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## SQUAMOUS-CELL EPITHELIOMA OF THE SKIN\*

A STUDY OF 256 CASES

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THE broad term "skin cancer" usually includes basal-cell epithelioma, or rodent ulcer, and squamous-cell epithelioma. As a matter of fact, the term skin cancer should include four types of epithelioma; that is, basal-cell, squamous-cell, melanotic and non-melanotic melano-epithelioma,<sup>4</sup> varying in degree of malignancy with their capacity to cause death in the proportion approximately of 35 for the first, 65 for the second, and 95 for the last two types on the basis of 1 to 100.<sup>3</sup> The recognition of the type of skin cancer being dealt with is of prime importance from the standpoint of prognosis. Carcinomas which originate in the sweat and sebaceous glands should not come under this term any more than carcinoma of the breast, as they originate from the germinal cells of specialized glands of dermal origin.

*Polymorphism of Epithelial Cells.*—No cells of the body are more prone to change their form than are epithelial cells. Not infrequently cells are seen in neoplasms, under the high power of the microscope, which bear a close resemblance to muscle-cells and fibroblasts, but since they can be traced directly to the basal layer of the skin, there can be no doubt with regard to their origin (Figs. 1, 2, 3 and 4).

Kettle, in his article "Polymorphism of the Malignant Epithelial Cell," states:

"That the malignant epithelial cell is capable of polymorphism is perfectly well recognized. The interchangeability of the acinus and the solid structure in adenocarcinoma is familiar to everyone, and the origin of a squamous-cell carcinoma from columnar epithelium has been reported on several occasions. Greater variations than these, however, are not, as a rule, considered possible. It is true Krompecher held that under certain conditions of growth and environment epithelial cells may assume a spindle form and may actually be converted into connective-tissue elements, but his views have not found general acceptance, and the doctrine of the specific nature of cell-growth is not seriously

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questioned. Without going so far as to claim that the adult epithelial cell can actually become changed into a connective-tissue cell, I am convinced that some carcinomata may possess such extreme powers of polymorphic growth that their cells, losing all trace of their epithelial origin, may become indistinguishable from connective-tissue elements."

Krompecher's view seems somewhat illusory, but considering that the entire body is developed from the fertilized ovum, his theory is brought within the range of possibility. Squamous epithelium does not originate from columnar epithelium, as the columnar cell is differentiated and cannot regenerate. When a squamous-cell epithelioma develops in an organ in which columnar epithelium is found normally, the gall-bladder, for example, the regenerative cells which, under ordinary circumstances produce columnar epithelium, produce squamous epithelium instead. The same process takes place in an everted uterus when protective instead of columnar epithelium is needed.

*Regeneration and Degeneration.*—I believe that the habitual use of the term "cancerous degeneration" is incorrect. MacCarty believes that cancer is a regenerative process and not a degenerative process. Cancer tissue like other tissues degenerates. The enzyme activity of the cancer cells may cause their death and that of other cells. Cancer cells may also be destroyed by being deprived of nourishment by fibrous connective tissue. Whatever affects the general metabolism of the body affects the cancer. As is well known, the cells of our bodies are subject to the two great processes of nature, anabolic and katabolic. the former builds up and the latter tears down. Nourishing diet, fresh air, sunshine, and rest help to cure tuberculosis, but not cancer, which is a part of the body, and when food is prepared and distributed to the normal cells it is also distributed to the cancer cells.

The chronic destruction of epithelial tissue often is followed by cancer, for example, on ulcer of the lip. The destruction of the epithelial cells is a katabolic process and the regeneration by the cells of the germinal layer is an anabolic process. If the anabolic process predominates, the ulcer is healed over by normal epithelium; if the katabolic process predominates, the ulcer continues to grow. If cancer develops on the border of the ulcer, however, the cancer has both regenerative and destructive properties. Cancer cells are undifferentiated cells which have taken over new properties besides their regenerative abilities; that is, the power to invade and migrate, thereby infringing on the rights of other cells, and, depending on their degree of cellular activity, producing death of the entire organism. I believe that pernicious anæmia, myelogenous leukæmia, lymphatic leukæmia, and, in fact, all malignant neoplasias are regenerative-destructive processes, probably following, in the large majority of instances, excessive chronic destruction of differentiated cells, such as pernicious anæmia following the chronic excessive destruction of red blood-cells, and lymphatic leukæmia and lymphosarcoma following

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the chronic excessive destruction of lymphocytes. Maud Slye, in her paper on the relation of pregnancy and reproduction to tumor growth in mice, concludes :

1. "Cancer and reproduction both being growth processes draw upon the same energy residuum and are made possible by the same food. Hence the food and energy used by one are withheld from the other.

2. "Therefore (a) if the female is constantly pregnant, energy and food are withheld from the tumor, and it grows with extreme slowness. (b) If there is a hiatus between pregnancies, or a termination of pregnancy, the energy which was running into reproduction is released and diverted into tumor which grows very rapidly. (c) If tumor growth considerably antedates impregnation, the currents of energy are already being used for tumor growth and are with difficulty diverted for pregnancy, probably never wholly so.

3. "Hence, when a female is well advanced in tumor growth before impregnation there are rarely any offspring brought to birth. When offspring are delivered they are few, small, undernourished and rarely suckled (which in mice means there is no lactation).

4. "When tumor growth is not interfered with by pregnancy, it is (a) extremely rapid in mice which are young, well nourished and vigorous; (b) less rapid in mice older or less vigorous or less nourished; (c) very slow in mice which are old, feeble, undernourished, or afflicted with a destructive complicating disease."

Miss Slye's conclusions are ample proof that cancer is a regenerative-destructive process.

*Cell Differentiation and Activity.*—In a recent paper on squamous-cell epithelioma of the lip,<sup>2</sup> I brought out the fact that the more an epithelioma tends to differentiate, the lower is the degree of malignancy. I believe this principle can be applied to malignant neoplasia in general. Very few melanotic or non-melanotic melano-epitheliomas show any tendency to differentiate, hence the high degree of malignancy; however, gland formations and squamous cells are sometimes found in these neoplasms.

The question has often been asked why the basal-cell epithelioma is of such a low degree of malignancy when it is made up of undifferentiated cells. It has been suggested that basal-cell epithelioma passes through a short cycle and differentiates into basal cells, while squamous-cell epitheliomas pass through a longer cycle in order to differentiate into squamous cells.<sup>5</sup>

It is well known that most of the cells of a basal-cell epithelioma bear a close resemblance to the normal basal or regenerative cells of the epidermis; however, sometimes there are cells in this type of neoplasm which contain round nuclei with deeply staining single nucleoli, "one-eyed cells"; sometimes the nuclei are irregular in outline and contain more than one nucleolus or none. I can see no differentiation in these cells; they bear a striking resemblance to the Grade 4 squamous-cell epithelioma or the melanotic epithelioma. Whenever these cells predominate in a basal-cell epithelioma it is best to give a guarded prognosis because they are liable very rapidly to infiltrate the surrounding tissues. There seems to be no reason why a basal-cell epithelioma with such active cells should not metastasize, and maybe they do.<sup>1</sup>



FIG. 1.—Squamous-cell epithelioma of the skin, showing polymorphism of the cells (low power).

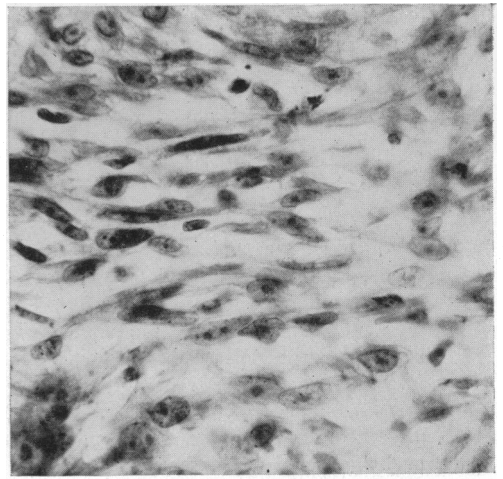


FIG. 2.—High-power magnification of section shown in Fig. 1. Note the close resemblance to fibrosarcoma.

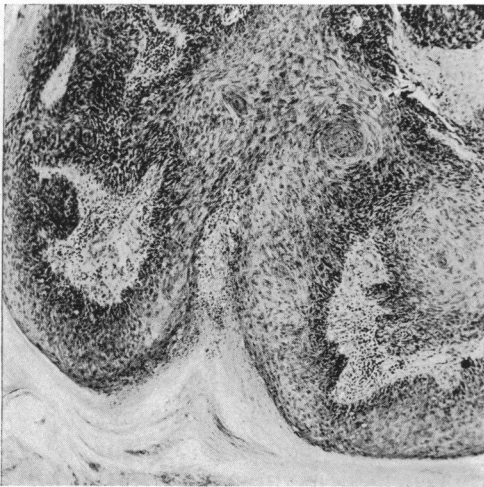


FIG. 3 (Case A33716).—Squamous-cell epithelioma of the skin showing a marked polymorphism of the cells (low power).

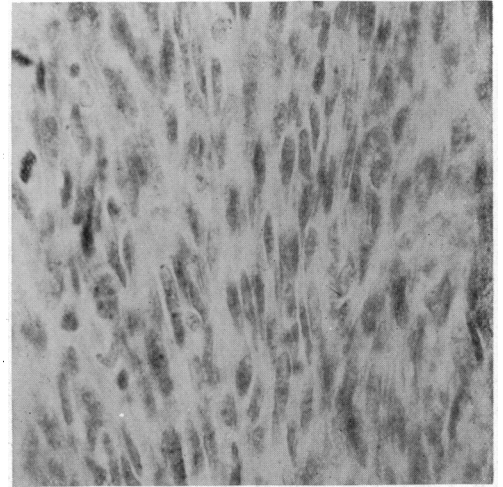


FIG. 4 (Case A33716).—High-power magnification of section shown in Fig. 3. Exact picture of myosarcoma.



FIG. 5 (Case A19884).—Grade 1, epithelioma; a, normal epithelium; b, epithelioma showing marked differentiation.

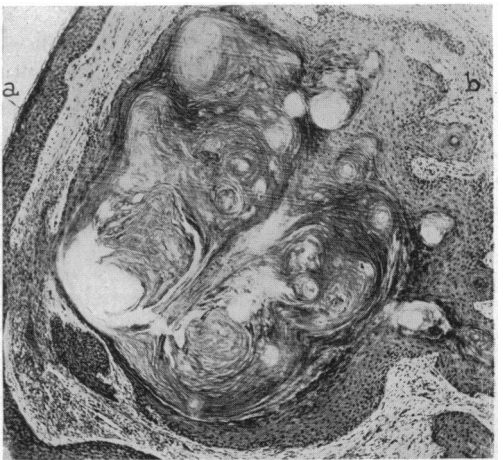


FIG. 6 (Case A66960).—Grade 1, epithelioma; a, normal epithelium; b, epithelioma showing marked differentiation.

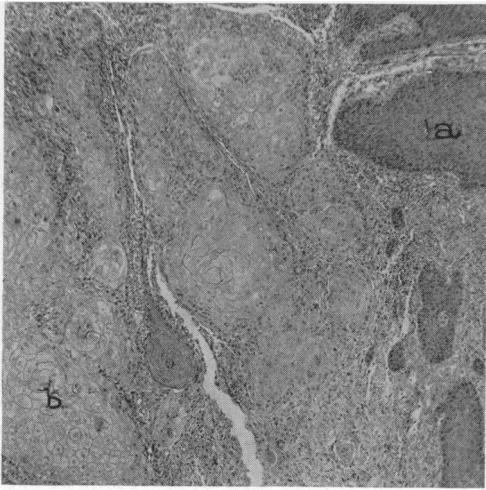


FIG. 7 (Case A95147).—Grade 1 epithelioma; *a*, normal epithelium; *b*, epithelioma showing marked differentiation.

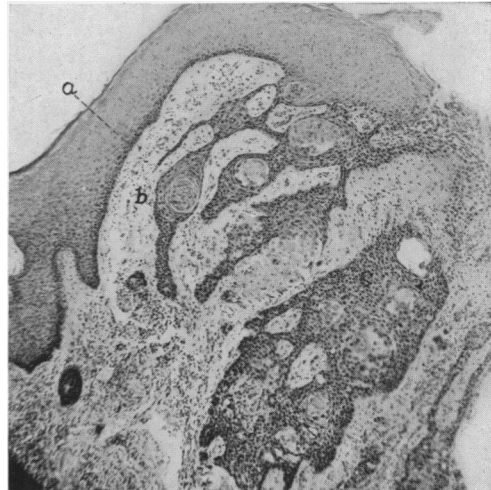


FIG. 8 (Case A75272).—Grade 2 epithelioma; *a*, normal epithelium; *b*, pearly body; *c*, undifferentiated epithelial cells.

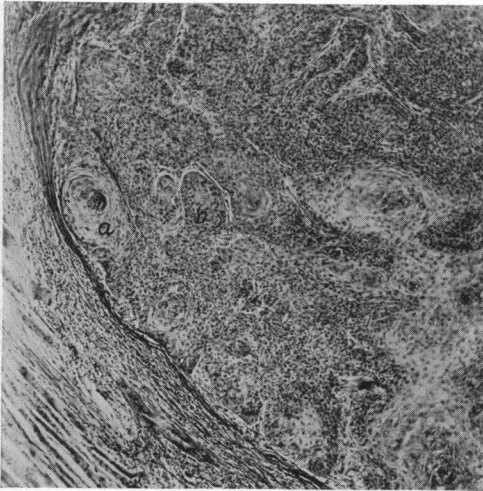


FIG. 9 (Case A90006).—Grade 2 epithelioma; *a*, pearly body; *b*, undifferentiated cells.



FIG. 10 (Case A34711).—Grade 3 epithelioma; *a*, normal epithelium; *b*, epithelioma.

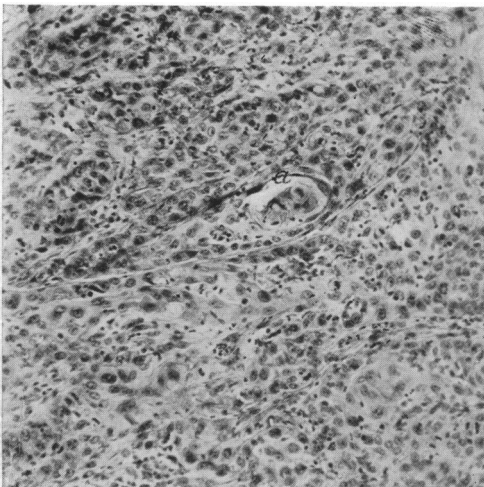


FIG. 11 (Case A53661).—Grade 3 epithelioma; *a*, epithelial cells showing practically complete differentiation.

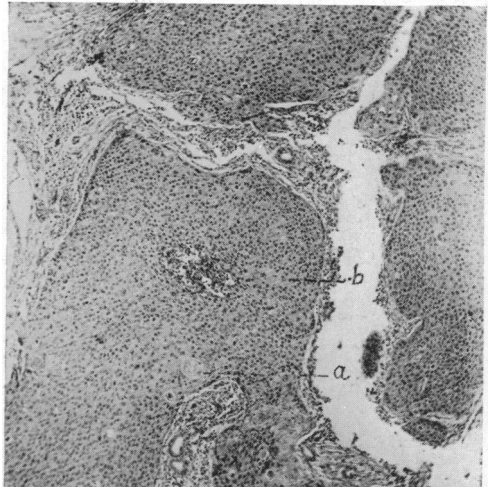


FIG. 12 (Case A220).—Grade 3 epithelioma; *a*, practically completely differentiated cells; *b*, undifferentiated cells.

Frequently areas of pearly bodies are found in a basal-cell epithelioma; these are due to the change from basal cells to squamous cells and from squamous cells to pearly bodies.

The same general plan will be followed in discussing squamous-cell epithelioma of the skin as that in squamous-cell epithelioma of the lip.<sup>2</sup> The degree of cellular activity is graded 1 to 4 on the same basis, namely, if the epithelioma shows a marked tendency to differentiate, that is, if about three-fourths of its structure is differentiated epithelium and one-fourth undifferentiated, it is graded 1 (Figs. 5, 6 and 7); if the percentage of differentiated and undifferentiated epithelium are about equal, it is graded 2 (Figs. 8, 9 and 10); if the undifferentiated epithelium forms about three-fourths and the differentiated about one-fourth of the growth, it is graded 3 (Figs. 11, 12 and 13); if there is no tendency for the cells to differentiate it is graded 4 (Figs. 14, 15 and 16). The number of mitotic figures and the number of cells with single large deeply-staining nucleoli, one-eyed cells, play an important part in the grading. With some experience in the grading of epitheliomas, a picture for each grade becomes fixed in mind, thereby making the grading rather easy. Not all cells with single deeply-staining nucleoli are malignant; however, when they are found in a neoplasm in large numbers it is best to treat the tumor as malignant or promalignant. These cells are regenerative, and, since malignant neoplasia is a regenerative-destructive process, their presence in malignant neoplasms is not out of order.

An endothelial leucocyte is also a one-eyed cell, but it differs from the true one-eyed cell of malignant neoplasia in that it lacks body. Not all malignant cells have a single nucleolus; some have more than one and others have none. As a rule, the more malignant the neoplasm, the more irregular and ill-defined are its cell nuclei; however, exceptions to this are not infrequently seen. A pearly body in a lymph-node is not itself cancer; neither are the large flat squamous cells with small nuclei which lie adjacent to it. The pearly body is a finished product which corresponds to the horny layer of the epidermis. The large flat squamous cell with a small nucleus is almost a finished product; the keratinization of this cell forms the basis of the pearly body (Figs. 17 and 18). The large flat squamous cell with the small nucleus and the pearly body are not cancer when found in a lymph-node, as they are incapable of regeneration. Cells which are incapable of regeneration are not cancer cells. On this reasoning, the basis of grading epitheliomas is formulated.

#### CONCLUSIONS

1. The term "skin cancer" is indefinite and should be discarded.
2. The use of the term "cancerous degeneration" also should be discontinued.
3. The capacity of a cancer to cause death should be known when a prognosis is given.

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4. Cancer is a regenerative-destructive process, resulting in the majority of instances from the interaction of anabolic and katabolic processes.

5. In most cases malignant neoplasia probably follows the chronic excessive destruction of differentiated cells.

6. As a rule, the more marked the differentiation in a squamous-cell epithelioma, the lower is the degree of malignancy.

7. Pearly bodies and large flat squamous cells with small nuclei are not cancer. Cancer is regenerative or undifferentiated cells.

8. The 256 cases in this series of squamous-cell epithelioma of the skin represent 12.8 per cent. of 2000 cases of general epithelioma observed in the Mayo Clinic from November 1, 1904, to July 22, 1915.

9. Squamous-cell epithelioma of the skin occurred more often in males than in females; the proportion is 4 to 1. It occurred in patients past middle life; their average age was fifty-nine and thirty-four hundredths years.

10. Squamous-cell epithelioma occurred most often in farmers; they represented 53.96 per cent. of the cases in males.

11. The site of the cancer was preceded by a mole, wart, pimple, scab, ulcer, leucoplakia, crack, wen, blister, or lump in 51.17 per cent. of the cases.

12. There was a history of injury in 23.82 per cent. of the cases; burns represented 24.59 per cent. of the injuries, and X-ray burns represented 20 per cent. of the burns.

13. The average duration of the lesion was 4.8 years and the average greatest diameter 3.85 cm.

14. Seventy-eight and four hundredths per cent. of all the lesions occurred above the clavicle.

15. Twenty-eight and twelve hundredths per cent. of the patients were treated with acid, paste or plaster, and so forth, before they entered the clinic.

16. Twenty-six and ninety-five hundredths per cent. of the patients were operated on before they entered the clinic.

17. Ninety-two and eighteen hundredths per cent. of the patients were operated on at the clinic.

18. Regional lymph-nodes or salivary glands were not removed in 77.96 per cent.

19. Of the 22.03 per cent. of the cases in which the regional lymph-nodes or salivary glands were removed, metastasis was demonstrated in 61.53 per cent.

20. The cervical lymph-nodes were involved in 31.25 per cent., sub-maxillary lymph-nodes in 28.12 per cent., the parotid lymph-nodes in 25 per cent., the parotid salivary gland in 25 per cent., and the axillary and inguinal lymph-nodes each in 15.62 per cent.

21. In a classification of the epitheliomas according to cellular activity, graded 1 to 4, Grade 1 represents 8.20 per cent.; Grade 2, 69.53 per cent.; Grade 3, 17.18 per cent., and Grade 4, 5.07 per cent.

22. The average duration of the lesion according to grade was longest



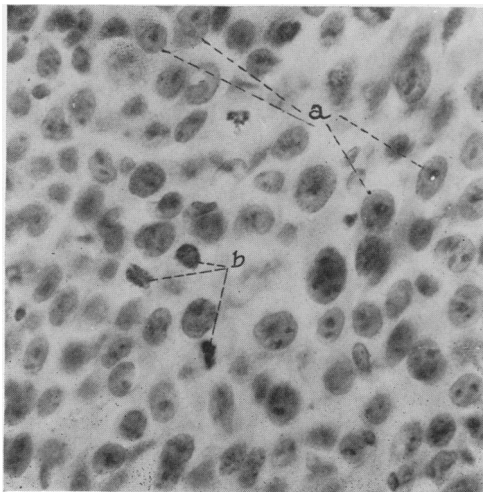


FIG. 13 (Case A38629).—Very malignant area of a Grade 3 epithelioma; *a*, "one-eyed cells"; *b*, mitotic figures. In some areas in this neoplasm the cells showed a tendency to differentiate.

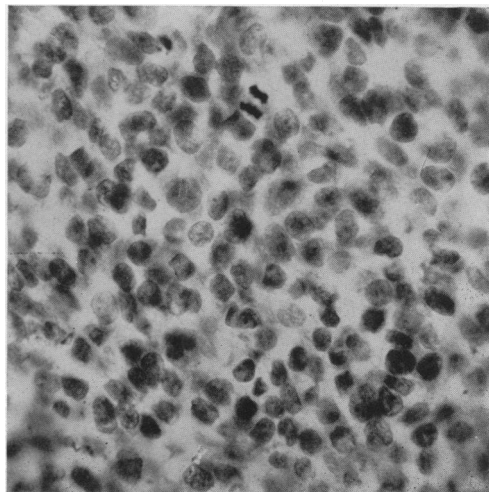
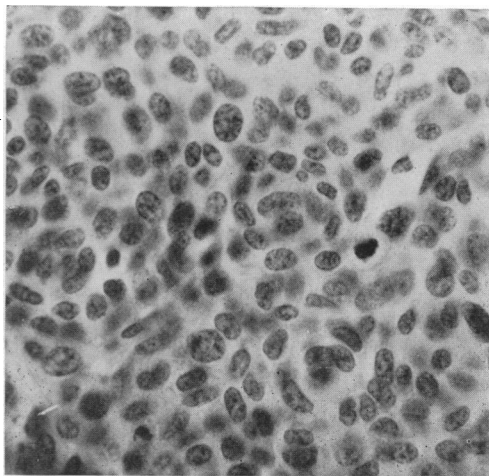
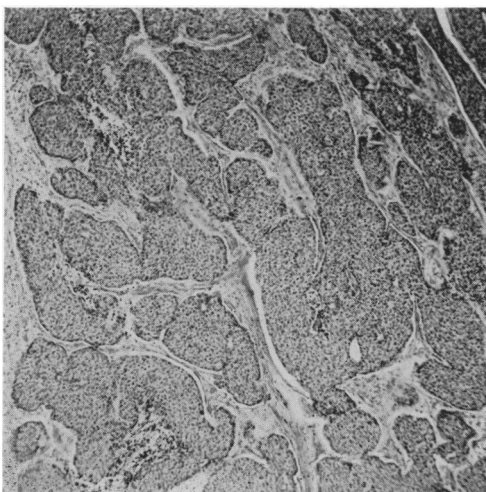


FIG. 16 (Case A118133).—High-power magnification of Grade 4 epithelioma similar to epithelioma shown in Fig. 15.



FIGS. 14 AND 15 (Case A90864).—Low-power and high-power magnification of a Grade 4 epithelioma, showing irregular pale-staining cells; very few one-eyed cells.

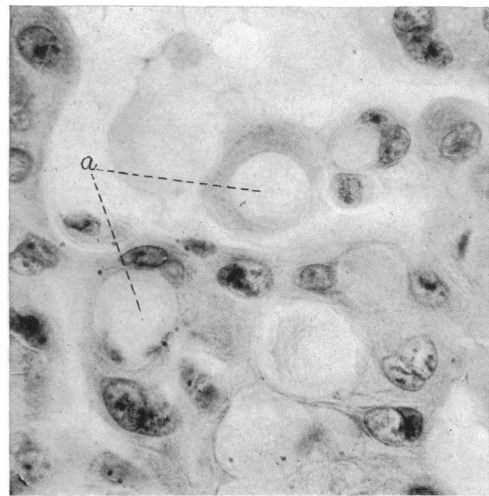
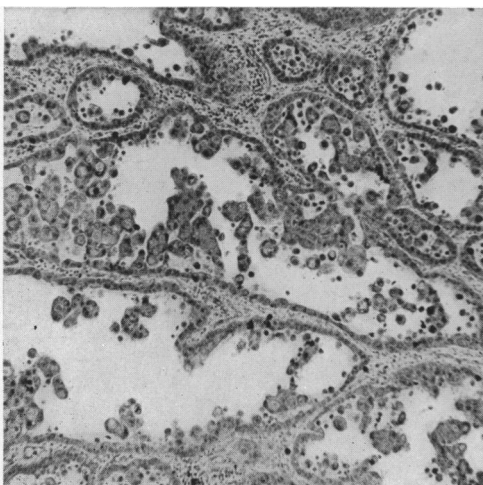


FIG. 17 (Case A56882).—Squamous-cell epithelioma of the skin, showing a number of cells undergoing keratinization (low power).

FIG. 18 (Case A56882).—High-power magnification of section shown in Fig. 17; *a*, cells becoming keratinized.



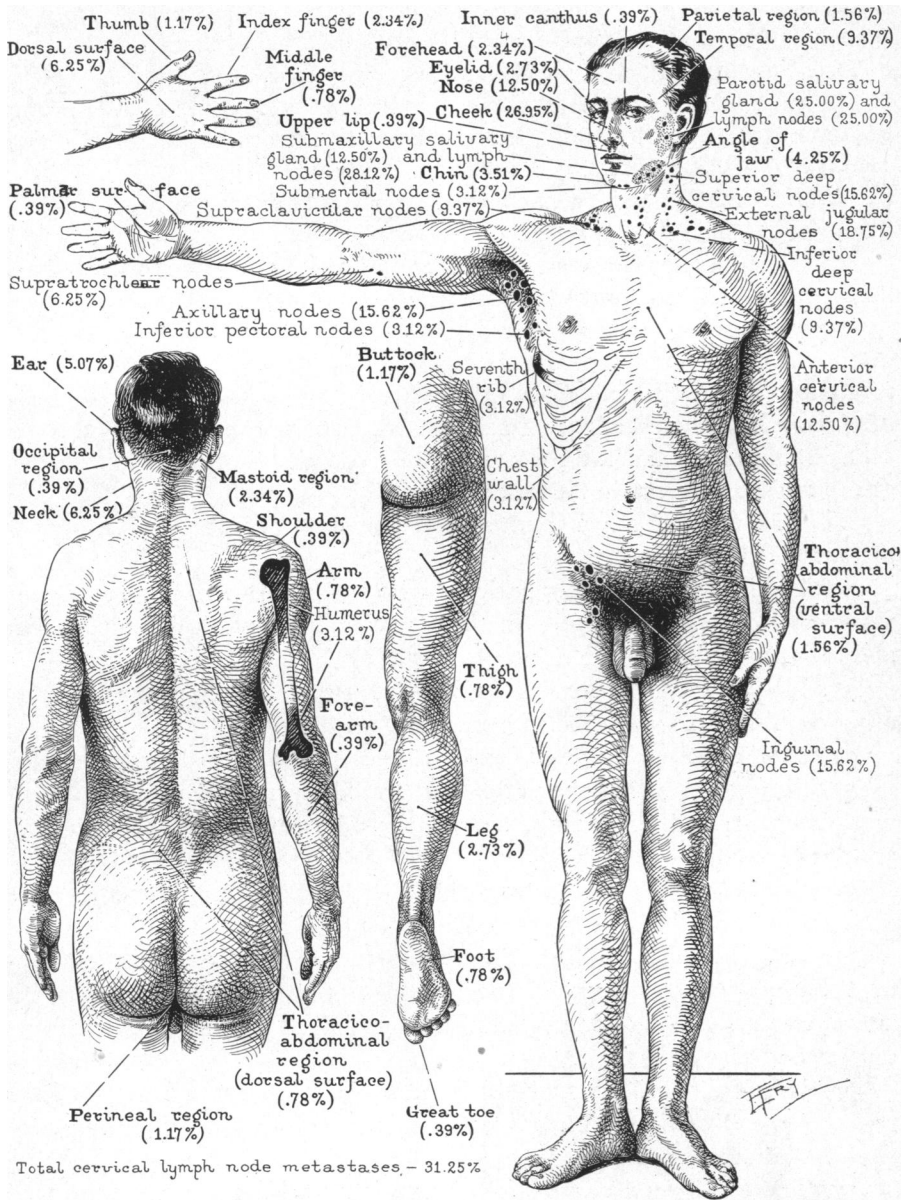


FIG. 19.—Percentages of points of origin in squamous-cell epithelioma of the skin and percentages of location of metastasis (location, dark letters; metastasis light letters).

in Grade 2, five and thirty-six hundredths years, and shortest in Grade 3, three and two hundredths years.

23. The average size of the lesion according to grade was largest in Grade 4, 5.4 cm., and smallest in Grade 1, 2.09 cm.

24. Fifty-one and seventy-seven hundredths per cent. of the patients operated on and traced are dead and 48.22 per cent. are alive.

25. Eighty-two and thirty-five hundredths per cent. of the living patients report good results, having been free from the disease on an average of seven and forty-four hundredths years.

26. Information received concerning the patients operated on who died, shows that 65.51 per cent. died of epithelioma.

27. Three (1.27 per cent.) of the patients who were operated on died before being dismissed from the Clinic; the actual operative mortality was 0.42 per cent.

28. Patients who were treated with pastes, plasters, and so forth, before entering the Clinic did not get such good total good results as those who were not so treated, 57.14 per cent. in the former group and 61.11 per cent. in the latter; the total poor results were 40 per cent. in the former group and 30 per cent. in the latter.

29. Ten and fifty-two hundredths per cent. of the patients with metastasis are living.

30. One of the two living patients who had metastasis reports a good result and one a fair result. In these patients the parotid lymph-nodes and salivary gland on one side only were involved.

31. No patient with cervical lymph-nodes or more than one group of any lymph-nodes involved has been reported living.

32. All the patients reported dead who had metastasis died of epithelioma.

33. Sixty per cent. of the patients operated on in whom no metastasis was demonstrated are living, all with good results, and 40 per cent. are dead.

34. Sixty-six and sixty-six hundredths per cent. of the patients reported dead who did not have metastasis died of epithelioma.

35. Fifty-three and fifteen hundredths per cent. of the patients operated on in whom no regional lymph-nodes or salivary glands were removed are living and 46.84 per cent. are dead; 81.35 per cent. of the living report good results

36. Fifty-four and seventy-six hundredths per cent. of the patients reported dead in whom no regional lymph-nodes or salivary glands were removed, died of epithelioma.

37. The total good results for the patients with metastasis are 6.66 per cent.; for those without metastasis, 77.77 per cent.; and for those in whom no regional lymph-nodes or salivary glands were removed, 66.33 per cent.

38. The total poor results without regard to grade for the patients with metastasis are 86.66 per cent.; for those without metastasis, 22.22 per

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cent.; and for those in whom no regional lymph-nodes or salivary glands were removed, 25.74 per cent.

39. The average duration of the lesion in the patients with metastasis was two and sixty-seven hundredths years; in those without metastasis, five and three hundredths years; and in those in whom no regional lymph-nodes or salivary glands were removed, four and seventy-eight hundredths years.

40. The average size of the lesion in the patients with metastasis was 6.3 cm.; in those without metastasis, 4.15 cm.; and in those in whom no regional lymph-nodes or salivary glands were removed, 3.08 cm.

41. The known causes of deaths from epithelioma were: Grade 1, 0; Grade 2, 61.29 per cent.; Grade 3, 85.71 per cent.; and Grade 4, 100 per cent.

42. The total good results for Grade 1 are 92.85 per cent.; Grade 2, 65.43 per cent.; Grade 3, 41.66 per cent.; and Grade 4, 0.

43. The total poor results for Grade 1 are 0; Grade 2, 25.92 per cent.; Grade 3, 54.16 per cent.; and Grade 4, 100 per cent.

TABLE I

*Squamous-cell Epithelioma of the Skin: Two Hundred and Fifty-six Cases (12.8 Per Cent. of Two Thousand Cases of General Epithelioma) from November 1, 1904, to July 22, 1915, Mayo Clinic.*

	No.	Per Cent.
Patients .....	256	
Males .....	205	80.078
Females .....	51	19.921
Age:		
Youngest patient .....		25.
Oldest patient .....		88.
Average age of patients .....		59.34
Occupation (males):		
Farmer .....	102	53.96*
Laborer .....	21	11.11
Merchant .....	11	5.81
Railroad employee .....	8	4.23
Physician: .....	6	3.17
Agent .....	4	2.11
Other occupations, 22 each under 2 per cent.....	37	19.57
Family history of malignancy .....	31	12.10
Previous lesion at site of cancer:		
Mole, wart, pimple, scab, ulcer, leucoplakia, crack, wen, blister, lump, etc.	131	51.17
History of injury .....	61	23.82
Burns, proportion of total injuries .....	15	24.59
X-ray burns, proportion of total burns .....	3	20.00
Average duration of lesion .....		4.8 years
Longest duration of lesion .....		35.0 years
Shortest duration of lesion .....		0.057 year
Greatest diameter .....		30.00 cm.
Average greatest diameter .....		3.854 cm.

\*A large proportion of patients coming to the Mayo Clinic are from rural communities.

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TABLE II

*Location of the Lesion (Fig. 19)*

	Cases	Per Cent.
Single lesion .....	247	96.48
Multiple lesions .....	9	3.51
Cheek .....	69	26.95
Nose .....	32	12.50
Temporal region .....	24	9.37
Neck .....	16	6.25
Hand (dorsal surface) .....	16	6.25
Ear .....	13	5.07
Angle of jaw .....	11	4.25
Chin .....	9	3.51
Eyelid .....	7	2.73
Leg .....	7	2.73
Forehead .....	6	2.34
Mastoid region .....	6	2.34
Index finger .....	6	2.34
Thoracico-abdominal region (ventral surface) .....	4	1.56
Parietal region .....	4	1.56
Thumb .....	3	1.17
Buttock .....	3	1.17
Perineal region .....	3	1.17
Thoracico-abdominal region (dorsal surface) .....	2	0.78
Arm .....	2	0.78
Middle finger .....	2	0.78
Thigh .....	2	0.78
Foot .....	2	0.78
Inner canthus .....	1	0.39
Occipital region .....	1	0.39
Upper lip (near nose) .....	1	0.39
Shoulder .....	1	0.39
Forearm .....	1	0.39
Hand (palmer surface) .....	1	0.39
Great toe .....	1	0.39

TABLE III

*Treatment Elsewhere of Squamous-cell Epithelioma of the Skin*

Non-surgical:

	No.	Per Cent.
One or more treatments with acids (carbolic, chromic, hydrochloric and nitric), alum (burnt), carbon dioxide, electricity, paste, potassium iodide, radium, Röntgen-ray (proportion of total non-operative methods of treatment, 50 per cent.) scarlet red and silver nitrate . . .	72	28.12
Surgical:		
One or more operations .....	69	26.95
Surgical and non-surgical:		
Operations without treatment with acids, alum, carbon dioxide, etc. . .	50	19.53
Treatment with acids, alum, carbon dioxide, etc., without operation . . .	53	20.70
Operation and treatment with acids, alum, carbon dioxide, etc. . . . .	103	40.23

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TABLE IV

*Patients Operated on at the Mayo Clinic*

Number of patients .....	236	(92.18 per cent. of 256)
Excision with knife immediately followed by cautery (one operation) .....	52	(22.03 per cent. of 236)
Excision with knife (one operation) .....	46	(19.49 per cent. of 236)
Block dissection of neck (unilateral) either alone or combined with other operations or methods of treatment before, at the same time, or after the block dissection was performed .....	9	(3.81 per cent. of 236)
Cautery (one operation) .....	8	(3.38 per cent. of 236)
Excision with cautery (one operation) .....	7	(2.96 per cent. of 236)
Excision with knife immediately followed by cautery (one operation) and later by skin graft (one operation) .....	7	(2.96 per cent. of 236)
Amputation of one or more fingers or of thumb and removal of regional lymph-nodes at the time of amputation or after amputation and either associated with or not associated with other operative or non-operative treatment before, at the time of, or after amputation..	6	(2.54 per cent. of 236)
Amputation of thigh or leg with or without removal of regional lymph-nodes and either associated or not associated with other operative or non-operative treatment before, at the time of, or after amputation .....	5	(2.11 per cent. of 236)
Amputation of arm, forearm, or hand with removal of regional lymph-nodes before or at the time of amputation, and either associated or not associated with other operative or non-operative treatment before, at the time of, or after the amputation .....	5	(2.11 per cent. of 236)
Excision with knife immediately followed by cautery (one operation) and followed later by cautery (one operation) .....	4	(1.69 per cent. of 236)
Cautery (two operations) .....	4	(1.69 per cent. of 236)
Block dissection of neck (bilateral) (two operations) accompanied by a complete evisceration of the left eye, excision of eyelids, and one supraclavicular lymph-node preceded by three excisions with knife immediately followed by cautery .....	1	(0.423 per cent. of 236)
Miscellaneous (various combinations of operations, radium and Röntgen-rays) .....	82	(34.74 per cent. of 236)
Inoperable .....	16	(6.25 per cent. of 236)
Operation refused after diagnosis had been made .....	4	(1.56 per cent. of 236)
Cases in which no lymph-nodes or salivary glands were removed .....	184	(77.96 per cent. of 236)
Cases in which lymph-nodes or salivary glands were removed (one or more groups) .....	52	(22.03 per cent. of 236)

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TABLE V

*Lymph-nodes and Salivary Glands Removed in Fifty-two Cases*

	Cases	Per Cent.
Submaxillary lymph-nodes .....	23	44.23
Submaxillary salivary glands .....	23	44.23
External jugular-nodes .....	20	38.46
Superior deep cervical-nodes .....	15	28.84
Anterior cervical-nodes .....	12	23.07
Inferior deep cervical-nodes .....	12	23.07
Cervical lymph-nodes .....	21	40.38
Parotid salivary gland .....	10	19.21
Parotid lymph-nodes .....	9	17.30
Submental-nodes .....	9	17.30
Axillary-nodes .....	9	17.30
Inguinal-nodes .....	6	11.53
Supratrochlear-nodes .....	3	5.76
Supraclavicular lymph-nodes .....	3	5.76
Chest wall .....	1	1.92

TABLE VI

*Pathologic Findings in Fifty-two Cases in which Lymph-nodes and Salivary Glands Were Removed*

	Cases	Per Cent
No metastasis .....	20	38.46
Metastasis .....	32	61.53
Inguinal lymph-nodes alone (one side) .....	5	15.62
Axillary lymph-nodes alone (one side) .....	3	9.37
Parotid salivary gland and lymph-nodes (one side) .....	5	15.62
Submaxillary lymph-nodes alone (one side) .....	2	6.25
Submaxillary salivary gland and lymph-nodes (one side) .....	2	6.25
Right and left external jugular, submental, left submaxillary and supraclavicular lymph-nodes .....	1	3.12
External jugular, anterior cervical, superior and inferior deep cervical lymph-nodes (one side) .....	1	3.12
Supratrochlear and axillary lymph-nodes, lower and upper end of humerus, chest wall including seventh rib, axillary line (one side).	1	3.12
Miscellaneous (submaxillary lymph-nodes and salivary glands, parotid lymph-nodes and salivary glands, cervical, supraclavicular, supra-trochlear, axillary, and inferior pectoral lymph-nodes, alone or in various combinations (one side) .....	12	37.50



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TABLE VII

*Metastasis in Thirty-two Cases (Fig. 19)*

	Cases	Per Cent.
Submaxillary lymph-nodes .....	9	28.12
Parotid lymph-nodes .....	8	25.00
Parotid salivary gland .....	8	25.00
External jugular lymph-nodes .....	6	18.75
Superior deep cervical lymph-nodes .....	5	15.62
Axillary lymph-nodes .....	5	15.62
Inguinal lymph-nodes .....	5	15.62
Submaxillary salivary gland .....	4	12.50
Anterior cervical lymph-nodes .....	4	12.50
Inferior deep cervical lymph-nodes .....	3	9.37
Supraclavicular lymph-nodes .....	3	9.37
Supratrochlear lymph-nodes .....	2	6.25
Submental lymph-nodes .....	1	3.12
Inferior pectoral lymph-nodes .....	1	3.12
Chest wall .....	1	3.12
Lower and upper ends of humerus .....	1	3.12
Seventh rib, axillary line .....	1	3.12
Cervical lymph-node involvement .....	10	31.25

TABLE VIII

*Grades in 256 Cases on a Basis of 1 to 4 According to Cellular Activity*

	Cases	Per Cent.
Grade 1 .....	21	8.20
Grade 2 .....	178	69.53
Grade 3 .....	44	17.18
Grade 4 .....	13	5.07

*Duration and Size of Epithelioma*

	Grade 1 Years	Grade 2 Years	Grade 3 Years	Grade 4 Years
Longest duration .....	20.00	35.00	10.00	20.00
Shortest duration .....	0.08	0.05	0.16	0.10
Average duration .....	4.76	5.36	3.02	3.30
	Cm.	Cm.	Cm.	Cm.
Largest size .....	4.30	30.00	14.00	15.00
Smallest size .....	0.50	0.30	1.20	0.60
Average size .....	2.09	3.70	4.61	5.40
	Grade 1	Grade 2	Grade 3	Grade 4
Operable epithelioma .....	21	164	39	12
Inoperable epithelioma .....	0	11	4	1
	Grade 1	Grade 2	Grade 3	Grade 4
Operation refused after diagnosis had been made .....	0	3	1	0

TABLE IX

*General Ultimate Results*

Patients traced (operable, 141; inoperable, 5; refused operation, 1) .....	147	(57.42 per cent. of 256)
Patients operated on .....	141	
Patients living .....	68	(48.22 per cent.)
Good result .....	56	(82.35 per cent. of 68)
Fair result .....	9	(12.23 per cent. of 68)
Poor result .....	3	(4.41 per cent. of 68)

*Duration of Life Since Last or Only Operation*

	Good result Years	Fair result Years	Poor result Years
Longest .....	13.16	12.05	5.23
Shortest .....	4.31	5.50	0.15
Average .....	7.44	8.78	3.28
Patients dead .....	73	(51.77 per cent.)	

*Deaths*

Patients .....	79	(53.74 per cent. of 147)
Patients with operable epithelioma .....	73	(92.40 per cent. of 79)
Patients with inoperable epithelioma .....	5	(6.32 per cent. of 79)
Patients who refused operation after diagnosis had been made .....	1	(1.26 per cent. of 79)

*Cause of Death of Patients Operated on: Data from Relative, Home Physician, or Pathologic Records of the Clinic*

	No.	Per Cent.
Known cause .....	58	
Epithelioma .....	38	65.51
Old age .....	4	6.89
Heart disease .....	4	6.89
Paralysis .....	3	5.17
Pneumonia .....	2	3.44
Arteriosclerosis .....	1	1.72
Acute gastritis .....	1	1.72
Carcinoma of pancreas .....	1	1.72
General infection .....	1	1.72
Carcinoma of prostate and pneumonia .....	1	1.72
Influenza .....	1	1.72
Tuberculosis .....	1	1.72
Unknown .....	15	

*Cause of Death of Patients Operated on Who Died at the Clinic*

Epithelioma and pneumonia (1.28 years after operation) ..	1	
Carcinoma of prostate and pneumonia (0.47 years after operation) .....	1	
Epithelioma and shock (0.027 year after operation).....	1	
Total .....	3	(1.27 per cent. of 236)
Actual operative mortality .....	1	(0.42 per cent. of 236)

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TABLE X  
*Patients Operated on, Treated with Pastes, Plasters, Acids, Etc., Before Entering the Clinic*

Information received	Grade				Total Results
	Grade 1	Grade 2	Grade 3	Grade 4	
Patients living					36 (54.54 per cent. of 66)
Good result	2 (10.52 per cent. of 19)	14 (73.68 per cent. of 19)	3 (15.78 per cent. of 19)		21 (58.33 per cent. of 36)
Fair result		1 (100 per cent. of 1)			1 (100 per cent. of 1)
Poor result					
Patients dead					15 (41.66 per cent. of 36)
Good result		1 (100 per cent. of 1)			1 (100 per cent. of 1)
Poor result		9 (69.23 per cent. of 13)	3 (23.07 per cent. of 13)	1 (7.69 per cent. of 13)	13 (36.11 per cent. of 36)
Cause unknown		1			1 (2.78 per cent. of 36)
<i>Total Results</i>					
Good (patients recovered from epithelioma and are living or recovered from epithelioma and died of other cause)					20 (57.14 per cent. of 35)
Fair (patient living with slight recurrence)					1 (2.85 per cent. of 35)
Poor (patients living with no improvement or died of epithelioma)					14 (40.00 per cent. of 35)
No information received					30 (85.71 per cent. of 35)

TABLE XI  
*Patients Operated on, Not Treated with Pastes, Plasters, Acids, Etc., Before Entering the Clinic*

Information received	Grade				Total Results
	Grade 1	Grade 2	Grade 3	Grade 4	
Patients living					46 (44.23 per cent. of 104)
Good result	4 (11.11 per cent. of 36)	27 (75 per cent. of 36)	5 (13.88 per cent. of 36)		36 (34.62 per cent. of 104)
Fair result	2 (25.00 per cent. of 8)	5 (62.50 per cent. of 8)	1 (12.50 per cent. of 8)		8 (7.69 per cent. of 104)
Poor result		2 (100 per cent. of 2)			2 (1.92 per cent. of 104)
Patients dead					58 (55.76 per cent. of 104)
Good result	6 (31.57 per cent. of 19)	11 (57.89 per cent. of 19)	2 (10.52 per cent. of 19)		19 (18.27 per cent. of 104)
Poor result		11 (44.00 per cent. of 25)	8 (32.00 per cent. of 25)	6 (24.00 per cent. of 25)	25 (24.04 per cent. of 104)
Cause unknown	2	10	2		14 (13.46 per cent. of 104)
<i>Total Results</i>					
Good (patients recovered from epithelioma and are living, or recovered from epithelioma and died of other causes)					55 (51.92 per cent. of 106)
Fair (patients living with slight recurrence)					8 (7.55 per cent. of 106)
Poor (patients living with no improvement or died of epithelioma)					27 (25.52 per cent. of 106)
No information received					66 (61.98 per cent. of 106)

TABLE XII  
*Patients with Metastasis Operated on with Removal of Regional Lymph-nodes or Salivary Glands*

Information received.....	Grade 2	Grade 3	Grade 4
Patients living.....			
Good result *.....	1 (100 per cent. of 1)		19 (59.37 per cent. of 32)
Fair result *.....		1 (100 per cent. of 1)	2 (10.52 per cent. of 19)
Patients dead.....			
Poor result.....	4 (30.76 per cent. of 13)		17 (89.47 per cent. of 19)
Cause unknown.....	2	5 (38.46 per cent. of 13)	
Good (patient recovered from epithelioma).....			
Fair (patient living with slight recurrence).....			
Poor (patients died of epithelioma).....			
Epithelioma.....			
No information received.....			13 (100 per cent. of 13)
* In the patient who reported a good result and in the one who reported a fair result, the parotid lymph-nodes and salivary glands on only one side were involved.			13 (40.62 per cent. of 32)

TABLE XIII  
*Patients Without Metastasis Operated on With Removal of Regional Lymph-nodes or Salivary Glands*

Information received.....	Grade 1	Grade 2	Grade 3
Patients living.....			
Good result.....	2 (33.33 per cent. of 6)	3 (50.00 per cent. of 6)	1 (16.66 per cent. of 6)
Patients dead.....			
Good result.....	1 (100 per cent. of 1)		
Poor result.....	2 (100 per cent. of 2)		
Cause unknown.....			
Good (patients recovered from epithelioma and are living or recovered from epithelioma and died of other cause).....			
Poor (patients died of epithelioma).....			
Epithelioma.....			
Heart disease.....			
No information received.....			
Epithelioma.....			
Heart disease.....			
No information received.....			

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TABLE XIV  
Patients Operated on Without Removal of Regional Lymph-nodes or Salivary Glands

	Grade 1	Grade 2	Grade 3	Grade 4	
Information received.....					111 (60 per cent. of 185)
Patients living.....					59 (33.15 per cent. of 111)
Good result.....	5 (10.41 per cent. of 48)	35 (75.00 per cent. of 48)	7 (14.58 per cent. of 48)		
Fair result.....	1 (12.50 per cent. of 8)	7 (87.50 per cent. of 8)			
Poor result.....		2 (66.66 per cent. of 3)	1 (33.33 per cent. of 3)		
Patients dead.....					52 (46.84 per cent. of 111)
Good result.....	7 (36.84 per cent. of 19)	10 (52.63 per cent. of 19)	2 (10.52 per cent. of 19)		
Poor result.....		14 (60.86 per cent. of 23)	7 (30.43 per cent. of 23)	2 (8.69 per cent. of 23)	
Cause unknown.....		2	8		
<i>Total Results</i>					
Good (patients recovered from epithelioma and are living or recovered from epithelioma and died of other cause)					67 (66.33 per cent. of 101)
Fair (patients living with slight recurrence).....					8 (7.92 per cent. of 101)
Poor (patients living with no improvement or died of epithelioma).....					26 (25.74 per cent. of 101)
<i>Cause of Death</i>					
Epithelioma.....					23 (54.76 per cent. of 42)
Old age.....					4 (9.52 per cent. of 42)
Paralysis.....					3 (7.14 per cent. of 42)
Heart disease.....					3 (7.14 per cent. of 42)
Pneumonia.....					2 (4.76 per cent. of 42)
Acute gastritis.....					1 (2.38 per cent. of 42)
Arteriosclerosis.....					1 (2.38 per cent. of 42)
Carcinoma of pancreas.....					1 (2.38 per cent. of 42)
Carcinoma of prostate and pneumonia.....					1 (2.38 per cent. of 42)
General infection.....					1 (2.38 per cent. of 42)
Influenza.....					1 (2.38 per cent. of 42)
Tuberculosis.....					1 (2.38 per cent. of 42)
No information received.....					74 (40.00 per cent. of 185)

TABLE XV  
*Patients With Metastasis and Patients Without Metastasis Operated on and Patients in Whom no Regional Lymph-nodes or Salivary Glands Were Removed*

	Grade 1	Grade 2	Grade 3	Grade 4
With metastasis.....	11 (34.2 per cent. of 32)	12 (37.5 per cent. of 32)	9 (28.12 per cent. of 32)	
Without metastasis.....	2 (10 per cent. of 20)	4 (20.00 per cent. of 20)		
Without removal of regional lymph-nodes or salivary glands.....	19 (10.32 per cent. of 184)	139 (75.64 per cent. of 184)	23 (12.5 per cent. of 184)	3 ( 1.63 per cent. of 184)
<i>Duration of Lesion Before Patient's Examination at the Clinic</i>				
With metastasis.....	Longest, 15 years	Shortest, 0.10 year	Average, 2.67 years	
Without metastasis.....	Longest, 20 years	Shortest, 0.8 year	Average, 5.3 years	
Without removal of regional lymph-nodes or salivary glands.....	Longest, 35 years	Shortest, 0.05 year	Average, 4.78 years	
<i>Size of Lesion at the Time of Patient's Examination at the Clinic</i>				
With metastasis.....	Largest, 30 cm.	Smallest, 1.5 cm.	Average, 6.3 cm.	
Without metastasis.....	Largest, 15 cm.	Smallest, 1.5 cm.	Average, 4.15 cm.	
Without removal of regional lymph-nodes or salivary glands.....	Largest, 30 cm.	Smallest, 0.3 cm.	Average, 3.08 cm.	

TABLE XVI  
*Duration of Life After Operation of Patients With Metastasis*

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Average of all grades
Information received.....						14 (43.75 per cent. of 32)
Patients living.....						
Good result.....	1	1				2
Fair result.....	1					4.8 years
Patients dead.....						
Poor result.....	4		3			11.8 years
						12
Longest.....		Years	Years	Years	Years	Average of all grades
Shortest.....		1.28	0.50	2.96	2.96	2.96
Average.....		0.15	0.31	0.027	0.027	0.027
No information received.....		0.68	0.41	1.58	1.58	0.98
						18 (46.25 per cent. of 32)



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TABLE XVIII  
*Duration of Life After Operation of Twenty Patients Without Metastasis*

	Grade 1	Grade 2	Grade 3	Grade 4		Average of all grades
Information received.....					8 (40.00 per cent. of 20)	
Patients living.....	2	3	1		6	7.29
Good result.....	2	3	1		6	7.29
Longest.....	7.26	7.97	8.90			8.90
Shortest.....	6.01	6.33				6.01
Average.....	6.63	7.18				7.29
Patients dead.....					2	
Good result.....					1	
Poor result.....					1	
Longest.....						1.33
Shortest.....						0.37
Average.....						0.85
No information received.....					12 (60.00 per cent. of 20)	

TABLE XVIII  
Duration of Life of Patients Operated on Without Removal of Regional Lymph-nodes or Salivary Glands

Patients living.....	Grade 1	Grade 2	Grade 3	49
Good result.....	5	37	7	
	Years	Years	Years	
Longest.....	6.49	13.14	10.88	
Shortest.....	4.93	4.31	6.04	
Average.....	5.70	7.74	7.59	
Fair results.....	1	7		
	Years	Years	Years	
Longest.....	1.59	12.50		
Shortest.....		5.50		
Average.....		8.38		
Poor result.....		2	1	
	Years	Years	Years	
Longest.....		5.23	0.15	
Shortest.....		4.46		
Average.....		4.84		
<i>Duration of Life of Patients of All Grades</i>				
Patients living:	Good result	Fair result	Poor result	
Longest.....	13.14 years	12.50 years	5.23 years	
Shortest.....	4.31 years	1.59 years	0.15 year	
Average.....	7.51 years	8.40 years	3.73 years	
Patients dead (not of epithelioma).....	6 years	10 years	2 years	
Good result				
Longest.....	8.16 years	9.02 years	6.40 years	
Shortest.....	0.43 year	0.26 year	5.34 years	
Average.....	3.96 years	3.55 years	5.87 years	
Poor result.....	13 years	7 years	2 years	
Longest.....	3.61 years	1.95 years	0.98 year	
Shortest.....	0.26 year	0.05 year	0.58 year	
Average.....	1.45 years	0.93 year	0.78 year	
<i>Duration of Life After Operation of Patients of All Grades</i>				
	Good result	Poor result	Average of all grades	
	Years	Years	Years	
Longest.....	9.02	3.61	9.02	
Shortest.....	0.26	0.05	0.05	
Average.....	3.92	1.22	2.45	

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TABLE XIX  
Results Following Operations

	Grade 1	Grade 2	Grade 3	Grade 4
Information received.....	16 (76.19 per cent. of 21)	92 (56.09 per cent. of 164)	26 (66.66 per cent. of 39)	7 (58.33 per cent. of 12)
Patients living.....	8 (50.00 per cent. of 16)	50 (54.34 per cent. of 92)	10 (38.46 per cent. of 26)	
Good result.....	7 (87.50 per cent. of 8)	41 (82.00 per cent. of 50)	8 (80.00 per cent. of 10)	
Fair result.....	1 (12.50 per cent. of 8)	7 (14.00 per cent. of 50)	1 (10.00 per cent. of 10)	
Poor result.....		2 (4.00 per cent. of 50)	1 (10.00 per cent. of 10)	
Patients dead.....	8 (50.00 per cent. of 16)	42 (45.65 per cent. of 92)	16 (61.53 per cent. of 26)	7 (100 per cent. of 7)
Good result.....	6 (100 per cent. of 6)	12 (38.70 per cent. of 31)	2 (14.28 per cent. of 14)	
Poor result.....		19 (61.29 per cent. of 31)	12 (85.71 per cent. of 14)	7 (100 per cent. of 7)
Not stated.....	2	11	2	
Total good result (patients re-covered from epithelioma and are living or recovered from epithelioma and died of other cause) 13 (92.85 per cent. of 15)		53 (65.43 per cent. of 81)	10 (41.66 per cent. of 24)	
Total fair result (patients living with slight recurrence).....	1 (7.14 per cent. of 14)	7 (8.64 per cent. of 81)	1 (4.16 per cent. of 24)	
Total poor result (patients living with no improvement or died of epithelioma).....		21 (25.92 per cent. of 81)	13 (54.16 per cent. of 24)	7 (100 per cent. of 7)
Total result not stated.....	2	11	2	

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