SQUAMOUS-CELL EPITHELIOMA OF THE LIP

A STUDY OF FIVE HUNDRED AND THIRTY-SEVEN CASES *

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Of all the malignant neoplasms with which man is afflicted, few cause more concern and inconvenience than that of epithelioma of the lip. In the past, pathologists have been content to classify cancer of the lip as cancer, without any distinction as to the degree of malignancy. It is a well established fact that some cancers of the lip are fatal to patients and others are not. There must be a reason for this. One theory is that some persons are resistant to cancer, and this seems to be borne out in a certain percentage of cases.

Undoubtedly, a large proportion of cancer cells are destroyed by the defense cells of the body; of these, the fibrous connective tissue cell is the most important, since it cuts off nourishment from the cancer cells.

The endothelial leukocyte and lymphocyte evidently also play an important rôle in the destruction of cancer cells, for practically always they may be seen in the neighborhood of a cancerous growth. Foreign body giant cells that are most probably formed from the endothelial leukocytes are not infrequently found lying adjacent to cancer cells.

The most important factor in squamous-cell epithelioma of the lip seems to be the degree of cellular activity. The cells of some epitheliomas of the lip show a marked tendency to differentiate, that is, to produce a growth similar to the normal; the pearly body is an example. The pearly body corresponds to the horny layer of the epidermis. In other squamous-cell epitheliomas there is no differentiation whatever. In the large majority of growths whose cells show no tendency to differentiate, or at least very little, there are many mitotic figures.

In studying these epitheliomas, therefore, it occurred to me that they should be graded according to differentiation and mitosis, special stress being laid on the former. The grading was made on a basis of 1 to 4, and absolutely independent of the clinical history. If an 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; if the differentiated and undifferentiated epithelium are about equal, it is graded 2; if the undifferentiated epithelium forms about three fourths and the differentiated about one fourth of the growth, it is graded 3; if there is no tendency of the cells to differentiate, it is graded 4. Of course 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.

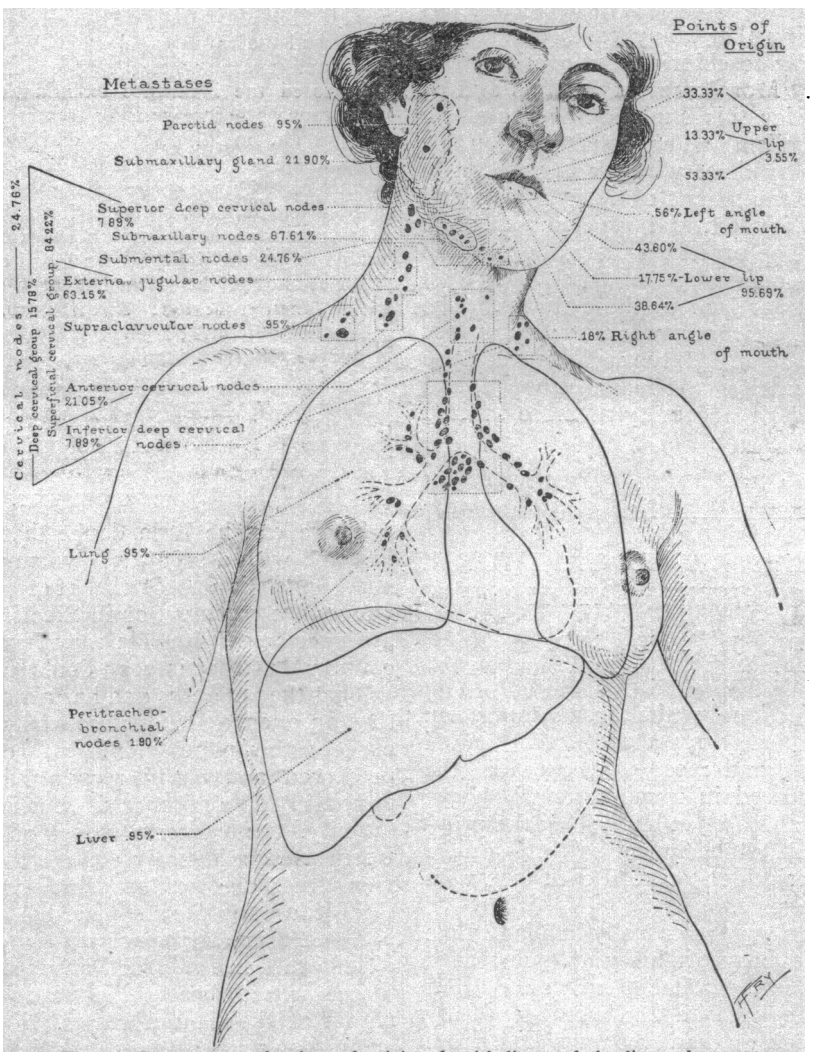

Fig. 1.—Percentages of points of origin of epithelioma of the lip, and percentages of location of metastasis.

Some epitheliomas of the lip are very active and from the start show little or no tendency to differentiate; some grow more malignant with time, and others increase in malignancy and then retrogress. Unquestionably an epithelioma of a low grade of malignancy is made more malignant by irritation with chemicals such as hydrochloric or nitric acid, silver nitrate or arsenic paste.

Chronic ulcers of the lip, like chronic ulcers of the stomach, should be examined very closely for cancer, provided syphilis has been eliminated. MacCarty [1] has demonstrated early cancer in the epithelium at or near the edge of gastric ulcers; practically the same process is found in early cancer or ulcer of the lip. In the lip the cancer starts in the stratum germinativum of the epithelium at or near the border of the ulcer. Not all cancers of the lip are preceded by ulcers, but the majority are.

I shall present the facts in statistical form and make the deductions, not from one, but from various standpoints: (1) the duration and size of the lesion; (2) the

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1. MacCarty, W. C.: Pathology and Clinical Significance of Gastric Ulcer: From a Study of Material from Two Hundred and Sixteen Partial Gastrectomies for Ulcer, Ulcer and Carcinoma, and Carcinoma. Surg., Gynec. & Obst. **10**: 449-462, 1910.

use or nonuse of tobacco; (3) the use or nonuse of caustics, pastes or plasters, etc., before treatment at the clinic; (4) metastasis or no metastasis; (5) cellular activity, and (6) other points of general interest.

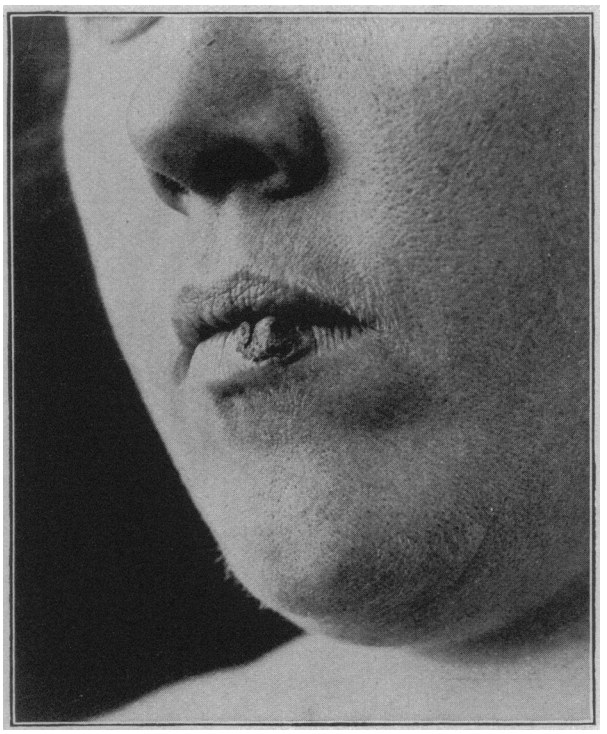

Fig. 2 (a 188878).—Typical elevated or wartlike epithelioma of the lip.

CONCLUSIONS

1. The 537 cases of squamous-cell epithelioma of the lip in this series represent 26.85 per cent. of 2,000 cases of general epithelioma.

2. Squamous-cell epithelioma of the lip occurs more often in males than in females; the proportion is 49: 1.

TABLE 1.—SQUAMOUS-CELL EPITHELIOMA OF THE LIP: FIVE HUNDRED AND THIRTY-SEVEN CASES (26.85 PER CENT. OF TWO THOUSAND CASES OF GENERAL EPITHELIOMA)

Patients	537	
		Per Cent.
Males	526	(97.95)
Females	11	(2.05)
Age:		
Youngest patient		21
Oldest patient		97
Average age of patients		57.3
Occupation:		Per Cent.
Farmer		56.7
Laborer		9.0
Merchant		3.83
Traveling salesman		2.87
Railroad employee		2.87
Carpenter		2.68
Lawyer		1.34
Blacksmith		1.15
Clerk		1.15
Other occupations 59, each below 1 per cent.		18.4
Family history of malignancy		14.9
Previous lesion at site of cancer:		
Sore or ulcer (coldsore, 10.6 per cent.)		63.3
Crack		4.1
Leukoplakia		3.7
Tobacco:		
Patients using tobacco		80.49
Patients not using tobacco		19.51
Females using tobacco (smoke)		45.45
Females not using tobacco		45.45
Methods of using tobacco:		
Patients who smoke only		69.82
Patients who chew only		6.31
Patients who smoke and chew		23.5
Patients who use snuff		0.35
Total number of smokers		93.33
Total number of chewers		29.82
Total number of snuffers		0.35
Methods of smoking:		
Pipe only		40.69
Cigars only		19.18
Pipe and other methods and with chewing		37.79
Cigars with other methods and with chewing		31.97
Total number of pipe smokers		78.48
Total number of cigar smokers		51.16
Total number of cigaret smokers		1.16
History of injury		8.38
		Years
Average duration of lesion		2.58
Longest duration of lesion		28.00
Shortest duration of lesion		0.08
		Cm.
Greatest diameter		12.5
Average greatest diameter		2.4
Origin of lesion:		Per Cent.
Lower lip		95.69
Upper lip		3.55
Left angle of mouth		0.56
Right angle of mouth		0.18
Lower lip:		
Left lower lip		43.60
Right lower lip		38.64
Middle lower lip		17.75
Upper lip:		
Left upper lip		53.33
Right upper lip		33.33
Middle upper lip		13.33

TABLE 2.—FIVE HUNDRED MEN WITHOUT EPITHELIOMA OF THE LIP

Average age, years	36.07
	Per Cent.
Users of tobacco	78.6
Nonusers of tobacco	21.4
Methods of using tobacco:	Per Cent.
Smoke only	82.95
Chew only	4.32
Smoke and chew	12.72
Snuff	0.20
Total number of smokers	95.67
Total number of chewers	17.04
Total number of snuffers	0.20
Methods of smoking:	
Pipe only	6.11
Cigars only	16.48
Cigarets only	26.32
Pipe and other methods, and chewing	31.91
Cigars and other methods, and chewing	42.02
Cigarets and other methods, and chewing	30.05
Total number of pipe smokers	38.03
Total number of cigar smokers	58.51
Total number of cigaret smokers	59.04

It occurs in patients past middle life; their average age is 57.3 years.

3. The disease occurs most often in farmers; they represent 56.7 per cent. of the cases.

4. A family history of malignancy plays a negligible part.

5. The site of the cancer was preceded by a sore or an ulcer in 63.3 per cent. of the cases.

6. About one fifth of all the patients do not use tobacco, while one half of the female patients do not use it.

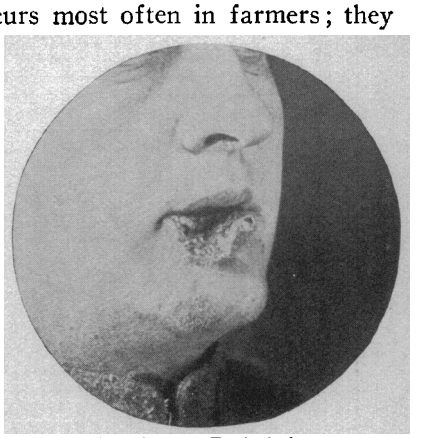

Fig. 3 (a 265421).—Typical depressed or ulcer-like epithelioma of the lip.

7. Of the patients using tobacco, 93.33 per cent. smoke; 78.48 per cent. of these use a pipe.

8. A comparison of 500 men without epithelioma of the lip with the 537 patients with epithelioma of the lip shows that the percentage of tobacco users and non-tobacco users is practically the same; 78.6 per cent.

users and 21.4 per cent. nonusers in the former group, and 80.49 per cent. users and 19.51 per cent. nonusers in the latter group, but that the average age of the men

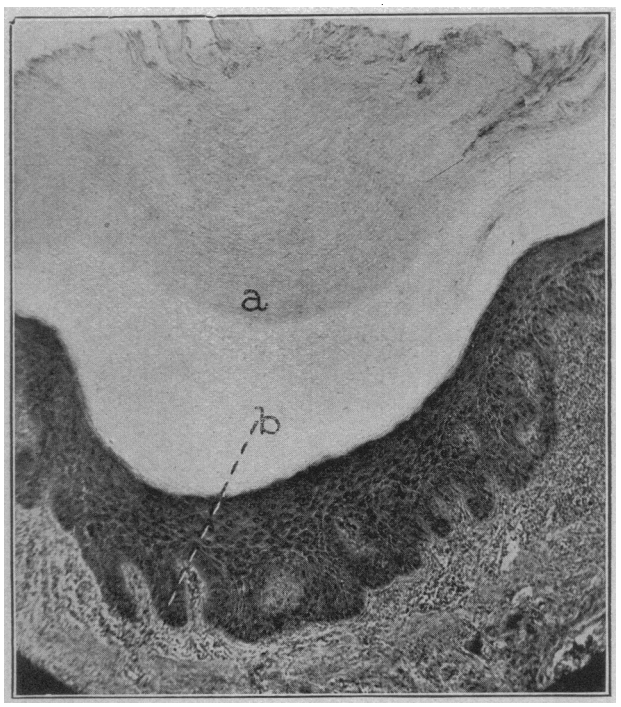

Fig. 4 (a 21283).—Marked leukoplakia of the lip, characterized by increase of (*a*) horny layer of epidermis, and (*b*) basal layer.

without epithelioma of the lip is about nineteen years less than the average age of the patients with epithelioma of the lip at the time of onset.

9. The most remarkable difference in a comparison of the patients with epithelioma of the lip and the men without epithelioma of the lip is in the method of smoking. The total number of pipe smokers in the former

TABLE 3.—TREATMENT ELSEWHERE IN SQUAMOUS-CELL EPITHELIOMA OF THE LIP

	Per Cent.
Nonsurgical:	
1. One or more treatments alone or in various combinations of acids, carbon dioxid, copper sulphate, electricity, mercury, paste or plaster, potassium iodid, radium, roentgen ray, scarlet red, shoemakers' wax, and silver nitrate	29.05
2. Paste or plaster alone or in combination with other nonsurgical treatments	51.28
3. Caustics (acids or silver nitrate) alone or in combination with other nonsurgical treatments	35.89
4. Roentgen ray alone or in combination with other nonsurgical treatments	18.58
5. Paste or plaster alone or in combination with other nonsurgical treatments (proportion of all epitheliomas of lip)	14.89
6. Caustics (acids or silver nitrate) alone or in combination with other nonsurgical treatments (proportion of all epitheliomas of lip)	10.42
7. Roentgen ray alone or in combination with other nonsurgical treatments (proportion of all epitheliomas of lip)	5.4
Surgical:	
1. One or more operations	17.87
2. Excision of growth from lip without removing lymph nodes	53.12
3. Excision of V from lip without removing lymph nodes	5.2
4. Excision of growth and one or more groups of lymph nodes	16.66
5. Excision of V from lip and one or more groups of lymph nodes	6.25
6. Miscellaneous	18.75
Surgical and nonsurgical:	
1. One or more operations and one or more treatments with acids, carbon dioxid, etc., alone or in various combinations.	4.65
2. Operations without treatment with acids, carbon dioxid, etc., before or after operation	13.22
3. Treatment with acids, carbon dioxid, etc., without operation	24.39
4. Operation and treatment with acids, carbon dioxid, etc.	37.61

TABLE 4.—PATIENTS OPERATED ON AT THE MAYO CLINIC

	No.
Cases (96.08 per cent. of 537)	516
1. Excision of submental lymph nodes, submaxillary lymph nodes and salivary glands of both sides, and V-shaped excision of epithelioma of the lip (one operation) (39.34 per cent. of 516).	203
2. V-shaped or quadrilateral shaped excision of epithelioma of the lip (10.85 per cent. of 516)	56
3. Excision of submental lymph nodes, submaxillary lymph nodes, and salivary glands of both sides and quadrilateral shaped excision of epithelioma of the lip (one operation) (4.84 per cent. of 516)	25
4. Excision of submental lymph nodes and submaxillary lymph nodes and salivary glands on one side, and V-shaped excision of epithelioma of the lip (one operation) (3.29 per cent. of 516).	17
5 Unilateral block dissection (one operation) (2.9 per cent. of 516)	15
6 Miscellaneous (various combinations of operations, cauteries, excisions of specimens for diagnosis, at one time or at different times) (38.76 per cent. of 516)	200
REMOVAL OF LYMPH NODES AND SALIVARY GLANDS	
Cases	449
1. Submental lymph nodes (97.1 per cent. of 449)	436
2. Submaxillary lymph nodes and salivary glands (unilateral) (12.91 per cent. of 449)	58
3. Submaxillary lymph nodes and salivary glands (bilateral) (84.18 per cent. of 449)	378
4. Cervical lymph nodes (16.7 per cent. of 449)	75
5. Block dissections (alone or combined with other operations) (10.02 per cent. of 449)	45
6. Cases in which the lymph nodes were removed months or years after the removal of the epithelioma of the lip (2.44 per cent. of 449)	11
7. Lymph nodes removed (one or more groups) (87.01 per cent. of 516)	449
8. Cases in which no lymph nodes were removed (12.98 per cent. of 516)	67
PATIENTS WITH INOPERABLE EPITHELIOMA	
Cases (3.9 per cent. of 537)	21

is 78.48 per cent. and the total number of cigaret smokers is only 1.16 per cent., while in the latter the total number of pipe smokers has dropped to 38.03 per

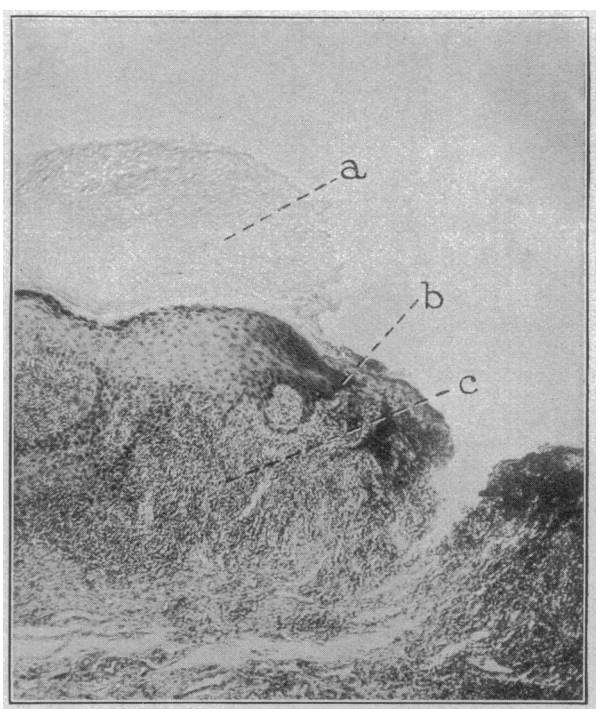

Fig. 5 (a 152243).—Ulcer associated with a leukoplakia of the lip: *a*, leukoplakia; *b*, junction of epidermis and ulcerated area; *c*, lymphocytes.

cent., and the total number of cigaret smokers has risen to 59.04 per cent.

10. A history of injury plays a negligible part.

11. The duration of the lesion shows a marked variation, from 0.08 years to 28 years, with an average of 2.58 years.

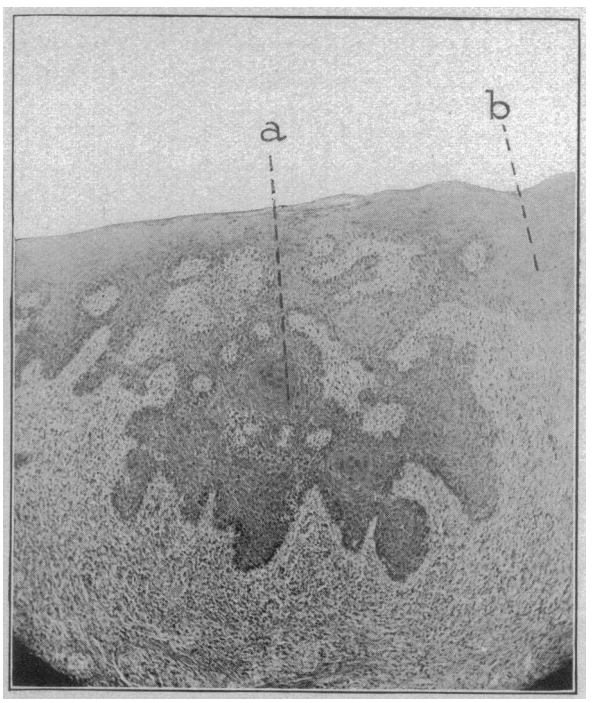

Fig. 6 (a 98158).—Grade 1 epithelioma of the lip with marked differentiation; low degree of malignancy; patient well five years after operation: *a*, epithelioma; *b*, normal epithelium.

12. The greatest diameter of any lesion is 12.5 cm.; the average, 2.4 cm.

13. The lesion originated on the lower lip in 95.69 per cent. of the cases, on the upper lip in 3.55 per cent., at the left angle of the mouth in 0.56 per cent., and at the right angle of the mouth in 0.18 per cent.

TABLE 5.—PATHOLOGIC FINDINGS IN CASES IN WHICH LYMPH NODES AND SUBMAXILLARY SALIVARY GLANDS WERE REMOVED

	No.	Per Cent.
Cases	449	
No metastasis found	344	76.62
Metastasis found	105	23.38
Submaxillary lymph nodes alone (one side)	44	41.90
Submaxillary lymph nodes and salivary glands (one side)	13	12.38
Submaxillary lymph nodes (one side) and submental lymph nodes	7	6.66
Submaxillary lymph nodes, salivary glands, and superior superficial cervical lymph nodes (one side)	6	5.71
Submental lymph nodes alone	5	4.76
Submaxillary lymph and superficial cervical lymph nodes (one side)	6	5.71
Submaxillary lymph nodes (both sides) and submental lymph nodes	5	4.76
Submaxillary lymph nodes (both sides), submental and anterior jugular lymph nodes (one side)	3	2.85
Miscellaneous (submaxillary lymph nodes and salivary glands, submental, cervical, parotid, supraclavicular and peribronchial lymph nodes; lung and liver, alone or in various combinations	16	15.23
Submaxillary lymph nodes, total involvement	92	87.61
Submaxillary salivary glands, total involvement	23	21.90
Submental lymph nodes, total involvement	26	24.76
Cervical lymph nodes (one or more groups)	26	24.76
Superior deep cervical nodes	3	7.89
Inferior deep cervical nodes	3	7.89
Exterior jugular nodes	24	63.15
Anterior cervical nodes	8	21.05
Supraclavicular nodes, total involvement	1	0.95
Parotid lymph nodes, total involvement	1	0.95
Peribronchial nodes, total involvement	2	1.90
Lung, total involvement	1	0.95
Liver, total involvement	1	0.95
Submaxillary lymph nodes, total involvement on both sides	13	12.38
Cervical nodes, total involvement on both sides	2	1.90

TABLE 6.—GRADE OF FIVE HUNDRED AND THIRTY-SEVEN CASES ON A BASIS OF 1 TO 4, ACCORDING TO CELLULAR ACTIVITY

	No.	Per Cent.
Grade 1	85	15.82
Grade 2	333	62.01
Grade 3	113	21.04
Grade 4	6	1.11

DURATION AND SIZE OF EPITHELIOMA ACCORDING TO GRADE

	Grade 1	Grade 2	Grade 3	Grade 4
	Years	Years	Years	Years
Longest duration	10.00	25.00	28.00	2.00
Shortest duration	0.10	0.08	0.08	0.91
Average duration	1.43	2.77	3.33	1.29
	Cm.	Cm.	Cm.	Cm.
Largest size	5.00	10.00	7.50	2.00
Smallest size	0.20	0.30	0.20	1.80
Average size	1.23	2.28	3.25	1.9

EPITHELIOMA PRECEDED BY ULCER

	No.	Per Cent.
Grade 1	52	15.29
Grade 2	225	66.17
Grade 3	60	17.64
Grade 4	3	0.88

PROPORTION OF EACH GRADE PRECEDED BY ULCER

Grade 1	61.17	per cent. of	85
Grade 2	67.56	per cent. of	333
Grade 3	53.09	per cent. of	113
Grade 4	50.00	per cent. of	6

INOPERABLE EPITHELIOMA ACCORDING TO GRADE

Grade 1	Grade 2	Grade 3	Grade 4
0	12	7	2

14. Twenty-nine and five hundredths per cent. of the patients were treated with acid, paste or plaster, etc., before they entered the clinic.

15. Seventeen and eighty-seven hundredths per cent. of the patients were operated on before they entered the clinic.

16. Ninety-six and eight hundredths per cent. of the patients were operated on at the clinic.

Fig. 7 (a 64692).—Grade 1 epithelioma of the lip showing marked differentiation, although it is of a slightly higher degree of malignancy than the epithelioma shown in Figure 5; patient well seven years after operation; *a*, completely differentiated area; *b*, partially differentiated cells; *c*, normal epithelium.

17. In 87.01 per cent., the regional lymph nodes were removed.

18. Of the 449 cases in which the lymph nodes or salivary glands were removed, metastasis was demonstrated in 23.38 per cent.; the submaxillary lymph nodes were involved in 87.61 per cent.; the submaxillary salivary glands in 21.90 per cent.; the submental lymph

Fig. 8 (a 99884).—Grade 2 epithelioma of the lip; not so much differentiation as in epithelioma shown in Figure 6; patient died from epithelioma of the lip four and one-half years after operation: *a*, completely differentiated area or pearly body; *b*, undifferentiated cells.

TABLE 7.—RESULTS

GENERAL ULTIMATE RESULTS

Patients traced (operable, 306; inoperable, 8) (58.47 per cent. of total)	314
Patients operated on	306
Patients dead (40.52 per cent.)	124
Patients alive (59.47 per cent.)	182
Good result (no recurrence (92.85 per cent. of 182)	169
Fair result (slight recurrence) (6.04 per cent. of 182)	11
Bad result (no improvement) (1.09 per cent. of 182)	2

DURATION OF LIFE SINCE LAST OR ONLY OPERATION, ACCORDING TO RESULT

	Good Result	Fair Result	Bad Result
	Years	Years	Years
Longest	14.39	13.68	2.80
Shortest	1.25	0.96	0.49
Average	7.76	6.8	1.65

MORTALITY

Deaths (42.05 per cent. of 314)	132
Deaths of patients with operable epithelioma (93.93 per cent. of 132)	124
Deaths of patients with inoperable epithelioma (6.06 per cent. of 132)	8

TABLE 7.—*Continued*

CAUSE OF DEATH OF PATIENTS OPERATED ON: DATA FROM RELATIVE, HOME PHYSICIAN, OR PATHOLOGIC RECORDS OF THE CLINIC

	No.	Per Cent.
Known cause	99	
Cancer of the lip	63	63.63
Heart disease	5	5.05
Nephritis	5	5.05
Pneumonia	4	4.04
Stomach trouble	3	3.03
Paralysis	3	3.03
"Following operation elsewhere"	3	3.03
Fall	2	2.02
Carcinoma of the stomach	1	1.01
Tumor of the stomach	1	1.01
Abdominal tumor	1	1.01
Diabetes	1	1.01
Carcinoma of the sigmoid	1	1.01
Sepsis	1	1.01
Tuberculosis	1	1.01
Hepatic disease	1	1.01
Cardiac and hepatic disease	1	1.01
Sarcoma of the liver	1	1.01
Lung trouble	1	1.01
Unknown	25	

CAUSE OF DEATH OF PATIENTS WHO DIED IN THE MAYO CLINIC (ALL OPERABLE)

Chronic nephritis and arteriosclerosis (more than 2 years after operation)	1
Epithelioma and abscess of the neck (52 days after operation)	1
Epithelioma (25 days and 4 months, respectively, after operation)	2
Pneumonia (few days after operation)	3
Sepsis (12 days after operation)	1
Total (1.55 per cent. of 516)	8
Actual operative mortality (0.77 per cent. of 516)	4

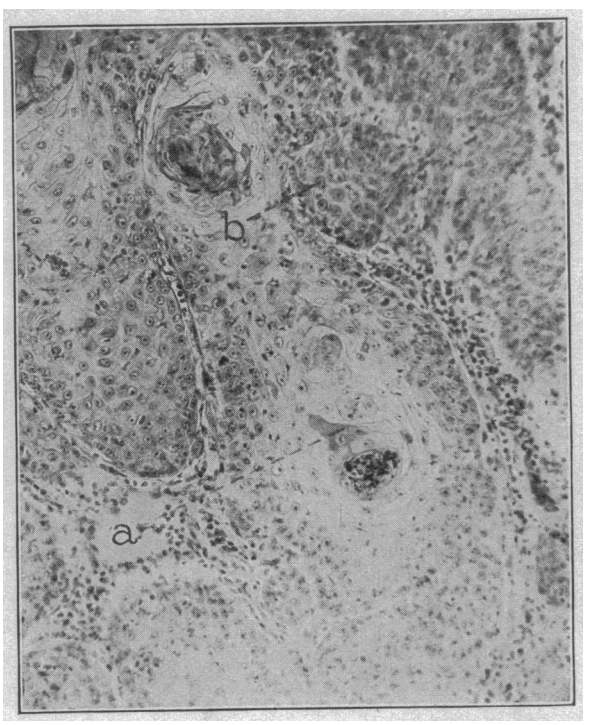

Fig. 9 (a 59017).—Grade 2 epithelioma of the lip; about the same degree of malignancy as in epithelioma shown in Figure 7; patient well more than seven years after operation: *a*, partially differentiated cells; *b*, undifferentiated cells.

TABLE 8.—TOBACCO USERS OPERATED ON

	Grade 1	Grade 2	Grade 3	Grade 4
Number of patients	37	118	37	3
Patients living	34 (91.81% of 37)	92 (77.96% of 118)	10 (27.02% of 37)	
Patients living, good result	33 (97.05% of 34)	85 (92.39% of 92)	10 (100% of 10)	
Patients living, fair result	1 (2.94% of 34)	6 (6.52% of 92)		
Patients living, poor result	.....	1 (1.08% of 92)		
Patients dead	3 (8.10% of 37)	26 (22.63% of 118)	27 (72.97% of 37)	3 (100% of 3)
Cause unknown	.....	6	5	1
Good result	2 (66.66% of 3)	6 (30.00% of 20)	7 (31.81% of 22)	
Fair result	1 (33.33% of 3)			
Poor result	.....	14 (80.00% of 20)	15 (68.18% of 22)	2 (100% of 2)

	Per Cent.
Total good result (patient recovered from epithelioma and is living, or recovered from epithelioma and died from other cause)	78.14
Total fair result (patient living with slight recurrence or died from other cause)	4.37
Total poor result (patient lived with no improvement or died from epithelioma)	17.48

TABLE 9.—NONUSERS OF TOBACCO OPERATED ON

	Group 2	Group 3	Group 4
Number of patients	7	37	7
Patients living	6 (85.71% of 7)	29 (78.37% of 37)	4 (57.14% of 7)
Patients living, good result	6 (100% of 6)	29 (100% of 29)	2 (50.00% of 4)
Patients living, fair result	.....	.....	2 (50.00% of 4)
Patients dead	1 (14.28% of 7)	8 (21.62% of 37)	3 (42.85% of 7)
Cause unknown	.....	1	
Good result	1 (100% of 1)	5 (71.42% of 7)	
Poor result	.....	2 (28.57% of 7)	3 (100% of 3)

TOTAL RESULTS

	Per Cent.
Total good result (patient recovered from epithelioma and is living, or recovered from epithelioma and died from other cause)	86.00
Total fair result (patient living with slight recurrence)	4.00
Total poor result (patient died from epithelioma)	10.00

TABLE 10.—PATIENTS OPERATED ON TREATED WITH PASTES, PLASTERS, ACIDS, ETC., BEFORE ENTERING THE CLINIC

Patients concerning whom information has been received	94
Patients living (53.19 per cent. of 94)	50

	Grade 1	Grade 2	Grade 3	Grade 4
Patients living, good result	5 (11.11% of 45)	34 (75.55% of 45)	6 (13.33% of 45)	
Patients living, fair result	.....	1 (33.33% of 3)	2 (66.66% of 3)	
Patients living, poor result	.....	1 (50.00% of 2)	1 (50.00% of 2)	
Patients dead	.....	.....	.....	44 (46.80% of 94)
Cause unknown	.....	4	3	
Good result	.....	5 (55.55% of 9)	4 (44.44% of 9)	
Poor result	.....	9 (32.14% of 28)	16 (57.14% of 28)	3 (10.71% of 28)

TOTAL RESULTS

Total good result (patient recovered from epithelioma and is living, or recovered from epithelioma and died from other cause)	62.06% of 87
Total fair result (patient living with slight recurrence)	3.44% of 87
Total poor result (patient living with no improvement or died from epithelioma)	34.48% of 87

TABLE 11.—PATIENTS OPERATED ON NOT TREATED WITH PASTES, PLASTERS, ACIDS, ETC., BEFORE ENTERING THE CLINIC

Patients concerning whom information has been received	212
Patients living (61.79 per cent. of 212)	131

	Grade 1	Grade 2	Grade 3	Grade 4
Patients living, good result	34 (27.64% of 123)	83 (67.47% of 123)	6 (4.87% of 123)	
Patients living, fair result	1 (12.50% of 8)	7 (87.50% of 8)		
Patients dead	.....	.....	.....	81 (38.20% of 212)
Cause unknown	.....	10	9	1
Good result	4 (16.00% of 25)	17 (68.00% of 25)	4 (16.00% of 25)	
Fair result	1 (100.00% of 1)			
Poor result	.....	18 (51.30% of 35)	17 (48.45% of 35)	

TOTAL RESULTS

Total good result (patient recovered from epithelioma and is living, or recovered from epithelioma and died from other cause)	77.08% of 192
Total fair result (patient living with slight recurrence or died from other cause)	4.68% of 192
Total poor result (patient died from epithelioma)	18.22% of 192

TABLE 12.—PATIENTS WITH METASTASIS OPERATED ON

Patients concerning whom no information was received	36 (34.29% of 105)
Patients from whom information was received	69 (65.71% of 105)
Patients living	12 (17.39% of 69)

	Grade 1	Grade 2	Grade 3	Total Number of Good Results
Patients living, good results*	.....	5 (50% of 10)	5 (50% of 10)	10 (83.33% of 12)
Patients living, fair result*	.....	.....	1 (100% of 1)	
Patients living, poor result*	.....	.....	1 (100% of 1)	

DURATION OF LIFE OF PATIENTS WITH GOOD RESULT FROM LAST OR ONLY OPERATION

Longest	11.73 years
Shortest	3.29 years
Average	6.18 years

Patients dead	57 (82.6% of 69)

Grade 1	Grade 2	Grade 3	Grade 4
.....	15 (34.09% of 44)	26 (59.09% of 44)	3 (6.81% of 44)

	Years
Longest duration of life from last or only operation of patients who died from epithelioma	2.5
Shortest duration of life from last or only operation of patients who died from epithelioma	0.066
Average duration of life from last or only operation of patients who died from epithelioma	0.79
Longest duration of life from last or only operation of patients who died from epithelioma or other cause	4.88
Shortest duration of life from last or only operation of patients who died from epithelioma or other cause	0.016
Average duration of life from last or only operation of patients who died from epithelioma or other cause	0.86

CAUSE OF DEATH

Epithelioma	44 (91.66% of 48)
Lung trouble	1 (2.08% of 48)
Sepsis	1 (2.08% of 48)
Heart disease	1 (2.08% of 48)
Pneumonia	1 (2.08% of 48)
Not stated	9

* In the ten patients with metastasis who reported a good result, and in the one who reported a fair result, the submaxillary lymph nodes on only one side were involved. In the one patient who reported a poor result, the submaxillary lymph nodes and the salivary gland on only one side were involved.

TABLE 13.—PATIENTS WITH METASTASIS IN SUBMAXILLARY LYMPH NODES ON ONE SIDE ONLY

Patients concerning whom no information was received	14 (30.81% of 44)	Patients living, fair result	1 (9.09% of 11)
Patients concerning whom information was received	30 (69.18% of 44)	Patients dead	19
Patients living	11	Patients dead from epithelioma	14 (82.35% of 17)
Patients living, good result	10 (90.9% of 11)	Patients dead from other cause	3 (17.64% of 17)
		Patients dead from cause not stated	2

TABLE 14.—PATIENTS WITHOUT METASTASIS OPERATED ON

Patients concerning whom no information was received 146
Patients concerning whom information was received 198
Patients living (76.26% of 198) 151

	Grade 1	Grade 2	Grade 3	Total Number of Good Results
Patients living, good result	35 25.00% of 140)	99 (70.71% of 140)	6 (4.28% of 140)	140 (92.71% of 151)
Patients living, fair result	1 (10.00% of 10)	8 (80.00% of 10)	1 (10.00% of 10)	
Patients living, poor result	.....	1 (100% of 1)	.....	
Patients dead	.....	.....	.....	47 (23.73% of 198)
Cause unknown	.....	10		
Good result	3 (12.50% of 24)	18 (75.00% of 24)	3 (12.50% of 24)	
Fair result	1 (100% of 1)			
Poor result	.....	9 (75.00% of 12)	3 (25.00% of 12)	

Total good result (patient recovered from epithelioma and is living or recovered from epithelioma and died from other cause) ..... 164 (87.23% of 188)
Total fair result (patient living with slight recurrence, or died from other cause) ..... 11 (5.85% of 188)
Total poor result (patient living with no improvement, or died from epithelioma) ..... 13 (6.91% of 188)

TABLE 15.—PATIENTS WITH AND WITHOUT METASTASIS OPERATED ON

	Grade 1	Grade 2	Grade 3	Grade 4
Patients with metastasis	.....	39 (37.14% of 105)	63 (60.00% of 105)	3 (2.85% of 105)
Patients without metastasis	67 (19.47% of 344)	248 (72.09% of 344)	29 (8.43% of 344)	

DURATION OF LESION BEFORE EXAMINATION AT CLINIC

	Years		Years
Longest duration (patient with metastasis)	28.00	Patient without metastasis	25.00
Shortest duration (patient with metastasis)	0.16	Patient without metastasis	0.08
Average duration (patient with metastasis)	3.27	Patient without metastasis	2.40

SIZE OF LESION AT THE TIME OF EXAMINATION AT THE CLINIC

	Cm.		Cm.
Largest size (patient with metastasis)	12.5	Patient without metastasis	10.00
Smallest size (patient with metastasis)	1.0	Patient without metastasis	0.2
Average size (patient with metastasis)	3.74	Patient without metastasis	2.01

ASSOCIATION OF EPITHELIOMA OF THE LIP WITH OTHER MALIGNANT NEOPLASMS

	Cases
Nonmelanotic melano-epithelioma on shoulder	1
Squamous-cell epithelioma of cheek	1
Squamous-cell epithelioma of bladder	1
Basal-cell epithelioma of eyelid	1
Adenocarcinoma of sigmoid	1
	5 (0.93% of 537)

TABLE 16.—DURATION OF LIFE AFTER OPERATION OF PATIENTS WITHOUT METASTASIS

ACCORDING TO GRADE

Good result:	Grade 1	Grade 2	Grade 3
Number of patients	35	98	6
	Years	Years	Years
Longest duration	14.39	14.31	12.22
Shortest duration	1.73	1.25	4.3
Average duration	7.59	7.54	7.17
Fair result:			
Number of patients	1	8	1
	Years	Years	Years
Longest duration	4.39	13.68	7.32
Shortest duration	.....	0.96	
Average duration	.....	7.54	

DURATION OF LIFE AFTER OPERATION OF PATIENTS OF ALL GRADES

	Good Result	Fair Result	Poor Result
	Years	Years	Years
Longest duration	10.19	.....	4.51
Shortest duration	0.36	.....	0.51
Average duration	4.47	6.73	1.85

DURATION OF LIFE AFTER OPERATION OF ALL PATIENTS WITHOUT METASTASIS

	Years
Longest duration	10.19
Shortest duration	0.36
Average duration	3.68

DURATION OF LIFE OF PATIENTS OF ALL GRADES

	Good Result	Fair Result
	Years	Years
Longest duration	14.39	13.68
Shortest duration	1.25	0.96
Average duration	7.53	7.2

DURATION OF LIFE AFTER OPERATION OF PATIENTS WITHOUT METASTASIS WHO ARE DEAD

Good result—Patients did not die from epithelioma:

	Grade 1	Grade 2	Grade 3
Number of patients	3	18	3
	Years	Years	Years
Longest duration	5.8	10.19	9.3
Shortest duration	3.5	0.36	2.02
Average duration	4.28	4.24	6.07

Fair result—Patients did not die from epithelioma but had slight recurrence:

Number of patients	1
	Years
Longest duration	6.93

Poor result—Patient died from epithelioma:

	Grade 2	Grade 3
Number of patients	9	3
	Years	Years
Longest duration	4.51	1.52
Shortest duration	1.00	0.51
Average duration	2.15	0.95

nodes in 24.76 per cent., and the cervical lymph nodes in 24.76 per cent.

19. In a division of the epitheliomas according to cellular activity, on a basis of 1 to 4, Grade 1 represents

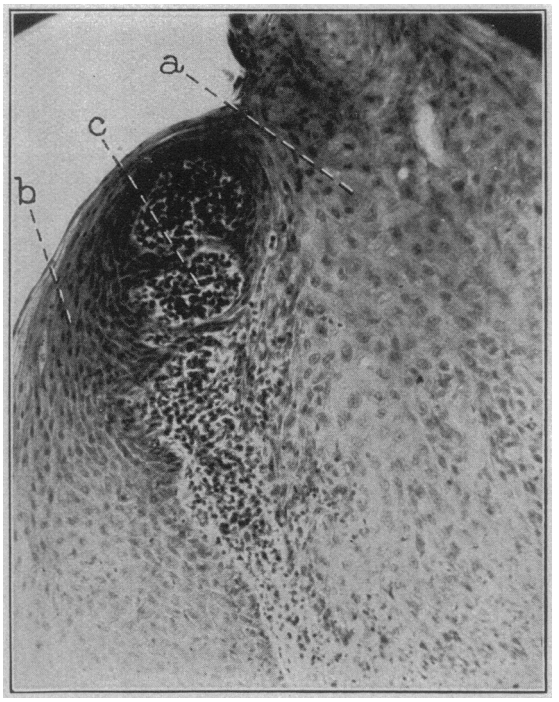

Fig. 10 (a 72479).—Grade 2 epithelioma of the lip: *a*, epithelioma; *b*, normal epithelium; *c*, lymphocytes

15.82 per cent.; Grade 2, 62.01 per cent.; Grade 3, 21.04 per cent., and Grade 4, 1.11 per cent.

20. The average duration of the lesion according to grade is longest in Grade 3, 3.33 years, and shortest in Grade 4, 1.29 years.

21. The average size of the lesion according to grade is largest in Grade 3, and smallest in Grade 1.

22. Of the patients operated on and traced, 40.52 per cent. are dead and 59.47 per cent. are alive.

23. Of the living patients, 92.85 per cent. report a good result, having been free from the disease on an average of 7.76 years.

24. Of the patients operated on who have died, concerning whom information has been received, 63.63 per cent. died from epithelioma.

25. Eight, or 1.55 per cent., of the patients who were operated on died in the clinic, while the actual operative mortality was only 0.77 per cent.

26. The users of tobacco who were operated on did not obtain quite so good total good results as the nontobacco users; 78.14 per cent. in the former, and 86 per cent. in the latter.

27. In the inoperable cases, the nontobacco users reached as high as 30.76 per cent.

28. The patients who were treated with pastes, plasters, etc., before entering the clinic did not get such good total good results as those who were not so treated; 62.06 per cent. in the former and 77.08 per cent. in the latter; moreover, 31.91 per cent. of the former who were operated on had metastasis, while only 19.48 per cent. of the latter operated on had metastasis.

29. Of the patients with metastasis, 17.39 per cent. are living and 82.6 per cent. are dead.

30. Of the living who had metastasis, 83.33 per cent. report a good result. In these patients the submaxillary lymph nodes on only one side were involved.

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

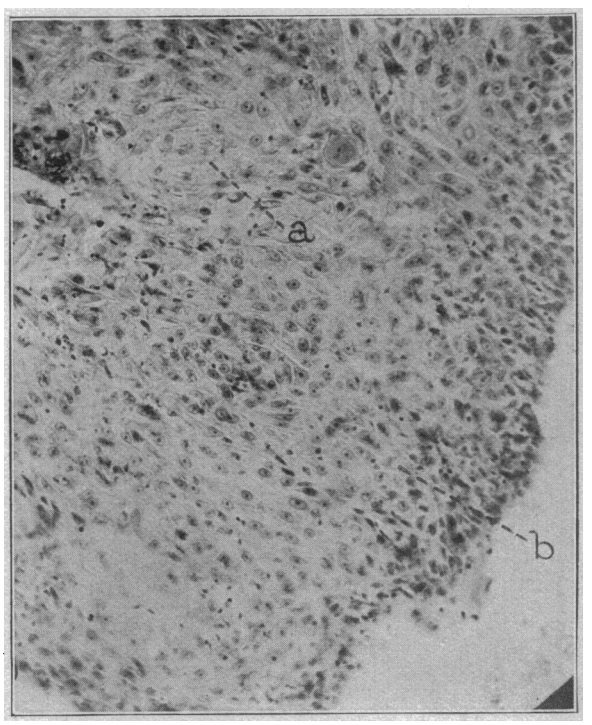

Fig. 11 (a 38260).—Grade 3 epithelioma of one of the left submaxillary lymph nodes, secondary to epithelioma of the lip; slight differentiation; the patient died from epithelioma five months after the last operation, and twenty months after the onset of the disease: *a*, partially differentiated cells; *b*, undifferentiated cells.

TABLE 17.—RESULTS FOLLOWING OPERATION ACCORDING TO GRADE

	Grade 1	Grade 2	Grade 3	Grade 4
Information received from patients operated on	45 (52.94% of 85)	192 (59.81% of 333)	65 (62.26% of 113)	4 (100% of 4)
Patients living	40 (88.88% of 45)	128 (66.66% of 192)	16 (24.6% of 65)	
Patients living, good result	39 (97.5% of 40)	119 (92.96% of 128)	13 (81.25% of 16)	
Patients living, fair result	1 (2.5% of 40)	8 (6.25% of 128)	2 (12.50% of 16)	
Patients living, poor result	.....	1 (0.78% of 128)	1 (6.25% of 16)	
Patients dead	5 (11.12% of 45)	64 (33.33% of 192)	49 (75.38% of 113)	4 (100% of 4)
Good result	4 (80.00% of 5)	23 (45.09% of 51)	6 (15.78% of 38)	
Fair result	1 (20.00% of 5)			
Poor result	.....	28 (54.90% of 51)	32 (84.21% of 38)	4 (100% of 4)
Not stated	.....	13	11	
Total good result (patient recovered from epithelioma and is living or recovered from epithelioma and died from other cause)	43 (95.55% of 45)	142 (79.32% of 179)	19 (35.18% of 54)	
Total fair result (patient living with slight recurrence or died from other cause)	2 (4.45% of 45)	8 (4.46% of 179)	2 (3.70% of 54)	
Total poor result (patient living with no improvement or died from epithelioma)	.....	29 (16.20% of 179)	33 (61.11% of 54)	4 (100% of 4)
Total result not stated	.....	13	11	

32. Of the patients reported dead who had metastasis, 91.66 per cent. died from epithelioma.

33. If a patient has the submaxillary lymph nodes on one side only involved, he has a 1 to 3 chance of getting a good result, and will be living and well on an average of 6.18 years after operation.

34. Of the patients operated on in whom no metastasis was demonstrated, 76.26 per cent. are living, and 23.73 per cent. are dead; of the living, 92.71 per cent. report a good result.

35. The average duration of the lesion in the patients with metastasis is 3.27 years, as compared with 2.40 years in those without metastasis; the average size of the lesion is 3.74 cm. in the patients with metastasis, as compared with 2.01 cm. in those without metastasis.

36. Among the known causes of death, deaths from epithelioma were as follows: none of Grade 1; 54.90 per cent. of Grade 2; 84.21 per cent. of Grade 3, and 100 per cent. of Grade 4.

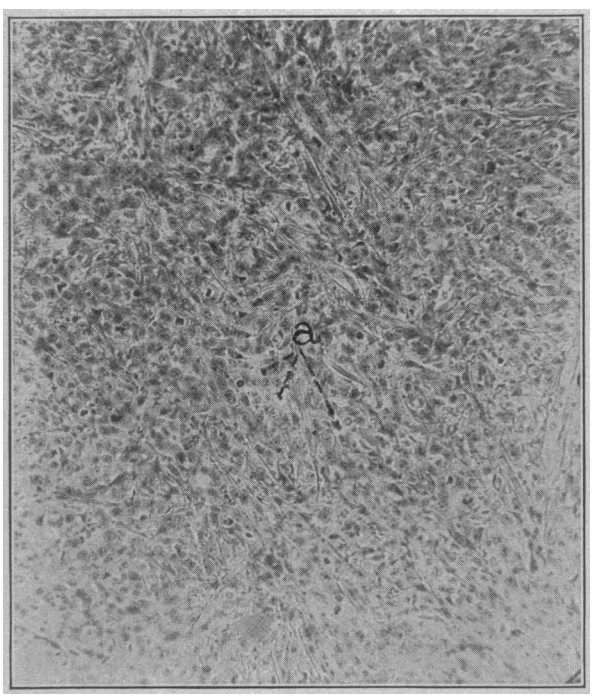

Fig. 12 (a 74162).—Grade 4 epithelioma of the liver secondary to epithelioma of the right side of the upper lip; no differentiation; numerous mitotic figures; high degree of malignancy; the patient died four and one-half months after the last operation, and eleven months after the onset of the disease, with metastatic epithelioma of the lymph nodes of the right side of the neck, right peritracheobronchial nodes, right lung, and liver: *a*, mitotic figures.

37. Some malignant neoplasm was associated with the epithelioma of the lip in 0.93 per cent. of the patients.

The First Book on Pediatrics.—The first book ever published on children's diseases is probably the work by Omnibono Ferrarii, printed in Bruges, 1557. The book is in Latin, in quarto, has 196 pages, besides three chapters with 12 pages of aphorisms. The book is dedicated to the College of Physicians and Philosophers of Verona. The dedicatory expresses the view that every person should have two purposes in life: First, avoid laziness so as not to waste his life, and second, show his gratitude to the persons from whom he has received any favors. According to the author, his book was written after having noticed that the ancient physicians who wrote about children did not say anything about nurses' diseases nor describe methodically the different diseases that might befall children.

THE INTESTINAL TUBE

ITS SIGNIFICANCE AND APPLICATIONS *

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In the descriptions contained in this article, I am dealing primarily with the introduction of the rubber tube into the intestine beyond the duodenum. I have therefore taken the liberty of referring to it as an intestinal tube, rather than a duodenal tube, for the latter might imply that its use is limited to the duodenum.

The primary purpose of this study of a series of roentgenograms of the intestinal tube in a given case is to demonstrate more clearly the principle of the detachable bulb, as outlined in a preceding communication.[1] In that article, I described a modification of the duodenal tube, which, I believe, enhances its usefulness in intestinal feeding. In the first place, several openings were made along the course of the tube, up to a distance of about 1½ inches from its end, each opening about the size of its lumen. The purpose of this was to minimize the possibility of occlusion which occasionally occurs. Of greater value was the change from an end-piece that was permanently attached during its sojourn in the intestine, to an end-piece that could be detached shortly after the tube had reached its destination. This modification was considered of importance because of the possibilities of danger resulting from a prolonged direct contact of a weighted substance with the delicate intestinal mucous membrane. The detachable bulb not only obviates this factor, but as a direct result, makes it possible to use the tube in the intestine over a longer period of time, a factor which might be of value in the more chronic affections. I was able to accomplish this modification by sewing the metallic bulb to the end of the rubber tube with catgut. Plain catgut was first used, but in a number of cases, owing probably to a contraction of the pyloric sphincter, the tube remained in the stomach for several hours and the gastric secretions had digested the catgut, causing the premature detachment of the bulb. Without a weight at the end of the tube, there was a tendency for it to remain coiled within the stomach, the end failing to pass into the intestine. After experimenting with different kinds of catgut, I decided on the use of chromicized catgut No. 4, as this gave the most satisfactory results.

To illustrate this principle more clearly, it was decided to take a series of roentgenograms from the time the tube was swallowed and the end had passed within the intestine, until the bulb had left the intestinal canal.

As soon as the clear bile colored fluid was obtained by aspiration, I had a roentgenogram taken, with the result shown in Figure 1. The roentgenogram was taken during the process of injecting a suspension of barium in buttermilk through the open end of the tube by means of a syringe. The picture obtained showed the end of the tube within the intestine. From then on, roentgenograms were taken at varying intervals, with the idea of obtaining information regarding the time when the detachment of the bulb from the end of the tube occurred; and finally, after the bulb had left

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1. Buckstein, Jacob: Experiences with Duodenal Feeding at U. S. Army General Hospital No. 41, J. A. M A. **73**: 670 (Aug. 30) 1919.