

RODENT ULCER

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When the Combined Clinic was started in 1948 at Grootte Schuur Hospital, its object was to bring into one treatment centre all cases of facial and mouth cancer and to provide a focal point where surgeon, radiotherapist, dermatologist and plastic surgeon could meet and see the patients in consultation, so that each patient could be assessed by all who were likely to have to treat him; later it was hoped to publish the results of treatment and reports of significant cases as they became available from time to time.¹⁻³ Since its inception, over 1,000 cases have been seen at this clinic and it is now possible to publish a resumé of the scheme of management evolved.

Until recently Grootte Schuur Hospital has been the only organization in the Western Cape equipped to handle these cases in significant numbers. The statistics obtained until 1956 and here presented include all the cases of rodent ulcer which have come up for treatment in the Western Cape in the last decade. Recently, other institutions have been opened.

THE ETHNIC FACTOR

The hospital serves about 2 million people, approximately evenly divided between Europeans and Coloured; relatively few (100,000) Bantu are domiciled in the area under discussion and for our purposes they are classified with the Coloured. Of the (approximately) one million Coloured, practically all come to this hospital for their radiotherapeutic treatment. While it is unusual for a Coloured patient to seek private treatment, this cannot be said of the Europeans, a proportion of whom (exact numbers unknown) prefer and can afford private treatment; in addition a fairly large number of Europeans who are employees of the South African Railways have their own practitioners who attend to their medical needs on a contractual basis. The figures that are therefore presented in this communication refer to all the Coloured cases in the population served by the hospital and to about 50% of the European cases.

The vast majority of the original European population of the Cape came from Holland and the German states along the Baltic coast, and there is an admixture of French (Huguenot) blood which, in turn, came from France. The number of blondes in this group (the Afrikaner) is relatively large; approximately 50% of the Afrikaner people have blonde hair, blue eyes and a light soft skin.

Since European and Coloured patients appear at the hospital in about the same numbers, any difference in the frequency of the disease in the two groups has statistical

significance. The relative number of cases of the various kinds of cancer of the face are shown in Fig. 1.

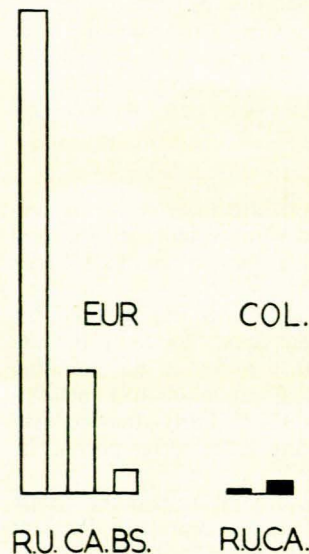


Fig. 1. Graphic representation of the varieties of facial cancer showing the disparity between the European and Coloured patients. RU=rodent ulcer. CA=epithelioma. BS=basis-squamous carcinoma. Eur=European. Col=Coloured.

It is obvious that rodent ulcer is far commoner in Europeans than in the Coloured. Even among the Europeans there is a sharp division in the incidence of the disease; the vast majority of our patients are fair-haired, blue-eyed people who lead open-air lives and whose skin is constantly exposed to the sun and the weather. Because the Afrikaner is traditionally occupied in agricultural pursuits, our patients are predominantly Afrikaner.

ACTION OF SUNLIGHT

A certain number of blondes are able to develop pigment and can tan, but the majority of them show varying degrees of erythema and tan with difficulty; it is apparent that their pigment mechanism for protection against the sun is not as efficient as that of the brunettes. Of the non-tanning blondes a large proportion develop skin troubles as a result of exposure to sunlight. This has been known for many years and, indeed, rodent ulcer of the face has for long been called 'sailor's wart' in Europe, where the condition is relatively rare, but has been noticed in sailors and in travellers to the tropics.

The Nordic individual who leaves his cool, rainy native land to settle in countries where the sun is less obscured is often called upon to pay for his enterprise by developing dermatoses, rodent ulcer, basi-squamous epithelioma and frank epithelioma on the exposed portions of his skin; it is this group of people who are our constant and most frequent patients. The problem is by no means restricted to South Africa; the number of rodent ulcers which are reported and treated in Australia is very great indeed. Those areas of

the United States south of the Mason-Dixon line contribute a fair number; and recently a large number of fair-haired people have settled in Israel, which in due course will doubtless contribute its share of facial cancers to the picture.

Pre-cancerous conditions are well known and this is a very common finding in many of our patients. It is the rule to find large areas of pre-cancerous skin and only a small area broken down into a rodent ulcer. The pre-cancerous condition, known as solar keratosis, is recognized by a roughening and a loss of the normal smoothness and greasiness of the skin.

The tendency to develop rodent ulcer is not confined to the blonde European, it is due to lack of protective pigmentation, and when albinism occurs among negroes these albino negroes almost invariably show malignant skin changes as a result of exposure to sunlight which are very similar to those shown by the blonde European. The conclusion is inescapable that lack of resistance to sunlight is not an independent racial phenomenon, but is related to the physical condition of the skin.

AETIOLOGY AND PATHOLOGY

All rodent ulcers are basal-cell carcinomata, and the origin of basal-cell carcinoma is in dispute. While most pathologists agree that the neoplasm originates in the deeper layer of the epithelium and thus retains the small-celled and dark-staining quality possessed by its parent tissue, others are of the opinion that a basal-cell carcinoma indistinguishable from these may originate in any of the skin appendages, and that the sweat glands, the sebaceous glands and the hair follicles may all be the original site of the lesion. It is impossible, however, in the present state of our knowledge of histology, to differentiate between basal-cell carcinomata originating in these different sites.

Once it starts to grow, basal-cell carcinoma appears as a small pearly area, typically with a small leash of blood vessels leading to it. It grows and spreads along the surface of the skin. Ulceration takes place and varieties are differentiated according to the degree of ulceration or of cyst formation. These cystic rodents appear to include small cysts and typically the area increases in size and attempts at healing occur, so that the circular area occupied by the rodent shows parts where healing has taken place. The disease has a great tendency to travel along tissue planes. If it reaches the conjunctiva it can be seen growing quite superficially on the mucous membrane. It shows a preference for travelling along fascial planes and lines of developmental fusion. If bone is invaded the basal-cell carcinoma travels along the periosteum for some time but sooner or later it invades the bone. If it succeeds in reaching a paranasal sinus it travels along the mucous membrane in unpredictable directions.

In the 1,200 or more rodent ulcers which have come under our notice not a single case of lymph-gland involvement has occurred, and we cannot with assurance record a single case of spread by the blood stream. For this reason we feel it is worth while making the local excision or treatment radical and effective because it is then possible to say with fair assurance that the condition is cured.

Mohs and Lathrop⁴ have pointed out, after cutting serial sections of excised rodent ulcers and reconstructing the tumour, that in certain instances relatively long processes of rodent ulcer are seen to invade and develop along nerve sheaths and into foramina in bone. We accept this finding,

though our own experience is that a radical excision is, as a rule, successful in the first instance.

STATISTICS

In the 9 years 1949-57, 1,209 cases of rodent ulcer occurring in 857 patients were treated by the radiotherapy department at this hospital. An analysis of 556 consecutive cases of these according to their sex and race is illustrated in Fig. 2.

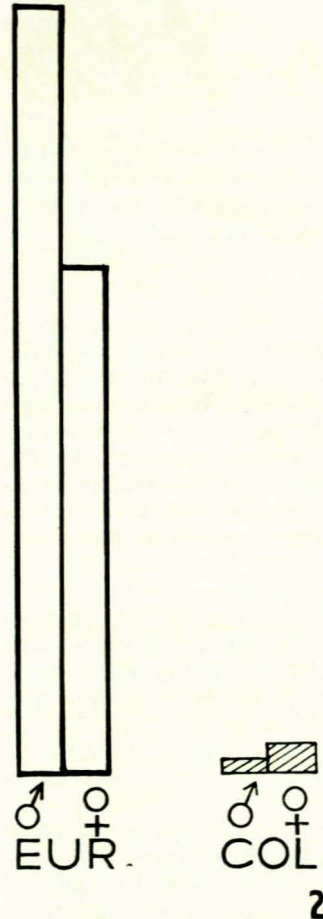


Fig. 2. Analysis of 556 consecutive cases of rodent ulcer showing race and sex distribution.

It will be observed that the number of Europeans is enormously larger than that of Coloured, viz. 804 Europeans against 29 Coloured, making the proportion about 27 to 1 in two hospital populations of approximately equal numbers. This means that the Coloured person's risk of getting a rodent ulcer is less than 3% of that of the European working and living under identical conditions. This is extremely significant. We shall show in a subsequent communication that somewhat similar figures are available for carcinoma of the lip and we hope to bring evidence to show that both these diseases are due to the effect of the sun's rays on specific skin organs.

Squamous carcinomata also show a greater incidence in Europeans than in Coloured, but the preponderance is less than with rodent ulcer—362 in European as compared with 32 in Coloured, the ratio being 11 to 1 as compared with 27 to 1 for rodent ulcer. Basi-squamous carcinomata have been found to occur in only 2 Coloured patients.

DIAGNOSIS

The diagnosis as a rule is simple. The patient, of typical colouration, complains of irritable skin on the face. He has noticed that it breaks down and ulcerates each winter but tends to heal in the summer; finally a persistent area of crusting is observed and, although this grows only very slowly, it never completely heals. The situation most commonly affected is a triangular area bounded laterally by a line drawn from the external canthus of the eyes to the middle of the upper lip, and above by the palpebral fissures; the nose is a very common site of trouble. The inner canthus of the lower eyelid is another site commonly affected, and so is the back of the ear. The dorsum of the hands on examination usually show roughnesses of varying degrees and often crusting, ulcerated areas. The rest of the glabrous skin, covered as it is by clothes and by hair, is normal.

If frank ulceration is present, it often does not appear as a typical rodent ulcer with a wire-like edge and healing at one or another part of its circumference. Indeed, it is poor judgment to wait for this typical appearance, and a snip for biopsy should be taken of every suspicious area. There is a clinical error of at least 5% but a pathologist can give the correct answer with ease and immediately in all cases.

The varieties of rodent ulcer classically described, viz. terebrant, cystic, ulcerating, etc., are not of clinical importance, for all are basal-cell carcinomata, all behave in the same way clinically, and all respond to the same treatment in their earlier stages.

TREATMENT

The treatment of rodent ulcer resolves itself into adequate therapy for a local disease; not a single case of distant metastases or lymph-gland involvement has been observed. Our aim has been to ensure local permanent cure at the cost of minimum deformity.

Preventive

As it is considered that facial cancers are due to the effects of actinic rays, patients are advised to wear broad-brimmed hats and to avoid the sun. It is felt, however, that this advice is usually too late to be of any value because cases seem to occur up to several years after patients have been warned and have avoided sunlight; it appears that once a lesion has started it progresses to neoplasia without needing to be actinically irradiated any further. However, we think it is wiser to prevent further radiation, and advise the patient to avoid exposure to the sun.

Sun protection creams. We have experimented with various sun protection preparations containing different chemical barrier creams⁵ in an effort to prevent recurrences in cases of severe solar keratosis with multiple rodent ulcers; but a report on the results of this therapy, which can only be a long-term one, is not yet available.

We intend trying to treat a series of cases with Meladinin⁶ in an effort to obtain pigmentation of these unprotected skins.

In the early stages, before the development of frank neoplasia, we treat the hyperkeratotic condition of the skin with ointments containing 5% salicylic acid. This, applied once or twice daily, suffices in a matter of 2-3 weeks to so smoothen the rough skin that it is possible to see immediately whether the area under suspicion is in fact neoplastic or not. The ointment has no obvious effect on the neoplastic areas, which after a fortnight stands out boldly and clearly on the smoothened skin.

Curative Treatment

To facilitate the description of the management of the frank, developed rodent ulcer, we divide them clinically into 3 types, viz.: (1) Small—less than 0.5 cm. in diameter, (2) average—larger than 0.5 cm. in diameter, and (3) complicated.

1. *Small rodent ulcers* are equally well treated by surgery or by radiotherapy; it is our custom to excise the ulcer surgically if it appears on an eyelid or on the pinna of the ear. In these cases radiotherapy presents difficulties and there is a risk of necrosis of the underlying cartilage or of damage to the lens if radiation is carried out on the pinna or on the eyelid; radiotherapy in divided doses up to 6,000 r is delivered over 14 days and it is sometimes difficult to

avoid these complications. Surgery avoids these risks, and in small uncomplicated cases gives excellent results if excision is adequate—it need only just clear the lesion—and if the scar is placed in one of the crease lines it often becomes completely invisible. Our plastic surgeons have had much experience in these excisions and their results, both cosmetic and curative, are very satisfactory in these selected cases.

If the rodent ulcer is very small (about the size of a grain of rice) excision biopsy is undertaken and is checked by the histologist for adequacy of the excision, as indeed is done as a routine where any excision is performed. Two sections at right angles to each other are taken to enable the pathologist to say whether the tumour has been completely excised or not; any fault in the excisional technique is noted and can be retrieved by radiotherapy after the excision wound has healed or by re-excising on a wider scale after healing is complete. Mohs and Lathrop⁴ use superficial chemical coagulation and repeated shavings histologically controlled to excise the tumour, but we have had no experience of this method.

2. The *average rodent ulcer* (0.5 cm. in diameter or larger), which forms the great majority of our cases, is treated with radiotherapy after biopsy, the aim being to deliver 6,000 r over the area with a margin of 1 cm. around the edge of the ulcer, over 14 days. The patient is seen at regular intervals until the immediate radiation effect has passed off. Healing is usually completed within 6 weeks and thereafter the patient is seen at the follow-up clinic, at first at monthly intervals, which are gradually lengthened until the visits are annual.

3. *Complicated rodent ulcers* are classified as such (a) if bone has been involved, (b) if they have been treated previously by radiotherapy and have recurred, and (c) if they have been treated at any time by a 'cancer paste'. The treatment of these cases is always surgical and the bone, if involved, must be completely excised. The local nature of the lesion makes it quite unnecessary to undertake wide resections; indeed, it is only necessary to clear the tumour by a small margin, and local recurrence is then very rare. However, *if bone is involved*, that bone requires to be completely removed. A certain number of these cases will prove on histological examination to have been clinically misdiagnosed, the clinical adherence to the bone being inflammatory in origin and not neoplastic; this is unavoidable.

If an air-sinus is invaded, the whole of that sinus should be widely exposed and its mucosal lining removed; if the mucosa proves to be invaded, the bones forming the walls of the sinus should be treated as if they were also directly invaded by neoplasm and removed. It is only in this ruthless way that excision of some of the more extensive types of rodent ulcer can be successfully undertaken. Any attempts to reduce the size of the excision will result in recurrence—usually in an inaccessible situation and often inoperable. The happy result of a successful first excision is so uniform and its failure so significant that nothing less than the most radical surgery at the first operation in these 'complicated' cases should be undertaken.

If the orbital cavity has been invaded, it is advisable to exenterate the orbit. A piece of tissue for microscopic examination is taken from the optic foramen and, if found invaded, radiotherapy is given and later a graft is inserted to blank off the raw cavity. This successfully holds the disease in check. This type of surgery as a rule leads to a certain

amount of deformity, which can be partly corrected later by the plastic surgeon.

In all our excisional work it has been the policy of the clinic that the person performing the excision of the original growth should not be responsible for the repair and *vice versa*. This is because of the psychological tendency to reduce the extent of the excision if one knows that a long repair lies ahead.

Apart from the smaller local excisions which our plastic surgeons undertake with the scalpel, excision with diathermy has much to recommend it. Diathermy wounds heal quite as well as ordinary surgical wounds made with the scalpel, there is less haemorrhage, and the superficial coagulum takes skin grafts successfully. Since the disease is only locally invasive, the strong argument in favour of diathermy that it seals the lymphatic channels does not apply, but using it certainly does facilitate operations in the deeper wounds.

Recurrence after radiotherapy. We recognise two types of recurrences after the radiotherapy, viz. (1) marginal recurrence and (2) central recurrence. While the marginal recurrence may be considered to be due to inadequate excision or radiation, it may also be explained on the basis of a separate origin in a disease which notoriously originates in multicentric foci. A central recurrence however, cannot be explained this way; it may be due to unrecognized extension of the growth into the underlying bone where it is relatively radio-resistant, or along a nerve sheath into a bony foramen where it is similarly protected.⁴ As a rule, the 'central recurrence' turns out to be a radionecrosis and, while this possibility is always in our minds, biopsy alone will show which is the true underlying factor.

Recurrences after radiotherapy are treated by excising the recurrence as well as all of the irradiated area and inserting a Thiersch graft to cover the defect, with no undercutting. This makes it possible to observe the lesion at follow-up through the thin skin pellicle and to carry out any further excisions should the need arise. We are opposed to second and further courses of radiotherapy because the extent of the reaction cannot be predicted and the effect on the tumour is usually incomplete.

Cancer-paste cases. It has been repeatedly observed that, regardless of what form of therapy has been given, the patient whose rodent ulcer has been treated with cancer paste has received such a trauma to the underlying stroma that radiotherapy is not effective; we now feel that a wide primary surgical excision offers these cases the only chance of a cure. Because of the damage to the stroma, the reaction to radiotherapy is also unpredictable, so that normal doses may lead to very extensive sloughing—an additional reason for advising surgery, which is definitive and free from this risk.

RESULTS

When the clinic was started in 1948, a great many very wide excisions had to be performed on long neglected cases (Fig. 3) but as the public has become educated and patients come for treatment sooner, these extensive excisions have become more and more rare. However, every now and then some individual who has neglected a rodent ulcer requires extensive operation; it is not always patients from the outlying districts who neglect these apparently innocent lesions.

We have not had a single case die of a rodent ulcer or as a result of its treatment. However, as many of our patients are in the 7th and 8th decades of life their normal life expectancy is not long (Table I). They die of intercurrent diseases—congestive cardiac failure, coronary disease, carcinoma of stomach or rectum, etc.

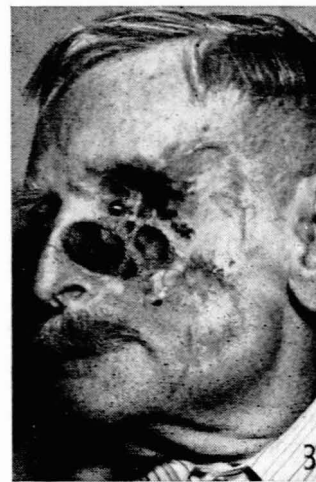


Fig. 3. A case of extreme deformity controlled for 8 years by surgery after radiotherapy had originally failed and still alive today.

The largest mutilations can be repaired by the plastic surgeon, if necessary by 'blanking out' the raw areas, usually with Thiersch grafts or in the larger excisions with pedicle grafts, and these elderly patients accept the deformity involved and are satisfied with the relief from pain that is normally obtained.

SUMMARY

1. In South Africa, Australia, the Southern States of the USA and Israel there has been a large influx of non-indigenous Nordic types.
2. These people consist of brunettes and blondes.
3. Brunettes are protected against sunlight by their capacity to sunburn and develop pigment.

TABLE I. AGE GROUPS OF 267 CONSECUTIVE CASES OF RODENT ULCER

	Under 30	30-39	40-49	50-59	60-69	70-79	80+
Cases ..	5	23	33	50	76	52	28
% ..	2	9	12.5	19	28.5	19.5	9.5

4. A large majority of the blondes burn and go red but never tan.
5. In this group of non-tanners many of those that lead outdoor lives develop hyperkeratosis.
6. Hyperkeratosis is the skin response of non-tanners to sunlight, just as tanning is the response of brunettes.
7. In the non-tanners, hyperkeratosis on the face is followed by the development of rodent ulcer, basi-squamous carcinoma and frank carcinoma.
8. The plan of management for treating these cases is indicated.

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REFERENCES

1. Schrire, T. (1956): *S. Afr. Med. J.*, 30, 173.
2. *Idem*, (1956): *Ibid.*, 30, 1185.
3. *Idem*, (1957): *Ibid.*, 31, 465.
4. Mohs, F. E. and Lathrop, T. G., (1952): *AMA Arch. Dermat. and Syph.*, 66, 427.
5. Kumler, W. D. (1952): *J. Amer. Pharm. Assoc.* 41, 492.
6. Schulze, B. V. and Leeming, J. (1955): *S. Afr. Med. J.*, 29, 147.