

CLASSIFICATION.

In morphology, pigmentation, derivation and other aspects, there appears according to various workers, to be as many differences between the basal cell carcinomata, or the melanomata themselves, as between the two groups. It seems thus, that until grounds for differentiating the two, are better defined, diagnosis in favour of one or the other must remain a matter of personal opinion. After all whether the mother cells are derived from the epidermis, including pigmented and non-pigmented naevi, or from the skin appendages, they are all of the basal cell type. The resultant tumours must, therefore, within the ordinary range of variance, have a similar structure. Although pigmented tumours have not as a rule been considered as basal cell carcinomata, there is no reason why, under certain circumstances, they could not be so termed.

It seems doubtful in any case whether pigmentation alone can be used as a differential criterion between the two. Furthermore, until the nature of naevi is better understood, one does not feel justified in assuming that the origin of tumours from them is sufficient reason to class them apart.

It has been stated by Wells (1925) that cells which do not normally form melanin, probably do not acquire this power in pathological conditions. This is, therefore, a very strong argument in favour of the basal cell origin of these tumours, since it is now a fairly well established fact from the work of Bloch^h and others, that this is the layer normally concerned with melanin production. (Owing to lack^{of} the necessary reagents, it was unfortunately impossible to apply the Dopa oxydase reaction to these tumours.) The above statement of Wells leads one to believe that pigmentation in skin tumours is a secondary characteristic and depends entirely on the pre-existence of the melanin producing

capacity in the basal cells from which the tumour takes origin. A point of particular interest in this connection is that the spinous cell carcinomata in the cases studied, never contained any pigment. Even in the combined forms the pigment was sharply localised to the basal cell portion of the tumour. As far as can be ascertained, spinous cell carcinoma^{ta} in general, do not contain melanin. This fact seems to prove that the spinous cell carcinoma takes its origin from the more differentiated layer of prickle cells, which, under normal conditions, in the skin are not capable of producing melanin. The spinous-cell carcinoma in the goat tumours must, therefore, be regarded as a separate tumour, which possibly develops as a sequel to the irritation due to the primary basal cell tumour. The "mixed forms" can then be classed either as atypical canceroids or as keratinising basal cell carcinomata. For the latter Krompecher has already made provision in his classification.

The basal cell tumours described, ^{could} have been called Melano-carcinomata and Amelano-carcinomata respectively. Such terms are vague and moreover, might lead to confusion. The word melanoma in veterinary practice is often loosely applied to any melanotic tumour, and very often to melanosarcoma. For this reason the term basal cell carcinoma has been used throughout to designate all the undifferentiated cell tumours of epidermal origin found in the Angora goat.

ⁿ Gans gives Krompecher's classification of basal cell tumours as follows:

Carcinoma baso-cellulare solidum.			
Ca	"	"	adenoides
Ca	"	"	parakeratodes
Ca	"	"	cysticum
Ca	"	"	hyalinicum
Ca	"	"	myxomatodes

The basal cell tumours studied in this paper would thus fall in part under the first three subdivisions of ^{the} above classification. No provision is made for pigmented tumours. It remains, therefore, to be proved by further detailed stud

of their finer morphology and genesis, whether a further subdivision to include them is justified or not.

PREDISPOSITION.

The etiology of cancer has so far baffled all attempts to elucidate it. The vast amount of work done in this connection has, however, not been altogether fruitless. The relationship between certain "predisposing factors" and the incidence of cancer has been closely studied, with the result that many aspects of the question are now better understood. Experiments and observations have thus far yielded overwhelming evidence in support of Virchow's Irritation theory, which today can practically be accepted as proved. (Lewin 1928) This leads one naturally to examine shortly the factors most likely to be involved in regard to ^hthe skin cancer now under consideration.

ENDOGENOUS FACTORS.

Breed ~~race~~. - It is evident that the Angora goat as a ^{breed} race is much more susceptible, or less resistant to skin cancer than the native or Boer goat, under similar environments. Points of difference between these ^{breeds} races might, therefore, yield a clue as to the reasons for such decreased resistance or increased susceptibility.

Heredity, inbreeding, constitution. ^{tu} - The Angora as has already been stated, is a highly specialised animal for the production of mohair. The organ concerned most in this specialisation is the skin. Inbreeding has and is frequently resorted to, in order to accentuate certain desirable qualities in the skin and hair. In doing this, it is possible that a latent, inherent predisposition to cancer has also been accentuated throughout the ^{breed} race. On the other hand, it may be that only certain strains transmit the predisposition. For the above reasons also the constitution of the Angora may have been weakened. As a result of her extensive work with

mice, Slye claims to have proved that the disposition to cancer is hereditary but that resistance is dominant over susceptibility. Little (1928), however, does not accept this theory, that cancer susceptibility is a simple mendelian recessive. Should breeding experiments of affected large animals be contemplated, the Angora goat would probably prove a suitable subject, on account of the relative frequency of spontaneous cancer.

Age.- Angora goats, on account of the mohair they produce are probably kept alive longer than other races which are usually destroyed for human consumption. Senile degenerative processes of skin and other ^{precancerous} changes associated with age, have not yet been studied.

Sex.- It is peculiar that nearly all animals affected are females. No explanation for this can be given at this stage.

ANATOMICAL DIFFERENCES - PIGMENTATION.

Amongst others one might mention the thinner and more delicate skin, the long hair and the greatly developed skin glands under tail. On account of the configuration of perineum, secretions, excretions and dirt are liable to stagnate, decompose and act as irritant and macerating agents in this region.

Pigmentation of the skin is one of the most striking differences between the Angora and the native goat. The latter have invariably a very heavily pigmented and tough skin. According to Wells (1925) the function of melanin is that of protection against light, especially the violet and ultra-violet rays. This protection is at least in part responsible for the relative infrequency of skin cancer in the coloured human races Wells (1925). It is significant also that the parts of ^{the} skin mostly affected are those not protected by long hair. In merino sheep, which also have a non-pigmented skin, the cancers thus far noted also affected the face and ears. The part played by the pigmented patches

or naevi is not yet ^u understood.

EXOGENOUS FACTORS.

Change of habitat. Although not native to this country, the Angora has become fairly well acclimatised. This, however, does not mean that climatic and other influences have no action on the susceptibility to cancer.

Irritants. Tumours in Angora goats can only rarely be traced to traumatic injuries in spite of the fact that the latter are frequent, ear marking, horning, e.g. 14505. One type of injury which seems to give rise to tumours more frequently than others is the fracture of a horn at its base, e.g. 17292, 17296.

As regards chemical and physical irritants, very little is known. Sunlight and maceration by decomposing secretions have already been mentioned. It is interesting to note that the Angora goat is highly refractory to the carcinogenic action of coal tar (See experiment 10).

~~Specific agents?~~

Other possibilities have been suggested as starting points for tumours, e.g. tick bites with resulting wounds and scratching.

"Piles" These anal tumours have often been called "bleeding piles" by farmers. The possibility of these tumours starting from haemorrhoids was not overlooked. This can, however, definitely be ruled out. Haemorrhoids, according to Fischer, are enlarged varices on the venous plexus either inside or outside the anal ^b ^t sphincter, under the mucous membrane of the anus. The tumours described are definitely associated with the epidermis.

Haemorrhoids are practically unknown in the lower animals, and further even in man, it is very seldom that they give rise to any malignant tumour.

In conclusion it is very difficult to pick out any one or more of the above factors and attach to it more

importance than to others. There may be other factors at play of which nothing is known. In all likelihood it is to the combined influence of all or most of these factors that the neoplasms are to be ascribed.

V Summary and Conclusions.

1. The South African Angora Goat is considered briefly in regard to its origin, appearance and habitat. Special attention is paid to the histology of the normal skin of those parts usually affected with cancer.
2. The occurrence of a type of skin gland in the depth of the subcutis, of the perineal region is recorded. It is not mentioned in text books on comparative histology. It is suggested that it may be a type of apocrine sweat gland.
3. Attention is drawn to the irregular distribution of melanin pigment in the skin, and the frequent occurrence of naeuous-like pigmented patches.
4. Skin cancer of the South African Angora goat is described apparently for the first time.
5. Its incidence is relatively high, especially when compared with the Native and Boer goats in this country, in which cancer is practically unknown.
6. Females are by far the most frequently affected.
7. The predilection seat of development is the perineum (anus and vulva). The ears, horn stumps, and the rest of the skin are also occasionally affected.
8. The material studied is derived from 16 cases. 13 were tumours of the perineum, one of the ear, one of the horn and one of the neck.
9. According to histological appearances, these tumours were divided into three groups, viz. I The undifferentiated epithelial cell tumour, or basal cell carcinoma, II The differentiated cell tumour, or spinous cell carcinoma, and III Mixed or combined forms of both.

10. In most cases of basal cell carcinoma, the relationship of the tumour cells to the basal cells of the epidermis can be seen clearly. Pigmentation is closely associated with this region.
11. Evidence from two cases 14774 and 9983, seems to point to the sebaceous gland, as the origin of at least some of these tumours.
12. As the tumour grows, the proliferating basal layer remains continuous with that of epidermis. In this way pigment forming cells as they occur in epidermis, become incorporated and proliferate in the tumour.
13. Spinous cell carcinomata seem to originate from already differentiated epithelial cells, as they have not the property of pigment formation.
14. It is suggested that these canceroids arise sometimes secondarily as the result of irritation due to pre-existing basal cell tumours.
15. The spirochaetes and bacteria found on the tumours are secondary saprophytes and cannot be regarded as the cause of these tumours.
16. Goats suffering from cancer often become fly struck. The fly larvae undoubtedly contribute additional suffering to the animal and may hasten death or metastasis.
17. Surgical treatment is fairly simple in the early stages, and in our hands has been entirely successful.
18. On account of the small individual value of the goat and the difficulty in obtaining veterinary assistance in this country, it is advisable at this stage to encourage culling off all affected animals.
19. Several attempts at transmission by contact, inoculation and transplantation failed.
20. The Angora goat is highly refractory to the carcinogenic action of coal tar.

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VII. PROTOCOLS.

In order not to encumber the text matter with rather lengthy descriptions of each individual case, the clinical observations, post mortem and histological findings are gathered together in protocol form under this heading. The cases are dealt with in the order in which they are arranged in the comparative table given above. A short comment on the diagnosis will also be found at the end of each description.

Clinical observations.No. 14771.

Angora she-goat, full mouth, in fair condition

6.9.26. In the recess under tail an irregular lobulated tumour is found measuring roughly 3,25 x 2,5 x 1 c.m. It is of a pinkish red colour, soft in consistence, giving one the impression of exuberant granulations. It is extremely vascular and bleeds easily on manipulation. It is covered by slimy greyish exudate, mixed with blood and in parts tending to form crusts. Attachment is by a short stalk to the right and above the anus, and involves only the skin, so that the tumour is freely movable over subcutaneous tissues. The anal opening is just covered by the edge of the tumour, but is otherwise quite patent and defecation is not hampered in anyway. The vulva is unaffected. The skin around vulva is pigmented in patches (melanosis).

22.4.27 Tumour has become rounded in shape, roughly the size of a walnut, it is still deep pink, soft and glistening, and covered by slimy material soiling and matting the breech hair. This is further increased by a purulent discharge from the vulva. A small elevation of skin is noticed near the dorsal commissure of vulva, this involves one of the black pigmented patches of skin mentioned above and is kept in a practically constant state of moistness, by the sticky exudate running down from tumour.

Smear preparations made from the surface of the tumour, show a rich mixed bacterial flora, with which is mixed numbers of spirochaetes and also fusiform organisms.

16.5.27 The tumour tends to spread out into a mushroom-like shape. It is still lobulated and pinkish red on the surface, like granulation tissue and bleeds as easily when touched. The swelling above vulva has extended downwards considerably and involves the whole of both tips of vulva.

The whole vulva shows diffuse swelling and is covered by slimy exudate. The most prominent part is near the dorsal commissure. The exudate has dried to tenacious crusts, firmly adherent to underlying tissue. When this is removed by force a bleeding, rough, black ulcer, with raised swollen edges is exposed. A smear from the surface of this ulcer shows that the black colour is due to a greenish black, granular pigment present in large amounts and partly lying freely, partly hoarded by large mononuclear cells.

Defecation is somewhat painful but takes place with little difficulty. The animal, however, appears to suffer great pain when manipulated in region of perineum and tail. Urination is normal and unhampered.

2.6.27. Practically the same, the vulva is covered by a hard tenacious crust which causes distortion of underlying tissues. There is a purulent discharge from vulva and from beneath the crust. Bleeding takes place when the crust is removed.

25.6.27 Anal tumour is about the same size, pinkish grey colour, covered by slimy stinking matter. The vulva shows the same swollen distorted appearance, with tenacious crust and black bleeding purulent ulcer beneath. The structure beneath the scab is moist and soft and gives the impression of being spongy.

4.7.27. Tumours still in the same state, the black vulvar tumour if anything smaller. Smears from surface show numerous spirochaetes, fusiform organisms and a varied mixture of other bacteria. Large quantity of greenish-black pigment, either free or hoarded in monuclear cells from surface of black tumour.

9.9.27. Size and appearance the same. The tumours are covered by the moist sticky exudate, which mixed with caked blood etc. matts and soils the perineum and surrounding hair.

14.9.27. This animal was given 1,0 g. Pot. iodide daily to see what effect this drug would have on the tumour.

27.9.27 Tumour somewhat reduced in size, now measures only 3 c.m. in its greatest diameter.

5.10.27 Dose of Pot. iodide increased to 2,0 g. daily no change can be noted in tumour above anus but the black vulvar tumour is somewhat decreased in size and covered by a scab. There is a slight watery discharge from the eyes but the appetite and condition of the animal does not seem to suffer.

7.10.27 Tumours appear to decrease in size. The black vulvar tumour has the appearance of drying up, and is covered by thick tenacious scab. This can only be removed with difficulty and causes great pain. Spirochaetes and bacteria still present on the surface of tumours.

13.10.27 Eyes inflamed and show a slight purulent conjunctivitis. There is a serous discharge from nostrils and dribbling of saliva from the mouth (Iodism). Dosing with Potassium iodide discontinued. Except for the somewhat drier appearance and slightly decreased size, there is no change in tumours.

15.10.27 Animal has a distinctly dejected appearance and stands hunched up, hardly feeds at all. Condition noticeably poorer, purulent conjunctivitis worse.

17.10.27 Emaciated condition, hunched up and listless conjunctivitis, and dribbling from mouth.

21.10.27. Very much weaker, emaciated, does not feed. Sero-purulent discharge from eyes and nostrils.

22.10.27 Lying down, unable to rise.

24.10.27 Died during the night.

Post mortem findings.

Cachexia, purulent conjunctivitis, catarrhal rhinitis catarrhal enteritis. The tumour under tail measures 2 x 1.5 x 0.5 c.m. It is pinkish red in colour, smooth and covered with slimy greyish exudate.

The tumour over dorsal commissure of vulva is pitch-black in colour, measures roughly 1 x 0,5 c.m. is fairly hard, covered by tough scab. The swelling extends downwards on either side of vulva. The rest of skin of vulva is black in patches, pigmentation extending inwards along the mucous membrane of 3 c.m. Death in this case is probably due to Potassium iodide poisoning.

Histological findings. Specimen No. 7447.

Anal tumour. Under low magnification the appearance is as follows: On the one side the normal epidermis with all its skin glands becomes abruptly replaced by a very vascular tissue with ragged surface, indented by fissures which throw it into rounded irregular lobes. In places the surface is covered by a thick layer of necrotic matter. This tissue on the other side becomes continuous with the epithelium of the anus. At this junction there is a circumscribed, thickened, convoluted, ^{Solid} solid nest of basal cells connected by a small bridge to the anal epithelium. The central cells are not quite differentiated into squamous cells, and there is no indication of keratinisation. This nest marks the end of the epithelium of anus. The vascular tissue mentioned above forms the boundary of the tumour proper. In between the numerous small blood vessels and capillaries engorged with

blood, there is a large amount of inflammatory exudate cells mostly neutrophiles and lymphocytes. Amongst this there stands out clearly, solid strands and nests of epithelial cells. These are mostly arranged in the form of strings of single cells bent to form ^rcrypt-like structures or growing into closely packed masses, mostly at the bottom of the fissures between lobes. These cells show no mitotic figures, but evidence of rapid amitotic division is not lacking, as cells with two or more neuclei^e are frequent, and many nuclei have several nucleoli. These cells have not the regular uniform appearance seen in 7256A, for instance, but show a slight tendency towards the squamous type, i.e. lighter staining and polygonal shape. There are numerous swollen faintly staining cells, with dark chromatic granules in place of nucleus, the so-called "cancer parasites", but no definite centres of keratinisation are present.

Diagnosis.

Basal cell carcinoma (Adenoid type.)

Vulva tumour. The vulva tumour is practically continuous with the anal part above, but is quite distinct in that it is pigmented and affects only the vulva and its mucosa. The mucosa of vulva for about 2-3 c.m. is of a pitch black patchy colour, but is otherwise smooth. The skin of vulva is somewhat swollen and shows loss of substance over a small area. This elevated portion is covered by a layer of necrotic matter mixed with a large amount of pigment. The underlying tissue shows numerous small blood vessels and capillaries. In between these and penetrating a small distance from surface only, there are numerous nests of epithelial cells of the squamous type, surrounded by germinal layer in more or less the typical canceroid fashion. These nests are separated by large numbers of inflammatory cells (lymphocytes, neutrophiles). There is a considerable amount of black pigment (melanin) sometimes associated with the

basal cells, but mostly in dark clumps in the interstitium i.e. ^mconnective tissue cells. Pigment was never seen within the horny centres of the above epithelial nests. From the entrance of the vulva, and for a short distance along the mucosa the structure changes. The horny epithelial nests are replaced by foci of uniform large polygonal round cells, all containing melanin in the form of diffuse fine granules. Their structure which is undoubtedly epithelial is thus not obscured. They are not too closely packed together, and have the same staining properties and shape, as the basal cells of epidermis. The only difference is that they appear much larger and the nuclei fainter. The pigment is in the form of a fine dust-like mantle around the nucleus, whereas in the deeper tissues the pigment is hoarded in the form of very compact and dark clumps, in connective tissue cells (histiocytes). The thickness of this pigmented layer of basal cells varies. In parts it is in the form of round circumscribed foci partly covered over by flat epithelium, but towards the deeper parts of ^{the}vulva the layer becomes thinner, and gradually merges into normal mucosa. The pigmentation there appears to be due entirely to melanin hoarded in the deeper connective tissue cells.

Diagnosis.

Pigmented baso-cellular carcinoma with squamous cell (canceroid) tendencies in parts.

Comments: Here is a good example of the mixed type of carcinoma that is often found. The anal tumour is a non pigmented basal cell carcinoma. The vulva tumour is ^adeeply pigmented variety of the same, with in addition the formation of canceroid "pearl nests" or keratinisation centres.

Several points of interest will be noted in this case.

1. The primary tumour was presumably a basal cell carcinoma of the anus, without apparent pigmentation.
2. There was a pre-existing melanotic patch of skin at the dorsal commissure of vulva.