. occupies the whole recess under ^{the} tail. It extends downwards between the tail folds on either side and covers the anus and the upper commissure of the vulva. It is attached above the anus over an area roughly 2.5 x 3 c.m. Its thickness varies from 2.5 c.m. above to 1 c.m. below. The tumour is practically pitch black in colour throughout. It is irregular in outline and presents a moderately lobulated appearance with a deep fissure running across its surface obliquely. It bleeds very easily on the slightest manipulation. On account of the weight of the tumour hanging from the skin and underlying tissue, the anus is not ^{well} closed properly, but its upper half overlaps the lower. Defaecation and urination are not, however, interfered with, and there are no signs of colateral inflammation.

18.10.26 The tumour has increased in size, it now measures 12 x 8 x 2½ c.m.

19.11.26 This goat was killed by an intratracheal injection of chloroform and ether. The whole perineum was excised, together with attached tumour with a view to utilising parts of it for transplanting experiments, and for histological examination, respectively. (For transplantation and transmission, see Experiment No. 2)

Histological findings Specimen No. 6377.

Under the low power lens this tumour presents a remarkably uniform structure as is seen usually in a sarcoma.

The cells are arranged in whorls according to the sweeping curves of the branching stroma coming out of the stalk. The surface is covered for the greater part by a necrotic layer of exudate and other cells. Directly under this is a zone conspicuous by the close proximity of blood vessels and capillaries. From the small amount of ^{connective tissue} ~~stroma~~, and the staining property of epithelial cells, it seems that active growth takes place in this region. Melanin is strewn throughout the tumour parenchyma. Under ^a the higher magnification it is seen that the distribution of the pigment is very irregular. Many of the epithelial cells contain a varying amount of pigment, but some have none at all. On the other hand, a fair number of cells are packed so full of it, that they appear as large black blotches in the field and are often aggregated together in bunches. Such clumps are seen fairly frequently in the connective tissue stroma and in the deeper parts where epithelium is not usually found. Such heavily packed cells are probably connective tissue cells whose function is the hoarding of melanin. The stroma carries much more pigment than the tumour parenchyma (See 7256B). Some of the melanin also lies free in the interstitial spaces, but of course this distribution may be accidental due to spreading during the cutting of the section. There are very few mitotic figures in the tumour cells. In other respects the structure agrees with that of specimen 7256B, C, D etc. In the deeper subcutaneous tissue the tumour parenchyma is bounded off by a thick connective tissue capsule. In parts of the tumour, foci of somewhat different cells can be seen, they are slightly smaller, rounder and stain a deep purple. They do not contain any pigment, but for the rest are arranged as the others.

In many places where the epidermis can be followed until it merges into the tumour, the typical "shelling out" effect of the altered basal or germinal cells into the

tumour parenchyma can be clearly observed. The epidermis shows acanthosis to a marked extent, and in one place goes over abruptly into solid strands of squamous cells, closely packed together and having many foci of keratinisation typical of cancrioid horn pearl formation. This part is limited in extent, and is separated by connective tissue from the rest of the tumour. It is, however, continuous with the acanthotic epidermis. It contains no pigment.

Diagnosis.

Pigmented baso-cellular carcinoma, with a small spino-cellular carcinoma next to it. Combined form.

CLINICAL OBSERVATION No. 17293.

Angora she-goat, aged. Very poor condition.

17.6.27. A large pinkish tumour is found to occupy the whole of perineal depression below the tail. The tumour is about 5 x 4 c.m. and attached by a very short stalk to a small area above the anus. The surface is nearly flat, but shows shallow fissures. The tumour is covered by a moist, sticky, greyish to brownish, foul smelling matter, which causes a general soiling and matting of hair around the breech. The vulva is unaffected, although the anus is partly overlapped by the edge of the tumour; defaecation does not seem to be much interfered with. When manipulated in region of tail the animal evinces considerable tenderness, and the tumour bleeds very easily on the slightest handling.

Smear preparations from surface shows a rich and varied bacterial flora, but no spirochaetes.

9.7.27 Matting and soiling of hair around perineum accentuated, evidently due to increased exudate from tumour. The tumour itself shows on its left surface a sunken patch of greenish grey, softer substance (gangrene)

15.7.27 Foul smelling and objectionable appearance tumour largely gangrenous on surface.

In order to check this process, the tumour was

cleaned with tincture of iodine, and then coal tar applied.

18.7.27 Gangrenous parts have sloughed off, leaving a relatively clean, granulomatous, pinkish tumour behind, a good deal smaller than before.

2.8.27 Greyish exudate has again increased and greenish patches of gangrene appear on surface of tumour. Rest of perineum moistened and macerating.

4.8.27 The dorsal commissure of vulva is swollen and is covered by semi-dry scabs. No spirochaetes can be found in smears made, although the bacterial flora is profuse.

8.8.27 Superficial gangrene of tumour present.

15.8.27 Profuse thick yellowish-grey stinking exudate soiling the whole perineum and matting the hair at sides.

26.8.27 A large crop of fly larvae found all round and under tumour.

2.9.27 The tumour is considerably reduced in size, due to sloughing off of gangrenous tissue. Fly maggots are present and seem to cause much discomfort to animal. It keeps its tail down and flicks it continually, often stamps its feet, and shows uneasiness generally.

6.9.27 Most maggots have disappeared, tumour moist, sticky, and slightly necrotic. Superior commissure of vulva is much swollen, moist and pink in colour, being continually smeared with exudate by action of tail.

13.9.27 Only a few large maggots left, there is ulceration on both anal folds of skin. Anus is practically covered over by edges of tumour, but defaecation apparently not interfered with. Vulva moist and swollen, scabs adherent over the tumour.

15.9.27 Hair shorn off. Condition of animal is rather poor, and skin shows scalliness, somewhat resembling dandruff.

21.9.27 Dosed from today, daily with Liquor-arsenicalis B.P., starting with 0.1 c.c. and gradually increasing to 0.4 c.c.

7.10.27 No change. Spirochaetes are found in the smear preparation from surface of tumour.

13.10.27 Discontinued arsenic. This had no effect on tumour which is still as before. Animal is noticed to lie down a good deal.

15.10.27 Animal lies down in corners with head bent towards tail as if to ward off flies. These seem to cause it a great deal of worry

19.10.27 Given Potassium iodide 2 grams - Liquor arsenicalis 0.4 c.c. daily from today. Tumour is about the same, covered by sticky, foul exudate and in parts with scabs.

25.10.27 Animal lying down a good deal and is in poor condition.

29.10.27 Slight inflammation of conjunctiva with watery discharge, discontinued the Potassium iodide but continued the Liquor arsenicalis. The anal tumour has decreased slightly in size.

2.11.27 The tumour now measures 3.5 x 2 x 1.5 c.m. the greatest length being transversely across from one side to the other. The perineal skin above vulva also much thickened and covered by scabs. Smear shows numerous spirochaetes, fusiform and other bacteria. Increased the daily dose of Liquor arsenic to 0.6 c.c.

9.11.27 Slight greenish gangrenous areas on tumour, vulva swollen and moist partly crusted over, and showing a few small prominences of skin, especially on left side. Given Potassium iodide 2 g, and Liquor arsenic.

10.11.27 Given Potassium iodide with arsenic as before.

12.11.27 Do. Tumour gangrenous, with profuse foul

smelling and sticky exudate.

14.11.27 Necrotic area sloughed off, leaving a fairly clean granulation-like pink surface of tumour. Given Potassium iodide and arsenic as before.

21.11.27 Potassium iodide has been discontinued, but the Liquor arsenicalis daily dosing is proceeding. The animal is in poor condition, lies in corners and away from the others, seems extremely worried by flies settling on the tumour and often bites at perineum. It occasionally groans when defecating and appears very tender when tail is elevated or tumour touched in anyway.

22.11.27 Liquor arsenicalis discontinued. Tumour shows no change. A slight sero-purulent discharge from the eyes (iodism).

28.11.27 Poor in condition and weak, lies down most of the time, but appetite still good.

13.12.27 Partial necrosis of tumour. Vulva moist, macerated and swollen in appearance. There is yellowish-grey excrescences on the lower part of left vulva lips. This is covered by crusts and is about the size of a pea. The lymphatic supra-mammary glands shows no enlargement on palpation.

30.12.27 Emaciated and weak, unable to follow other goats. Small protuberance on left lip of vulva grows very slowly and is usually covered by crusts.

14.1.28 The anal tumour assumes a flattened, pink, cauliflower-like appearance, occupying the whole of space under tail and partly covering anus. The vulva is swollen and moistened by the exudate, and the protuberance on the left side has grown to the size of a hazel nut. The animal shows much uneasiness and scratches frequently at perineum, although no maggots are visible.

30.1.28 Fly larvae present in large numbers,

tumour is somewhat enlarged. The whole perineum has a repulsive appearance owing to foul smelling brownish exudate, soiling all neighbouring tissues. The maggots swarm all over and are eating into the tumour. Goat is still very sensitive and bleats weakly when handled e.g. lifting tail. It is emaciated in spite of fair appetite. Continual irritation is shown by running around and flicking tail, stamping feet, biting at tumour and lying down in corners etc.

25.2.28 Tumour slightly decreased in size owing to necrosis and burrowing action of maggots. Smaller tumour of vulva is the size of a hazel nut and has a greyish, granulated rough surface being covered by sticky exudates and scabs. The other side of vulva is swollen.

15.3.28 Animal is so emaciated and weak that it lies down most of time. The anal tumour has a very irregular cauliflower-like surface covered by slimy exudate and necrotic matter.

27.3.28 Tumour enlarged somewhat, tends to bulge out the tail folds on either side. The whole mass is not thicker than 2 c.m. being pitted and fissured in the centre with a raised swollen border all round. The anus is exposed and is fringed by a ragged edge of granulematous growths. Animal evinces considerable pain in defecation, ^{it} groaning and straining^s, and only a few pellets are voided at a time. The whole vulva is swollen and macerated, the lower part of left lip carries a growth with rough, greyish, granular surface about 2.5 c.m. in diameter.

11.4.28 The right supramammary gland shows a decided enlargement, it feels hard and about the size of a wall nut. The left one is about the size of a french bean and softer on palpation.

18.5.28 Right horn broken off short, frontal sinus teeming with fly larvae and necrotic matter, treated and

tarred. The anal tumour is one large ragged mass of stinking, partly necrotic, slime covered tissue. It is roughly rounded in outline and occupies the whole space between tail folds. It is shallow and contains deep fissures and burrows which are filled with maggots. The edge all round is ragged, swollen and elevated, so that the whole tumour may now be regarded as a huge ulcer, which is confluent with the tumour on vulva. Faeces now seem to emerge from a fissure on the bed of the ulcer. The anus has been more or less completely broken down. Urination takes place without difficulty. The animal strains and groans whenever it passes faeces and bleats whenever any of the affected parts are handled.

The surrounding hair is much soiled and matted together by a profuse, slimy, stinking brownish exudate, to which dirt sticks and forms crusts in many places.

The animal is very weak, but still shows signs of great distress from irritation of perineum and tumour. The right supramammary lymphatic gland on palpation, feels the size of a wall nut and is fairly firm. The left is still the size of a large bean.

23.5.28 Found dead in the morning.

Post Mortem Findings.

Extreme cachexia and anaemia. Fractured right horn with necrosis of frontal sinus. Sarcosporidia in oesophagus; hydropericardium. Large ulcerating tumour roughly circular in outline, with deeply fissured and pitted bed. The raised and much swollen borders cause great distortion of vulva to the right side. Its diameter is 7 c.m. and it extends from the recess under the tail, down to the dorsal commissure of the vulva, and then down the left lip at the lower part of which is a greyish, rough protuberance, covered by a scab. The deep crevices

in the bed of ulcer are filled with fly larvae which are actively eating away deeper into tissues. The anus has completely disappeared, the rectum opening directly on to the floor of ulcer. The vulva is patent in spite of distortion due to swelling.

The right supramammary gland shows at one side a small metastatic focus about 1.5.c.m. in diameter. There is a large abscess in the pelvic region outside the rectal wall. This contains a mass of thick yellowish pus.

Histological Findings. Specimen 8059

Section of this tumour at its junction with normal skin shows various transitory stages, very clearly. The epidermis very abruptly becomes enormously thickened, sending down long blunt and sharper processes into corium. These consist of flat prickle cells. Almost immediately, marked cornification takes place. The most superficial areas show large nests of keratinising flat cells with nuclei still more or less retaining their outline. The surrounding flat cells are paler in colour with vesicular nuclei and usually flattened concentrically around the pearls. This tendency to horn formation is marked even in cells fairly deep near the basal layer. There are very numerous isolated cells, or groups of two or three which show the peculiar swelling out and hyalinisation of cytoplasm and the disintegration of nucleus to dark chromatic mass or granules. In parts this leads to the formation of most weird shapes of giant cells. See fig. The cytoplasm reaches an enormous size, stains faintly, but is not quite hyalinised. The nuclei show rapid division to form ^aconglomerate of several nuclei, or else they disintegrate to form a large dust-like chromatin masses enclosed as it were in a delicate membrane.

Further towards the centre of the tumour the pearl nest formation become less frequent, the squamous cell strands become more solid and branch frequently in all

directions, penetrating to varying depths in the intermuscular spaces. There is ^a strong supporting connective tissue stroma. The surface is covered by an irregular necrotic layer of tumour cells and exudate in parts showing great excavations or fissures. The stroma is more or less infiltrated with polymorph neutrophiles often forming small abscesses. Skin glands are totally absent from the tissue below the tumour. The supramammary gland shows large dense foci of typical flat squamous epithelial cells with centres of keratinisation (Cancroid).

Diagnosis.

Spino-cellular carcinoma (cancroid) with metastasis in supramammary lymphatic gland.

Clinical Observations No. 17294.

Angora she-goat, aged, poor in condition.

17.6.27 A small tumour 2 x 1 c.m. is attached above and to the left of anus. It is covered by a thick crust of dry exudate and dirt, which is securely adherent to the underlying tissues. The surrounding skin and hair are quite dry and fairly clean. A smear from surface scraping was made, but show^{ed} only a small number of bacteria. No spirochaetes were present.

30.6.27 The thick crusts covering tumour were removed with some difficulty, and left a raw bleeding protuberance.

9.7.27 Thick scab firmly adherent to the tumour, when removed leaves a bleeding protuberance, each time smaller than before. ~~as~~ A thick layer of tumour seems to come off with the scab on removal.

22.7.27 Hard circumscribed crust covers just a small raised nodule about 1 c.m. in diameter, the remainder of original tumour. There are about 2 or 3 small excrescences covered by thick tenacious crusts next to it. On removal small bleeding excoriations are left.

2.8.27 The same elevations of varying sizes,

covered by dry scabs are present. There is no tendency to produce moist exudate, the covering scabs are partly of a horny nature.

15.9.27 Animal shorn, condition has improved markedly result of advanced state of pregnancy. Perineum the same.

23.9.27 The elevated areas at perineum are reduced in size and covered by small crusts only. The tumour has disappeared completely, although the site still shows a bleeding excoriation when the scab is removed.

5.10.27 Goat has given birth to one kid during the night. This kid is very weak, and is unable to feed.

13.10.27 Kid fees ^d fairly well after some difficulty had been experienced in getting it to learn to stand and suckle. Its legs are very weak, and inclined to give way under the body, spreading out at right angles to body on either side. The goat itself shows a few small pustules on perineum, which is partly covered by brownish discharge from vulva. The recess above anus shows a few small elevations of skin not covered by crusts, but presenting a superficial excoriation.

19.10.27 Crusts have reappeared on the small raised excoriations. The perineum otherwise shows a few scattered pustules extending down the escutcheon to udder.

29.10.27 Pustules healed up, few small dry crusts above anus.

2.11.27 Photographed perineum after removing the dry crusts and dirt, leaving the small excoriations bare.

13.12.27 The crusts on being left undisturbed thicken considerably and even become partly horny and pendulous, being very firmly adherent to underlying skin. Small surface erosions of skin can be seen at various places near anus and vulva.

3.1.28 Pendulous crusts have fallen off leaving small ulcers which heal partly and form new scabs.