TUMOURS OF SALIVARY TISSUE.

A clinico-pathological and experimental study.

by

J. Malcolm Cameron, M.B., Ch.B.

Thesis submitted for the degree of Doctor of Medicine

of the University of Glasgow.

))))))))))))))))))))

INDEX

INTRODUCTION.

"Tumours of the Salivary Gland are a pathological puzzle and a source of unsatisfactory speculation."

Bland-Sutton, J., (1906).

This thesis has been composed and written by myself. It is a record of the work which was begun whilst in the Pathology Department, Southern General Hospital, Glasgow, and continued during the tenure of the McIntyre Clinical Research Scholarship at the Glasgow Royal Infirmary.

Four hundred and one examples of tumours of salivary tissue were collected. Of these, 88 presented at the Western Infirmary, and the Southern General Hospital, Glasgow (1950-55) and the others at the Glasgow Royal Infirmary (1935-56). All the cases were reviewed clinically and a familiar incidence was encountered on three occasions. A detailed pathological study was made

on the cases seen at the Southern General Hospital, and the blood-group of the patients was determined in 341 cases. In amplification of the pathological study, attempts were made to produce salivary tumours experimentally in animals. In vitro studies with radio-active sulphur (Sulphur-35) were made on 10 consecutive cases of human salivary tumour.

The presentation of this thesis is not an indication that no further investigations of Salivary Tumours is contemplated, but rather that the findings have now reached a stage beyond which a general survey, such as is attempted here, would be unwieldy, and an attempt has been made to strike a balance between literary, clinical and experimental research.

PART I.

Review of the literature.

Tumours of Salivary Tissue.

"This bizarre lesion....."

Furstenburg, (1941).

Since the first attempt by Berard (1841), tumours of salivary tissue have not been satisfactorily classified either clinically or pathologically. Attention has been focused mainly on the so-called "mixed tumours", and the other varieties have often been neglected.

The term "adenoma" was introduced by Lebert & Broca (1850) for benign tumours of the Parotid gland, and most writers consider them as only a variant of pleomorphic adenomata, namely the most slowly growing and innocous variety. According to Willis (1953) pure adenomas are slowly growing, encapsulated, lobulated epithelial tumours and there is no sharp line of demarcation on structural grounds between simple adenoma and pleomorphic adenoma. Some 40 cases have been described in European literature;

the first in British literature was by Dunlop (1879) in a 36 year old female patient at the Glasgow Royal Infirmary. Only a few American workers, (Schutz, 1926; McFarland, 1927; Slaughter et al, 1953 and Ross, 1955) have reported cases; it is interesting to note that McFarland (1936) later reports that the case he described originally as a true simple adenoma was in fact a pleomorphic adenoma. Eggers (1928) classifies two of his seven palatal tumours as adenomata.

Pleomorphic Adenomata.

The vast majority of salivary growths are pleomorphic adenomata, the so-called mixed salivary tumours - a term dating from Minssen's report in 1874. Although the first published reports of such tumours are generally credited to C.G. Siebold (1793) and J.P. Siebold (1797), little of morphological interest has been added since it was first recognised as a clinical entity in 1853 by Paget.

The first complete record and review of the literature was by Wood (1904) and subsequent reviews of note were undertaken by Wilson & Willis (1912); Heineke (1913); Kennon (1921), and McFarland (1926, 33, 36, 42, 43). Ewing (1940) states that "no simple source of mixed tumours meets all the requirements", while Fick (1909) and Patey (1931) rightly suggest that confusion over terminology has been due to its uncertain aetiology, and such hyphenated monstrosities as chondro-myxo-haemato-endothelio-sarcoma have been used.

Originally, most of the German pathologists considered them of connective tissue origin, and any epithelial structures as vestiges of the gland in which they occurred. Billroth (1859), Virchow (1863) and Kaufmann (1929) were of the opinion that they were of mesenchymal origin, while Wartmann (1879) expressed the opinion that they were derived from lymphatic endothelium. Volkmann (1895) thought he had proved the endothelial origin as did Martini

(1907), von Hansemann (1910), and others. This theory was, however, adversely criticised by Hinsberg (1899), Cuneo & Veau (1900), Wood (1904), Chevassu (1910) and Ssobolew (1912) who suggested a branchio-genic origin, which was originally suggested by Cohnheim (1876) and Birsch-Hirschfield (1894). This theory would explain the presence in some tumours of areas of "cartilage"and "bone". Wilms (1899) and Marchand (1910), together with others, regarded them as composite tumours in which the epithelium plays the most important part, and traced them to an origin analagous to that of teratomata, except that the embryonic rudiment is separated at a later stage. Pitance (1897) thought that some developing buds were broken off and detached in the later development and formed the nucleus of a tumour. Other suggested theories at this time include that of Forgue & Massabuau (1908) that they should be classified as embryomata along with testicular tumours. Teratomata of the neck have been

reported by McGregor & Wartmann (1906) and more recently by Thomas (1957) and Edwards (1958), but these are quite different. Another theory which did not get many supporters was that of Krompecher (1908) who regarded them as basal cell tumours.

Fraser (1918) with his work on dogs believed he had experimental proof that they arose from the ducts of adult glands. McFarland (1926) supported by Kux (1931) and Hempleman and Womack (1942) suggested that the origin was probably sequestration of embryonal cells, this was in agreement with Forman and Warren (1918). Many agree on the pure epithelial nature of the tumours - Fick (1909); Bottner (1921); Fry (1928); Patey (1931); Zymbal (1933); Harvey et al (1938); Muir (1941); and others who have accepted without question the belief that they contain "cartilage", have devised various explanations as to the origin of the "cartilage". Harvey et al (1939) suggested that it was not true cartilage but pseudo-cartilage or a

myxo-chondroid substance developed probably by degeneration; the epithelial cells of which are isolated in a retraction space in the acellular homogeneous mucoid matrix giving all the appearances of cartilage cells within their capsule. Fry (1928) suggests that a similar appearance is given by a ring of deeply staining mucin round isolated cells.

By far the majority of pleomorphic adenomata arise in the parotid gland, less commonly in the submandibular, and rarely in the sublingual gland. They are, however, also found in the palate and various parts of the oro-facial region such as the lips, nose, pharynx or lacrimal glands; arising probably from serous or mucous glands. Submandibular tumours have been specially considered by Chevassu (1910) and Dockerty & Mayo (1942), while Paget, S. (1886); Eggers (1928); D'Aunoy (1930); Davis (1935) and Stobie (1935) have discussed palatal tumours. Lacrimal gland tumours were considered by Verhoeff (1904)

and those of the lip by Paget, J. (1851) and more recently by Bernier (1946).

The commonest age of first appearance of the tumour is between the third and fourth decade, but no age is exempt. Byars et al (1957) state that 5% occur before the age of 18 years, while McFarland (1926) considered 66% occurred before the age of 40 years and 90% before the age of 50 years. Occasionally the condition is first encountered in infancy; Pailler (1903) reported a case of a mixed tumour in a child of eleven months and Wood (1904) in an infant of seven months. Examples reported appearing in the first decade of life include Chevassu (1910) and Zymbal (1933) at 9 years; and Fry (1928) at 10 years. Schilling (1921) reported a case occurring in a 41 year old man that had been present since he was 1 year old. McFarland (1942) out of 380 cases found 8 occurring in the first decade. The tumours exhibit a slow imperceptible, intermittent growth and the shortest reported duration

before operation was 6 months (Bland-Sutton, 1906). The longest periods recorded prior to operation vary from 40-60 years in the cases reported by Street (1913) and Ross (1955) respectively.

Although in recent years, most reported series show a predominance of females, most earlier workers stated that the sexes showed little difference in their liability to pleomorphic adenomata of salivary tissue. In spite of the literature being mainly of European and American cases, they have been reported to occur in Chinese (Balme, 1912 and Yen, 1915); and in Hindus (Davidson, 1910 and Street, 1913), while McFarland (1942) reported seven in black-skinned people. Hickey (1957) considers pleomorphic salivary adenomata of the palate and tongue relatively common in Sudan.

In some cases, gross deformity has been produced yet the host shows little ill-effect. According to Heister (1739) he had never met any directions for the removal of

the parotid or submaxillary glands, though these glands indeed "frequently indurated and enlarged to a monstrous size". Removal of the tumour was considered dangerous and unjustified, often the patient refused surgery as in Cotterill's (1907) case, (Fig.1), which has been regarded by McFarland (1943) and others as the largest tumour recorded. The reported weight of 26 lb. was only an estimate, as the patient refused operation. As these tumours have in the past received only a passing mention, details were often scanty and the weight, when it was mentioned, was not necessarily accurate. Witness Keen's (1904) case which was said to

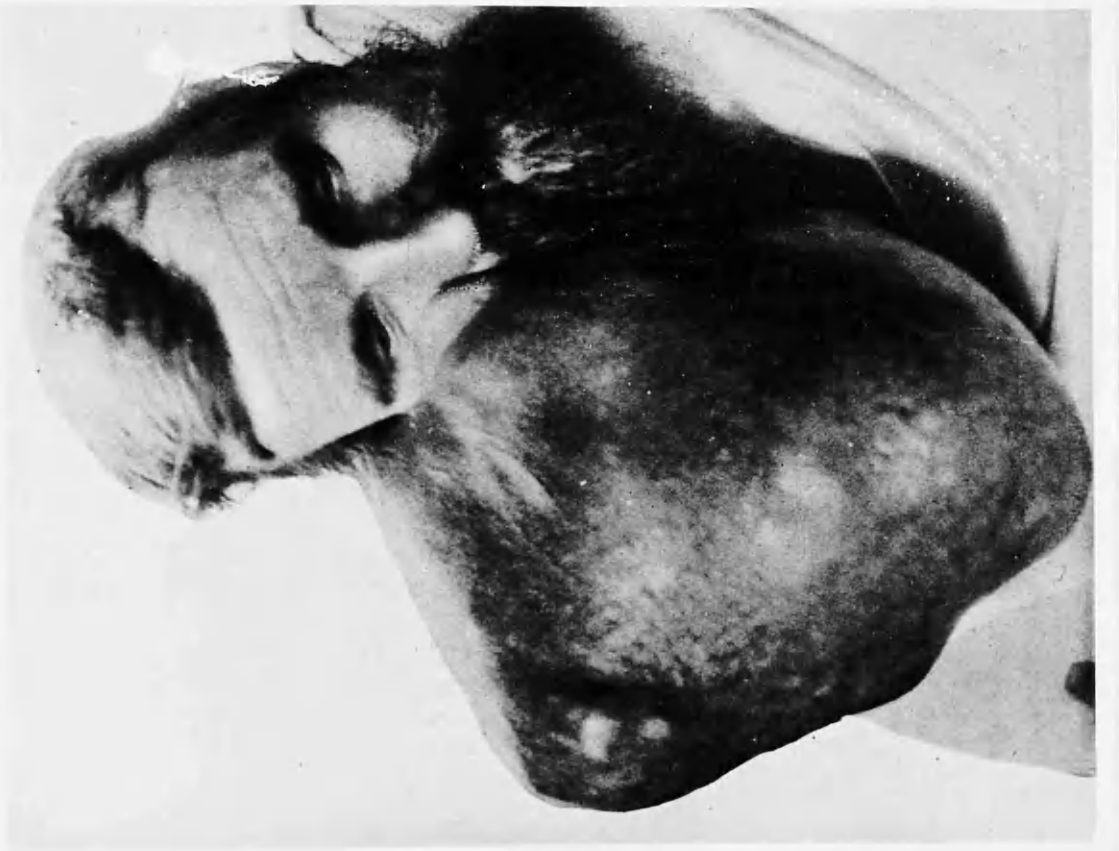


Fig. 1.

Photograph of Cotterill's case.

(by permission of the
publishers, W. Green & Son,
Ltd., Edinburgh).

be 7lb.; the excised tumour weighing only 4¾lb. at operation, but an allowance was made of 2lb. for the fluid lost when the tumour was "burst" a year before the operation. Amongst the largest surgically treated and confirmed histologically as "mixed" are those shown in the following Table. In the case of

Short & Puller (1955) is included in this series (Case No. 22) as she had been treated at the Glasgow Royal Infirmary between 1935-56.

TABLE VI.

Other giant parotid tumours classified histologically as "mixed".

AUTHOR.	WEIGHT.	SIZE.	SEX.	AGE at onset.	DURATION in years.
Spence,(1863).	3.1 kg.	$9\frac{1}{2}$ x $8\frac{3}{4}$ x $7\frac{3}{4}$ inches.	F.	18	16
Rouville & Martin, (1904)	2.95 kg.	____	F.	14	30
Ahlbom,(1935).	2.25 kg.	____	F.	30	17
Frazell,(1954).	1.27 kg.	22 cm. diam.	F.	38	6
Cade,(1954).	1.99 kg.	19 x 15 x 13 cms.	M.	54	18
Short & Puller, (1955).	2.8 kg.	30 cm. diam.	F.	33	16

Opinions vary slightly as to the recurrence rate, for example, Wood (1904) quotes 30%; Benedict & Meigs (1930) 42.5%; Stein & Geschickter (1934) 20%, and McFarland (1942) 25%. Such recurrences are more frequently encountered in parotid tumours, probably because of anatomical relations (Patey, 1940).

Carcinomata.

There is often no sharp line of demarcation between an unusually active pleomorphic adenoma and a frank carcinoma. As Fry (1928) suggests, however, there are varying degrees of malignancy and that the incidence is higher than is generally appreciated, reports varying from 10-50%. On an average, according to Foote & Frazell (1954), the age incidence is 10 years older than in pleomorphic adenomata, while Quattelbaum et al (1946) give the average age as 49.8 years. Dick (1954), however, reported a case of a small cell carcinoma arising in the left cheek of a two day old boy. Like other tumours of Salivary tissue, the parotid gland is the commonest site (Sirsat, 1953), followed by the submandibular and sublingual glands - the palate being an intermediate site. As a rule such cases are unilateral and apparently malignant from the onset, the growth being accordingly more rapid and there is a shorter

interval before patients present for treatment. In malignant salivary tumours there appears to be no preference for side, and there is little difference in the sex distribution as reported by previous workers. According to Redon (1953), less than 10% survive 5 years after receiving treatment.

Unlike other salivary tumours, the features of Salivary Carcinomata appears to be perineural involvement with pronounced infiltration (Bauer & Fox, 1945; Quattelbaum et al, 1946). So pain and paralysis are common features, as is rapid increase in size. According to Ross (1955), pain is a feature in 50% and 25% show severe paralysis. The capsules of the tumour can rarely be separated from the underlying tissue and they are often fixed to the skin. Metastases do occur; 5 of McFarland's (1942) 13 fatal cases, and 5 of 8 fatal cases in 5 years quoted by Quattelbaum et al (1946), showed pulmonary metastases.

Salivary Adenolymphomata.

Salivary adenolymphomata are a class unto themselves; various names have been applied to them including among others, papillary cystadenoma lymphomatosum, branchiogenic cystadenolymphoma, oncocytoma and Warthin's tumour. They were first reported by Hindelbrandt in 1898 but were only established as a distinct morphological entity in 1910 by Albrecht & Arzt, being composed mainly of epithelial and lymphoid tissue in or near the parotid gland. Nicholson (1923) reported the first case in British literature. No case, according to Carmichael et al (1935), has been correctly diagnosed before operation; this statement, however, is inaccurate, as some can be diagnosed correctly.

As with pleomorphic adenomata various theories as to their origin have arisen. Noteworthy one being branchiogenic - suggested by Ssobolew (1912) and supported by others, although not in vogue to-day. Another suggested by Warthin (1929), after whom the tumour is

is sometimes called, is that they arise from the epithelium of the embryonical pharyngeal entoderm or the upper respiratory tract displaced to the region of the parotid gland. Among those supporting this theory are Gaston & Tedeschi (1946), Kawson & Horn (1950), Robinson & Harless (1943) and Kraissl & Stout (1933). A third more acceptable theory, originally postulated by Albrecht Arzt (1910) and recently supported by Harris (1937) and Martin and Ehrlich (1944) is that they represent heterotropic salivary gland rests situated in lymph glands adjacent to or in the parotid. Jaffé (1932) pointed out that such tumours are usually situated on the external surface of the gland although the capsule of the tumours may fuse with the capsule of the gland. He regarded lymph tissue as not an essential part of the tumour but merely as a remnant of a lymph node. Yet another theory was recently postulated by Thomson & Bryant (1950) who made an extensive study of the subject, including detailed examination of human embryos; normal human salivary glands; branchiogenic cysts,

sinuses and 23 tumours. On their findings they relate the tumours to "neoplastic proliferation of the parotid ducts included in lymph glands". Hamperl (1931) suggested the oncocytes as the site of origin, but Ackerman (1943) considered oncocytomata as a different entity from adenolymphomata. Meza-Chávez (1949), however, showed the occurrence of oncocytes in normal parotid glands - being found in 9 out of 100 glands from 51 persons.

Adenolymphomata are rarely found in sites other than the parotid gland (Plaut, 1942). A few bilateral cases have been reported (Nino, 1940; Oughterson, 1941; Ramage et al, 1943; Lederman, 1943; Martin & Ehrlich, 1944; Lawrence & Procita, 1948; Foote & Frazell, 1953, and Schulenberg, 1954). They occur at any age, but are generally encountered in the seventh decade. Plaut (1942) gives the figure as 84% occurring after the age of 40 years. The youngest case recorded is in a boy aged 2½ years (Stohr & Risack, 1926) and the oldest in a man aged

92 years (Carmichael et al, 1935). Most previous workers have shown a decided sex difference; it being more common in female patients. A few malignant cases, have been recorded, (Ssobolew, 1912; Stohr & Risack, 1926; Lederman, 1943; Lloyd, 1946; and Gaston & Tedeschi, 1946), otherwise recurrences are rare.

Miscellaneous Tumours.

Numerous other salivary tumours, reputed to have arisen in or adjacent to the Salivary glands have in the past been classified as sarcomas. Other less common tumours include:-

a). neurofibromata (McFarland, 1926; Wheelock & Madden, 1949),

b). lipomata (Dockerty & Mayo, 1942),

c). angiomata (McFarland, 1926; Wheelock & Maddin, 1949),

d). rhabdomyomata (Prudden, 1883; Wood, 1904),

e). leiomyomata (Wheelock & Maddin, 1949),

f). lymphangiomata (Kennon, 1921; Wheelock & Maddin, 1949),

g). malignant melanomata (Rodriquez, 1889; Gilis & Godlewski, 1905 and Haggard, 1919).

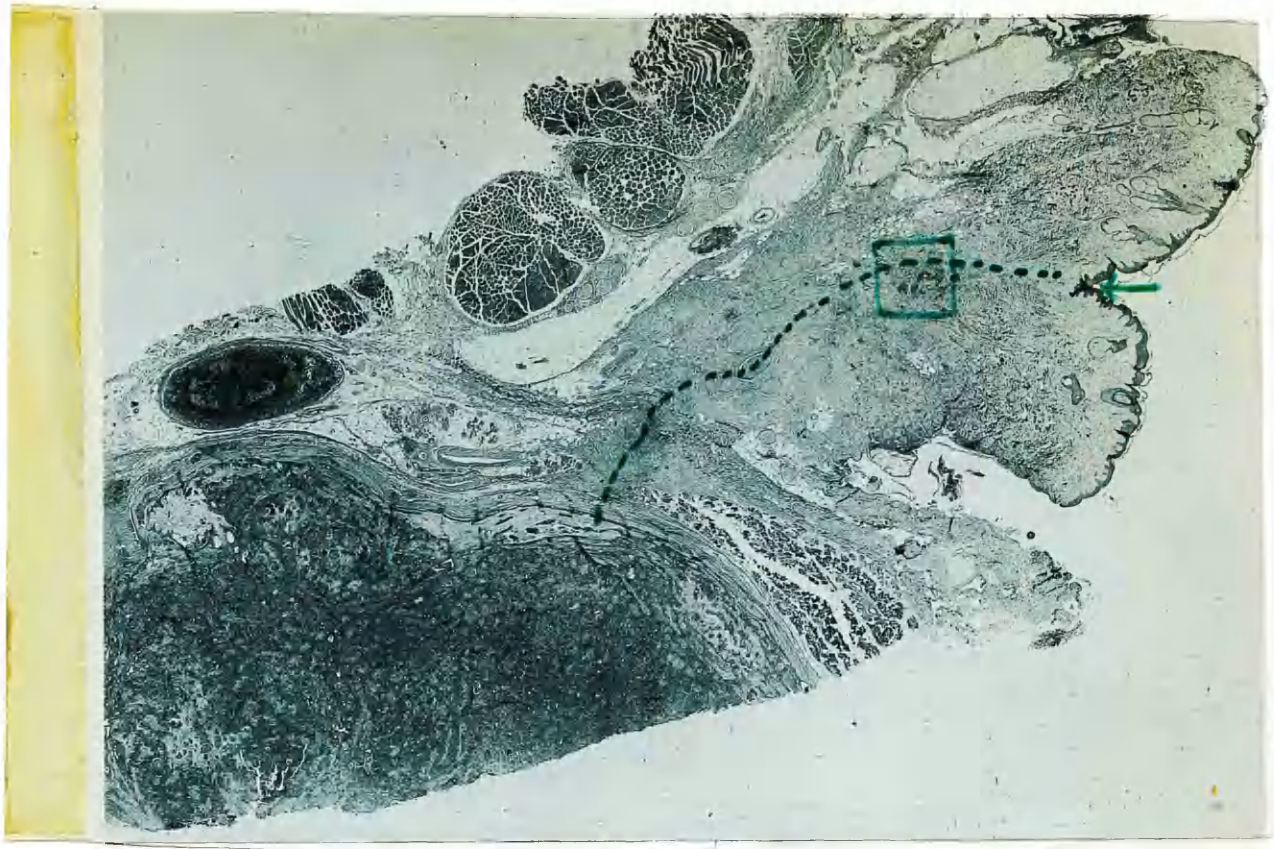
Haemangiomata, however, deserve brief comment - usually of the hypertrophic variety and found in infants

or children, are the commonest cause of chronic unilateral parotid swelling in the first year of life.

Treatment

Tumours of salivary tissue are either potentially malignant, borderline, or definately malignant (Ross,1955), and should, therefore, not be neglected. Patey (1940) suggested that there should be no hurry to operate and that the pre-operative period should be used to observe and determine the rate of growth and the presence or absence of pain or paralysis. Sialography has not in the past been used very extensively, but careful study of radiographs does add another very worthwhile, yet unessential, pre-operative examination. A concise portrayal of the method is given by Blady & Hocker (1938-9).

Minor operations such as enucleation are inadequate and should be condemmed, while biopsies are generally considered, howadays, as just meddlesome surgery.



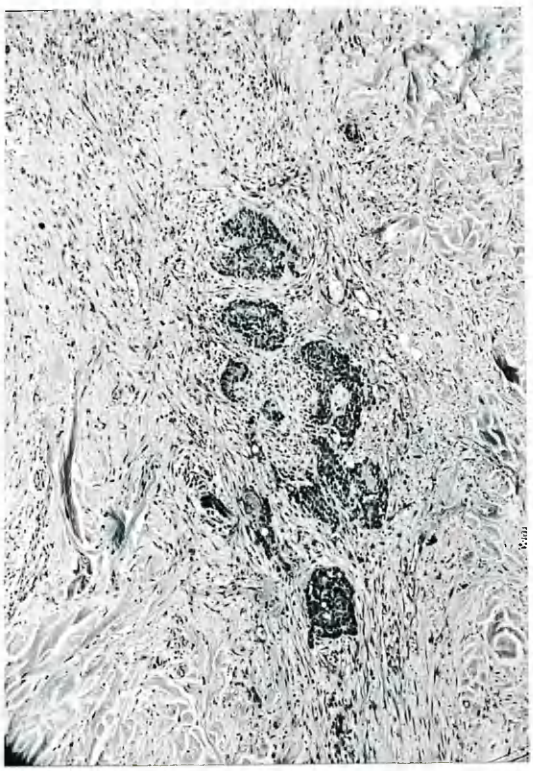
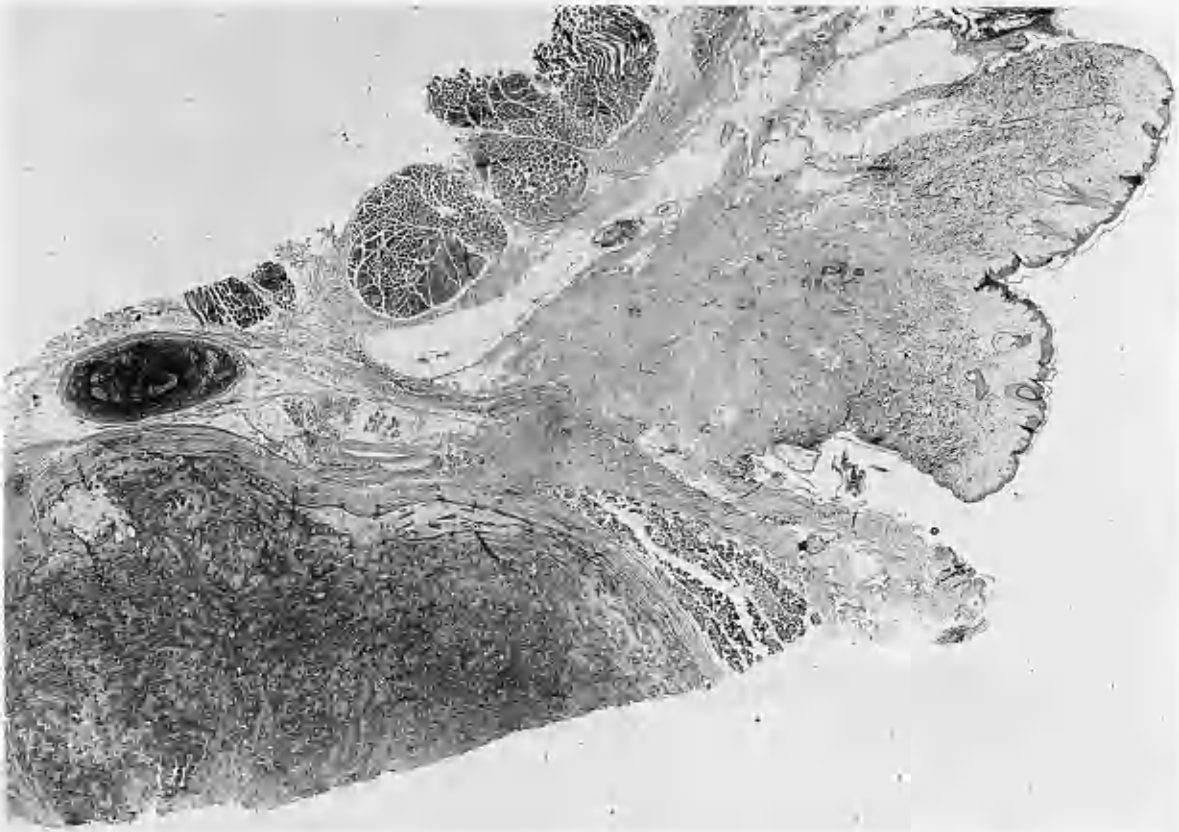


Fig. 2. (above) shows a nest of tumour cells implanted in a needle tract. The dotted line is the needle tract, as indicated by scar formation and recent healing. Fig. 3 (left) H.P. cell nest.

(by kindness of Dr. Ackerman and also the photomicrographs).



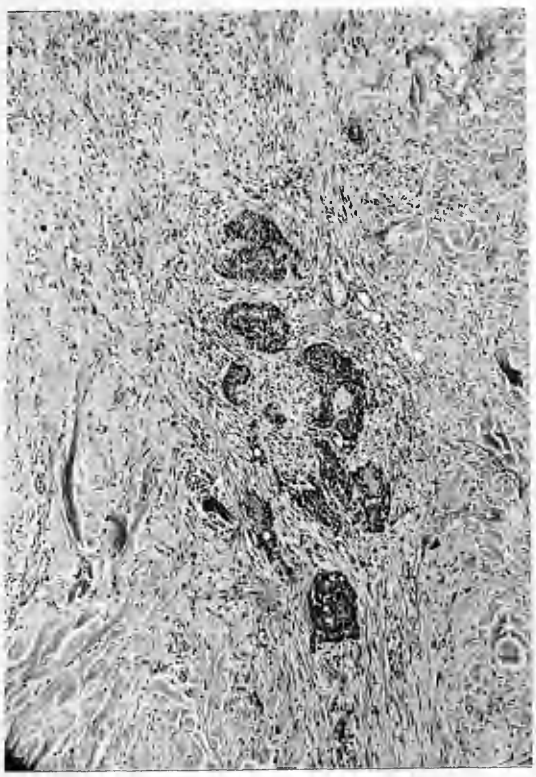


Fig. 2. (above) shows a nest of tumour cells implanted in a needle tract. The dotted line is the needle tract, as indicated by scar formation and recent healing. Fig. 3 (left) H.P. cell nest.

(by kindness of Dr. Ackerman and also the photomicrographs).

Although preliminary biopsies are advocated by Byars et al (1957), they demonstrate (figs. 2 & 3) how a nest of tumour cells can become implanted in a needle tract of an aspirated biopsy. These "key-hole" operations, besides being inadequate, tend to spread the tumour cells and make a recurrence almost a certainty. Parotidectomy is replacing enucleation as the standard treatment of salivary tumours - partly because of the belated recognition of the frequency of infiltrating types which cannot be removed by enucleation due to satellite tumours closely associated with the larger one (Fitzgibbon, 1953)- suggestive of multicentric origin. Parotidectomy was established in the 1940's as the routine treatment for parotid tumours by Janes, (1940); Bailey, (1941); and Redon, (1953 & 5). Janes (1957), rather than accept the multicentric origin theory for multiple recurrence, considers them due to "seeding of the wound through rupture of the tumour capsule".

One of the reasons for inadequate surgery is the inherent fear of damage to the facial nerve (Patey, 1940). A paralysed face is a real calamity and a very difficult fact to explain to a patient, especially those who appeared to have only a movable nodule prior to surgery, but which, in fact, are only the "top of the mountain" (Ross, 1955), such dumb-bell tumours are described by Proby (1924); Leriche (1935) and Patey (1957). Due to the extremely low recurrence rate of the French workers, Redon & Belcour (1955) and Moyse (1955), the case for routine superficial lobectomy is strong. Holmberg & Glover (1951) state that surgical excision is the correct form of treatment, as the majority of salivary tumours are radio-resistant (Patey & Thackeray, 1954). Radio-therapy is, however, of value pre-operatively (Patey, 1940) to toughen up the capsule. It is also used beneficially post-operatively, but according to most its record as the sole form of treatment is NOT convincing.

PART II.

Clinical material and results of investigations.

The classification of salivary tumours used throughout this thesis is a modification of that of Willis (1953), and the classification along with the number of cases is shown in the following table.

TABLE II.- CLASSIFICATION OF SALIVARY TUMOURS

TYPE		No.	%
I	Simple Adenoma	–	–
II	Pleomorphic Adenoma	315	78.5
III	Carcinoma	64	16.0
IV	Adenolymphoma	16	4.0
V	Miscellaneous	6	1.5
TOTAL		401	100

The distinction between simple adenoma and pleomorphic adenoma is so artificial that the first two types can be grouped together. Not a case was found which could be classified wholly as a simple adenoma. With this in mind, only the last four types of salivary tumour will be considered.

Pleomorphic adenomata.

There are in this series 315 examples of pleomorphic adenomata, constituting 78.5% of the total. By far the majority of them arise in the parotid gland, less commonly in the submandibular, and rarely in the sublingual. The site distribution reported by several workers is contrasted with the present series in the following table.

TABLE III.

Showing the site distribution of 315 pleomorphic salivary adenomata as compared with that of previous workers.

Author.		Parotid.	Submandib.	Subling.	Palate.	Lip.	Misc.	Total.
Present series.	R.	142	8	0	14	9	7	315
	L.	123	11	1				
	Total.	265	19	1	14	9	7	315
Wood,(1904).		35	13	0	3	4	4	59
Shreiner & Mattick,(1929).		45	7	0	1	9	4	66
Patey,(1931).		38	6	1	5	1	3	54
Zymbal,(1933).		55	2	0	0	1	0	58
Harvey et al,(1938).		230	21	2	6	9	7	275
Willis,(1953).		35	6	1	5	1	0	48
Ross,(1955).		84	9	0	3	0	2	98

It will be seen that the parotid gland accounts for just over 80% of such tumours. Other series vary from 70% (Sirsat, 1953) to 98% (Montella & Fontana, 1956). Of

Of these 265 tumours occurring in the parotid gland, 142 cases (53.6%) occurred on the right side - this slight preference for the right side, although not statistical, agrees with the findings of Wilson & Willis (1912) and Benedict & Meigs (1930); while McFarland (1943) states that the left is more frequently involved. From these findings there would be apparently no preference for any side.

The commonest age of first appearance of the tumour was between the third and fifth decade; almost 60% occurred before the age of 40 years and 90% before 60 years of age. Table IV shows the decade distribution of the age at the first appearance of the tumour in the cases in this series. Of the four occurring in the first decade, the earliest age of first appearance was 3 years of age, being treated conservatively until 42 years of age. The remaining three all appeared at 9 years of age with surgery being undertaken 3, 4, and 5 years later, respectively. Most tumours exhibited a slow, intermittent growth and on an

Table IV

Shows the decade distribution of the age at first appearance of the tumour.

Decade.	I	2	3	4	5	6	7	8	9	IO	Total.
Male.	I	I7	20	34	2I	I5	9	5	I	0	I23
Female.	3	2I	4I	46	40	26	I2	2	I	0	I92
Total.	4	38	6I	80	6I	4I	2I	7	2	0	3I5

Table V.

Shows the decade distribution of the age at the time of the first operation. This Table should be compared with the previous Table, in order to determine the rate of growth.

Decade.	I	2	3	4	5	6	7	8	9	IO	Total.
Male.	0	I0	I7	27	28	I8	I3	9	0	I	I23
Female.	0	9	34	35	4I	49	I4	9	I	0	I92
Total.	0	I9	5I	62	69	67	27	I8	I	I	3I5

average 6 years elapsed from the time of first appearance until the initial operation. Table V shows the decade distribution of the age at the time of the first operation in this series. The longest duration before being subjected to surgery, was, in this series, 39 years. There would appear to be a predominance of females in the 315

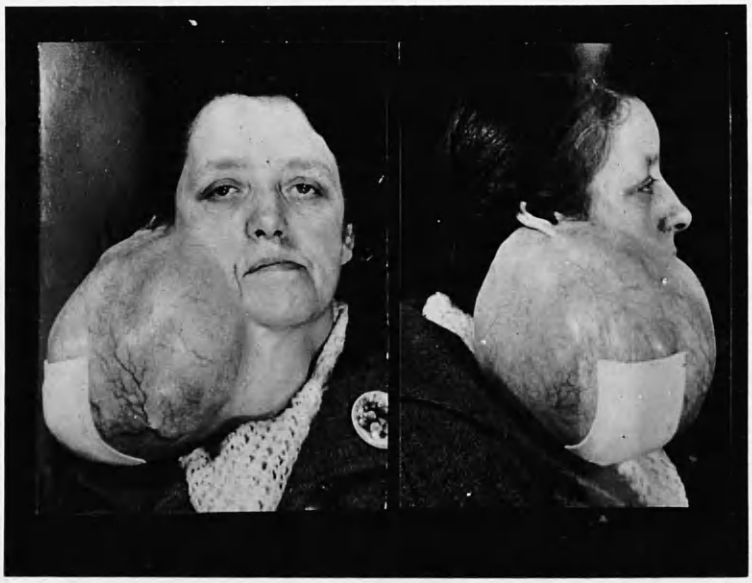
TABLE VI.

Shows the sex distribution of the pleomorphic adenomata in the present series as compared with the figures given by previous workers.

Author.	Male.	Female.
Wood,(I904)	25	2I
Chevassu,(I9I0)	30	27
Wilson & Willis,(I9I2)	30	26
Böttner,(I92I)	I0	I5
Fry,(I928)	II	I4
Ahlbom,(I935)	I06	I48
McFarland,(I942)	I84	2I2
Willis,(I953)	I6	34
Fitzgibbon,(I953)	I9	23
Present series,	I23	I92

cases of pleomorphic adenomata. The figures of previous workers, together with the present series, are seen in Table VI. Although most of the patients were British, two were Hindus. The largest tumour met with in this series was that reported by Short & Puller (Case No.221), included here because she was treated at the Glasgow Royal

Fig.4. Photograph of the largest tumour met with in this series.



Infirmary between 1935-56. The recurrence rate was 29.5%, and details of these recurrences together with

TABLE VII.

Shows the recurrence rate of Pleomorphic Adenomata at their sites of origin.

	Parotid.	Submandib.	Subling.	Palate.	Lips.	Misc.	Total.
Recurrences	78	7	I	2	I	4	93
Non-recurrences	I87	I2	0	I2	8	3	222
Total.	265	I9	I	I4	9	7	315

their sites are seen in Table VII. The average time interval between the original operation and subsequent excision in this series was 4 years. These tumours must be differentiated from tuberculosis, actinomycosis, and chronic adenitis due to oral-aural sepsis (Boyd,1938). Most can diagnose with a fair degree of accuracy a salivary tumour, but to differentiate salivary tumours

among themselves is probably an almost impossible task before operation. All such tumours, however, should be looked upon as malignant or potentially malignant until proved otherwise.

Not one reference was found of any previous report of pleomorphic adenomata affecting more than one member of a family. Yet, in the present series, familial incidence was found on three occasions.

A. On 2/9/52 a man aged 51 years presented at the Southern General Hospital with a left-sided submandibular tumour of 1 year's duration which was excised. Histology of the tumour tissue showed

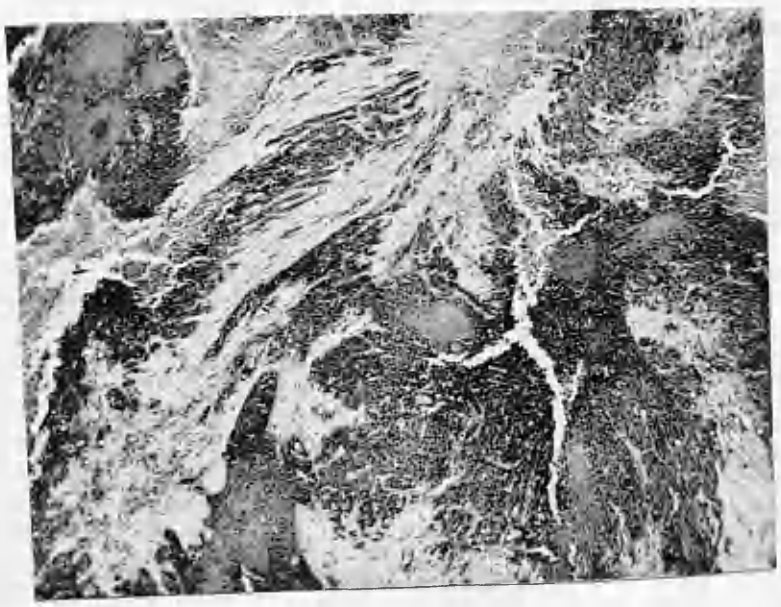


Fig.5. Photomicrograph of the father's tumour. (HxE. x 50).

epithelial islets in a myxomatous stroma, with extensive areas of squamous metaplasia (Fig.4). He died on 11/8/54 having had, in the interval, two recurrences with the same histological picture. On 3/4/53 his 21 year old son presented with a left-sided parotid tumour of two years

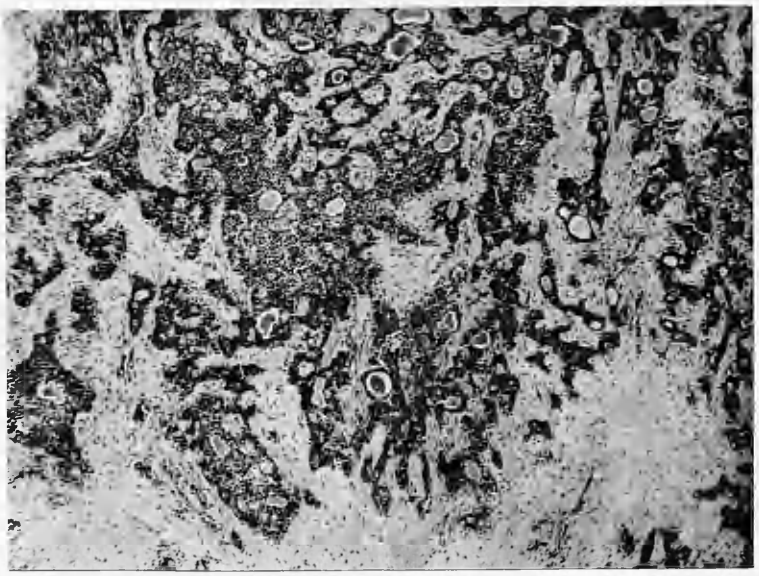


Fig.5. Photomicrograph of the son's parotid tumour. (H. and E. x 50).

duration. Histologically the tumour had the appearance of a typical "mixed" parotid tumour (Fig. 5). He has had, to date, no recurrence. The daughter, when aged 21 years had, on 6/12/55, a right-sided parotid tumour excised, after it had been present for two years. This tumour showed a typical pleomorphic adenoma with a predominance of matrix and relatively few

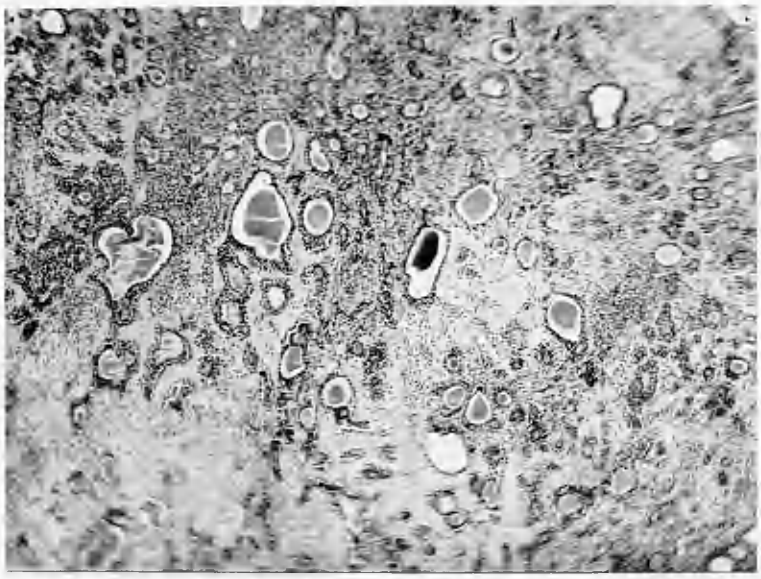


Fig. 6. Photomicrograph of the sister's tumour. (H.and E. x 50).

epithelial elements (Fig.6.)

B. A 21 year old man was seen in December 1956 at the Glasgow Royal Infirmary with a recurrent right-sided parotid tumour. Previous excision having been on 30/7/49 when it was reported as a typical pleomorphic adenoma. Subsequent excision in January 1957 revealed a more cellular pleomorphic adenoma (Dr. A. Currie). It was noted that his father (54 years old) had a right-sided parotid tumour of 12 years duration. He has, to date, refused operation, but clinically the diagnosis is without doubt (Prof. W. A. Mackey).

C. At the follow-up of this series a 25 year old married woman was seen at the Glasgow Royal Infirmary in December 1956, where, on 23/4/47 she

had had a tumour excised from her left parotid region, having been present for the previous 2 years. This tumour had been reported as a typical "mixed" parotid tumour with extensive areas of myxomatous stroma. When seen in December 1956 she had no sign of any recurrence and volunteered the information that her 50 year old mother had had a "lump" removed from the left side of her face when 18 years of age, somewhere in England. She had been told that it was likely to recur as it was a "mixed cyst of her saliva glands". To date, however, there has been no recurrence.

In Table VIII it is seen that in family A there is histological proof in all three cases (Dr. A. Dick).

FAMILIAL INCIDENCE OF "MIXED SALIVARY TUMOURS"

a.	**Father aet 51**	**– 2. 9. 52**	**– Mixed submandibular tumour**
	Son aet 21	**– 3. 4. 53**	**– Mixed parotid tumour**
	Daughter aet 21	**– 6. 12. 55**	**– Mixed parotid tumour**
b.	**Father aet 54**	**– 3. 12. 56**	**– Clinical Mixed parotid tumour**
	Son aet 14	**– 30. 7. 49**	**– Mixed parotid tumour**
c.	**Mother aet 18**	**– 1924 in England**	**– "Mixed cyst of Saliva Gland"**
	Daughter aet 16	**– 23. 4. 47**	**– Mixed parotid tumour**

In "B" clinical observations must be relied upon since the father prefers, in the meantime, to retain his tumour; while in family C, the history of pelomorphic adenoma in the mother is so circumstantial as to be almost certainly valid.

Carcinomata.

There will be seen from the following two tables that the age incidence at the time of first appearance of salivary carcinomata is between the fifth and eighth decade. In view of the more rapid increase in size and the associated symptoms of pain and/or paralysis, there is a shorter interval before the patient received treatment - in this series 2-3 years on an average.

In no case in this series was bilateral salivary carcinomata diagnosed, and like other tumours of salivary tissue, the parotid gland was the commonest site, followed submandibular gland, palate and one in each of the

TABLE IX.

Shows the decade distribution of the age at the onset of Salivary Carcinomata.

Decade.	I	2	3	4	5	6	7	8	9	I0	Total.
Male.	I	3	2	I	8	9	7	7	I	0	39
Female.	I	I	3	0	3	5	8	4	0	0	25
Total.	2	4	5	I	II	I4	I5	II	I	0	64

TABLE X.

Shows the decade distribution of the age at the time of the first operation for Salivary Carcinomata. To be compared with Table IX, in order to determine the rate of growth.

Decade.	I	2	3	4	5	6	7	8	9	I0	Total.
Male.	0	I	I	3	5	I0	9	9	I	0	39
Female.	0	2	0	2	I	5	9	6	0	0	25
Total.	0	3	I	5	6	I5	I8	I5	I	0	64

following sites, the sublingual gland, nose, tongue, and lip. This is shown in Table XI which also shows that in this series there would appear to be no preference for side in salivary carcinomata.

TABLE XII.

Shows the sex distribution of Salivary Carcinomata in this series at their sites of origin.

	Parotid.	Submandib.	Subling.	Palate.	Lips.	Nose.	Tongue.	Total.
Male.	27	6	0	5	0	I	0	39
Female.	20	I	I	I	I	0	I	25
Total.	47	7	I	6	I	I	I	64

TABLE XI.

Shows the site distribution of Salivary Carcinomata.

	Parotid.	Submandib.	Subling.	Palate.	Lips.	Nose.	Tongue.
Right.	24	3	0	6	I	I	I
Left.	23	4	I				
Total.	47	7	I	6	I	I	I

In malignant salivary tumours there appears to be a slight predominance in males - this difference in the sex distribution does not appear to have been so marked in previous reviews. (Table XII).

As will be seen in Table XIII, recurrences were noted in 58 of the 64 cases and in the remainder, death had occurred in 4 very shortly after operation due to other causes.

TABLE XIII.

This Table shows the recurrence rate in Salivary Carcinomata in relation to the site of origin.

	Parotid.	Submandib.	Subling.	Palate.	Misc.	Total.
Recurrences.	41	5	I	6	3	58
Non-recurrences.	6	2	0	0	0	8
Total.	47	7	I	6	3	64

In 4 of the 8 non-recurrences, death occurred shortly after the first operation due to natural causes.

The incidence of salivary carcinomata is much higher than is generally appreciated - in this series it accounts for 16% of the total of salivary tumours. Various reports of previous reviews, together with the present value, is

given in Table XIV.

TABLE XIV.

Showing the percentage incidence of Salivary Carcinomata.

Nasse,(I892)	II%.
Wood,(I904)	25%.
Kennon,(I92I)	22%.
Benedict & Meigs,(I930)	42%.
Stein & Geschickter,(I934)	I5%.
Slaughter et al,(I953)	26%.
Ross,(I955)	22.8%.
Present series,	I6%.

Adenolymphomata.

They occupy about 4% of the salivary tumours in this series and are a class unto themselves. Unlike Carmichael et al (1935), three at least of these tumours

were diagnosed correctly before operation. All but one of the 16 adenolymphomas occurred in the parotid gland, the one abstainer occurred in the right tonsil. In this series bilateral adenolymphomata was found in four cases - of the remainder 7 occurred in the left parotid and 4 in the right parotid gland. The finding of previous workers, that they were commonder in females was not shown in this series (Table XV).

TABLE XV.

Shows the sex ratio of Adenolymphomata in the present series as compared with that in previous reviews.

Author.	Female.	Male.	Ratio.
Carmichael et al,(I935).	24	4	6:I
Plaut,(I942).	50	I2	9:2
Martin & Ehrlich,(I944).	20	2	I0:I
Gaston & Tedeschi,(I946).	73	I7	9:2
Lloyd,(I946).	5	I	5:I
Hevenor & Clark,(I950).	I9	I	I9:I
Present series,	8	8	I:I

Not a single case was found in the first three decades of

TABLE XXVI.

Shows the decade distribution of the age at the first appearance of Adenolymphomata.

Decade.	I	2	3	4	5	6	7	8	9	IO	Total.
Male.	0	0	0	I	I	I	3	2	0	0	8
Female.	0	0	0	2	I	2	I	2	0	0	8
Total.	0	0	0	3	2	3	4	4	0	0	I6

TABLE XVII.

Shows the decade distribution of the age at the time of the first operation for Adenolymphomata.

Decade.	I	2	3	4	5	6	7	8	9	IO	Total.
Male.	0	0	0	I	I	0	3	2	I	0	8
Female.	0	0	0	I	I	I	3	2	0	0	8
Total.	0	0	0	2	2	I	6	4	I	0	I6

life, in this series. The age distribution at the onset and at the time of first operation is shown in Tables XVI and XVII. There was no recurrence noted in any case to date, and no case was reported as malignant.

Miscellaneous Tumours.

In this series, only six tumours were included to come under this catergory. They included two melanomas, two reticulum cell sarcomas, a recurrent leiomyosarcoma, and a fibroma. Recurrences had occurred in all but the fibroma, and death had occurred in all the patients before the follow-up was possible.

Histological Review.

Reference has already been made to the varied structure of pleomorphic adenomata and now only the commonest variations which were encountered will be shown. The findings recorded in this section accord with the descriptions of earlier workers, in particular of Zymbal (1933) and of Willis (1953); the former giving by far the best account of the microscopical structure of salivary tumours.

In some tumours, many or all the possible variations of structure may be found in close juxtaposition with all gradations between them; while in others, one or another structural variant predominates. The following types of structure will be described in turn:-

a). normal salivary tissue,

b). atypical glandular tissue with or without epithelial sprouting,

c). solid epithelial formation,

d). epithelial masses with cystic spaces,

e). cornifying squamous metaplasia,

f). variations in the proportions of the epithelial elements and the matrix, and finally,

g). areas of "pseudo-cartilage".

a) Normal salivary tissue.

Salivary glands are termed compound racemose glands, consisting of numerous lobes, which are made up of lobules, connected together by dense areolar tissue, vessels and ducts.

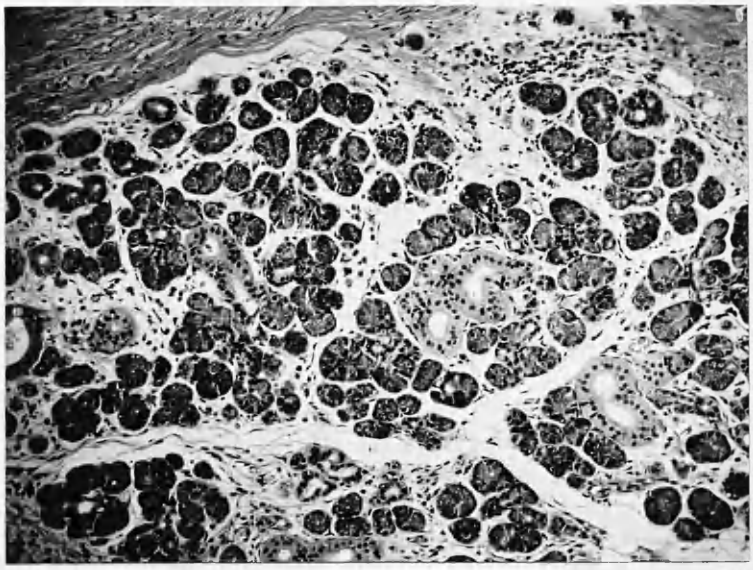


Fig.7. Photomicrograph of normal salivary tissue. (H.andE.x 100).

Each lobule consists of a ramifaction of a single duct, the branches ending in slightly dilated ends and alveoli on which the capillaries are distributed. The alveoli of salivary glands are of two kinds, mucous and serous. The

cells of the mucous alveoli are columnar in shape and the nucleus is usually situated near the basement membrane and is flattened. The cells in the serous alveoli fill the cavity almost completely in the resting condition. The cells are more cubical and the nucleus is spherical and central in position. The ducts are lined at their origin by low cubical epithelium, but as they enlarge the epithelial cells change to columnar type; near the opening into the mouth the epithelium becomes stratified. The photomicrograph (Fig.7.) shows a typical normal salivary tissue.

b). Atypical glandular tissue.

This is seen in a great variety of forms. They may be acinar or ductular in type; cystic or papillary; and they may contain mucoid or hyaline material. Predominance of the goblet-cell epithelium is sometimes seen as in the cases of, Schilling (1921), Lepp (1939), De & Tribedi (1939), Skorpil (1940), Linell (1948), and Cooray

et al (1950). On occasions it is associated with squamous-cell epithelium and some workers believe such tumours to form a distinct group of "muco-epidermoid" tumours and state that they account for approximately 50% of salivary tumours. Stewart et al (1945) found 45 cases out of 700 salivary tumours; the site of origin would appear to be in the salivary ducts. Hartz (1946) was the first to describe such a tumour accurately. Foote & Frazell (1954) rather than subdivide them into benign and malignant, use the terms high and low grade malignancy. They found 51 low-grade and 47 high-grade tumours out of a total of 900 cases (1929-49). According to Du Plessis (1957), in 28% of normal parotid glands sebaceous glands may arise from the parotid ducts, thus explaining the site of origin of such "muco-epidermoid" tumours.

The classical ductular type is seen in Fig. 8., while a relatively common pattern (Figs.9 & 10) is that in which the glandular tissue merges into the mucinous matrix. This

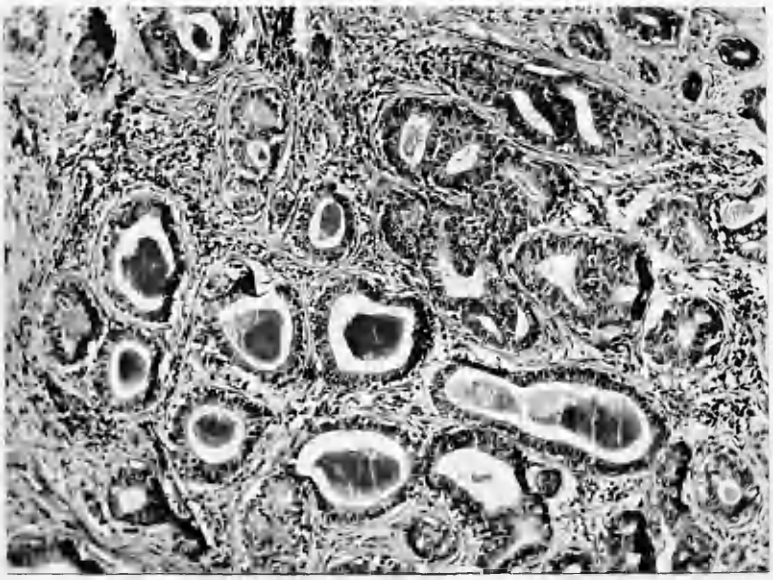
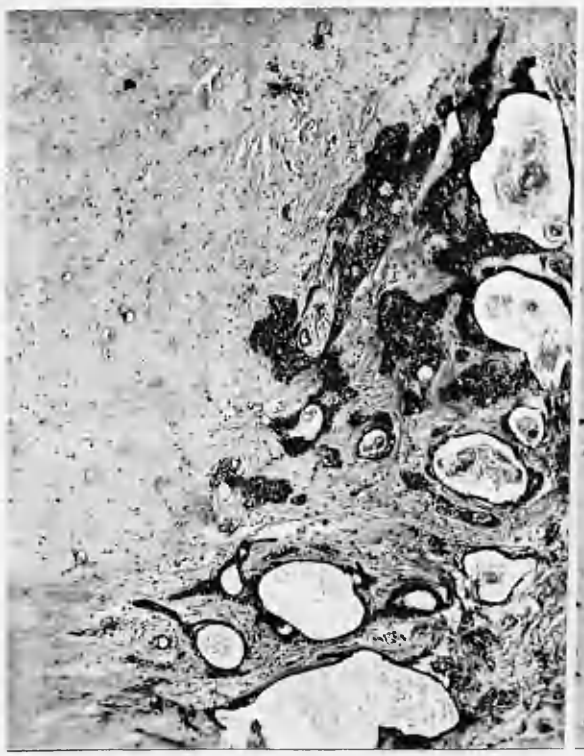
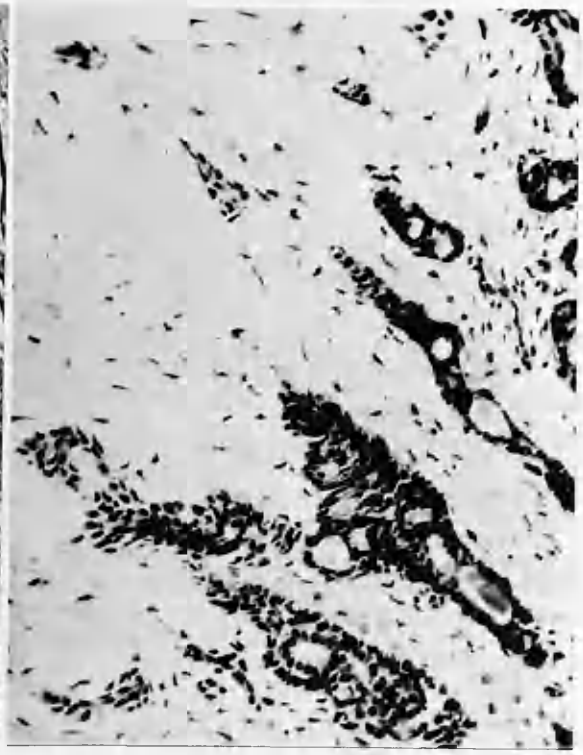


Fig. 8. Photomicrograph showing a glandular type of pleomorphic adenoma. (H.& E. x 100).

finding is well described by Zymbal (1933), and is shown by epithelial sprouting from the glandular formations. This fraying out of the epithelium is a common way of development of the so-called "mucoid tissue".





Figs. 9 & 10 Glandular tissue merging into mucoid matrix.
H. & E. X 50 H. & E. X 100.

A feature not uncommonly encountered is the presence of extensive areas of hyalinisation (Figs. 11 & 12).

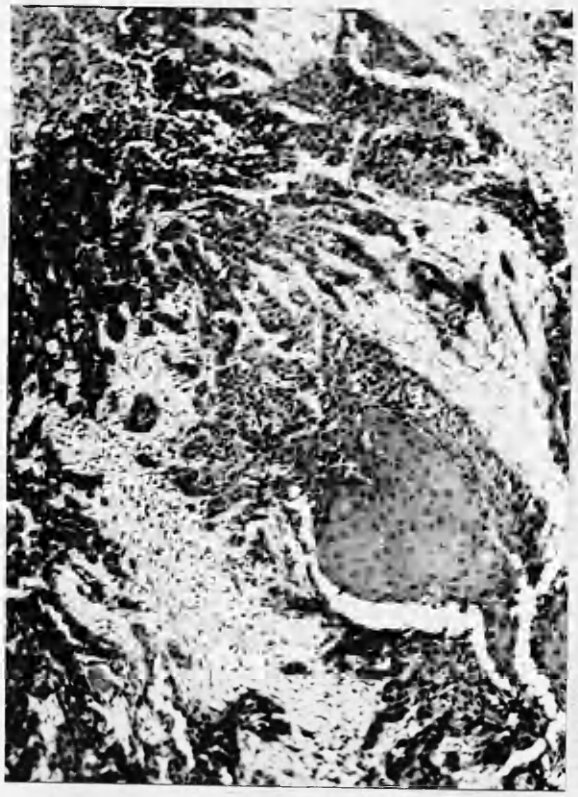


Fig.11. Photomicrograph showing areas of hyalinisation. (H. & E. x 100).

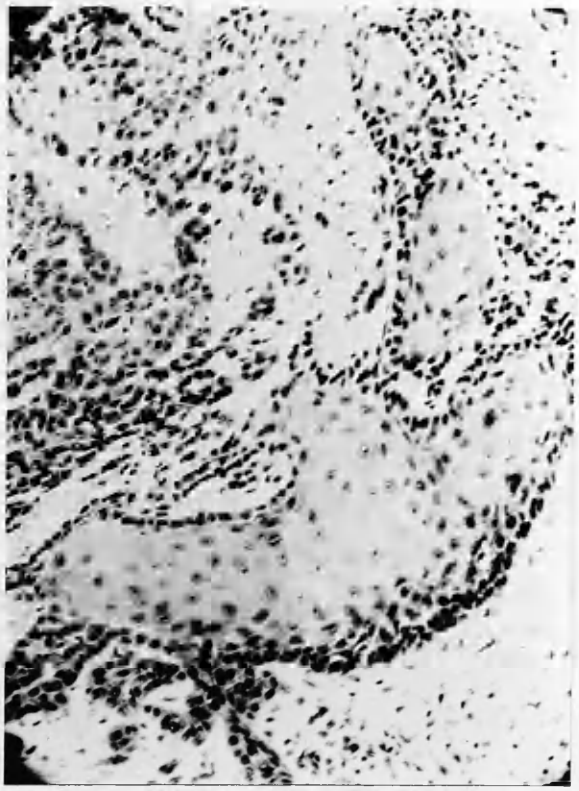
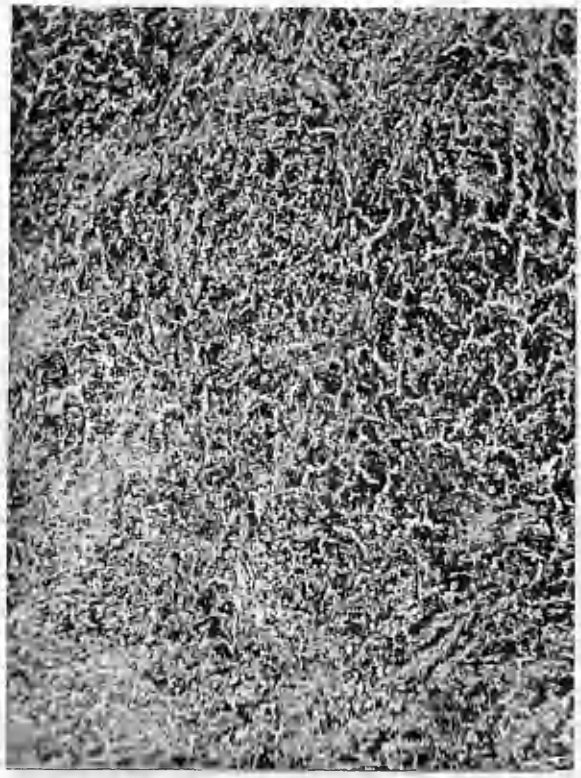


Fig.12. A more high-power view is seen. (H. & E. x 250).

c). Solid epithelial formation.

These are again of very diverse appearance. Many tumours contain a fairly solid glandular epithelium.



The case illustrated in Fig. 13 was the only one in the series which bore any resemblance to a simple adenoma. In solid epithelial tumours of this type, the glandular structures may be arranged in tubular or cylindromatous fashion, as in Fig. 14.,

Fig. 13.
(H. & E. x 50).

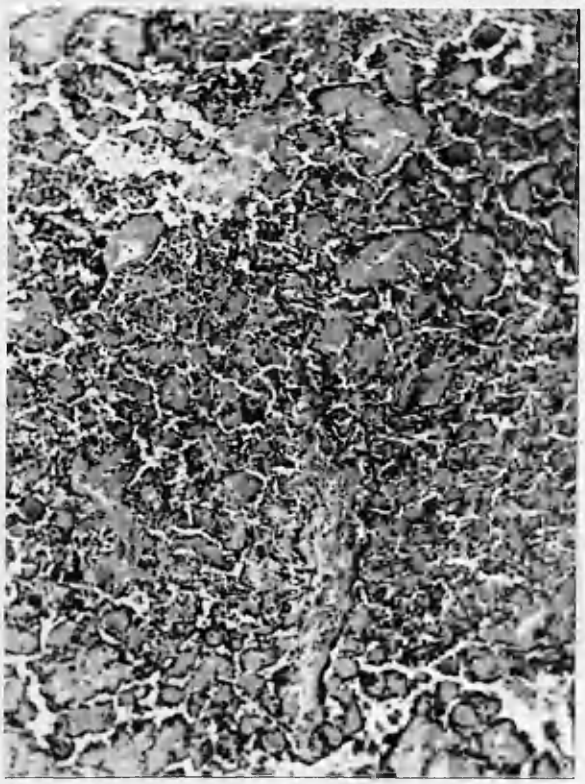


Fig.14.
Photomicrograph of a tubular or cylindromatous type of pleomorphic adenoma.
(H. & E. x 100).

or acinar formation (Fig.15) or on occasions may be more papilliform (Fig.16). In the histological study of salivary tumours, numerous sections must be examined in order to get a clear view of the predominant pattern.

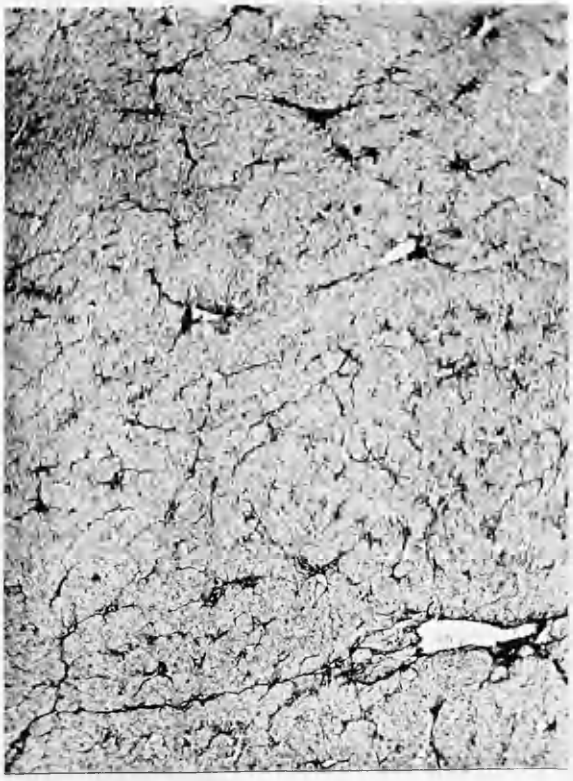


Fig. 15.
Acinar formation.
(H. & E. x 50).

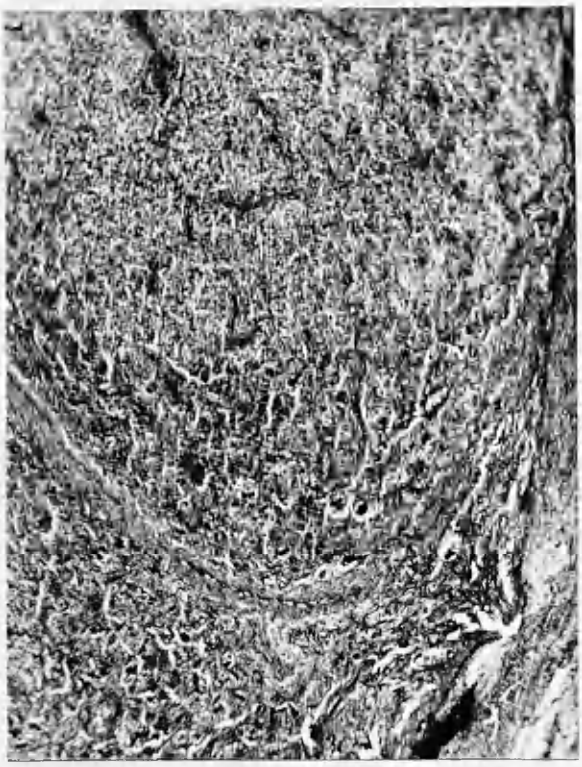


Fig. 16.
Papilliform type.
(H. & E. x 50).

d). Epithelial masses with cystic spaces.

In large epithelial masses, rounded or irregular spaces may appear chiefly by the collection of secretory products of the cells. Sometimes the

secretory spaces assume a characteristic structure, cribriform in type (Fig.17), which resembles that seen in mammary tumours (Willis, 1953).

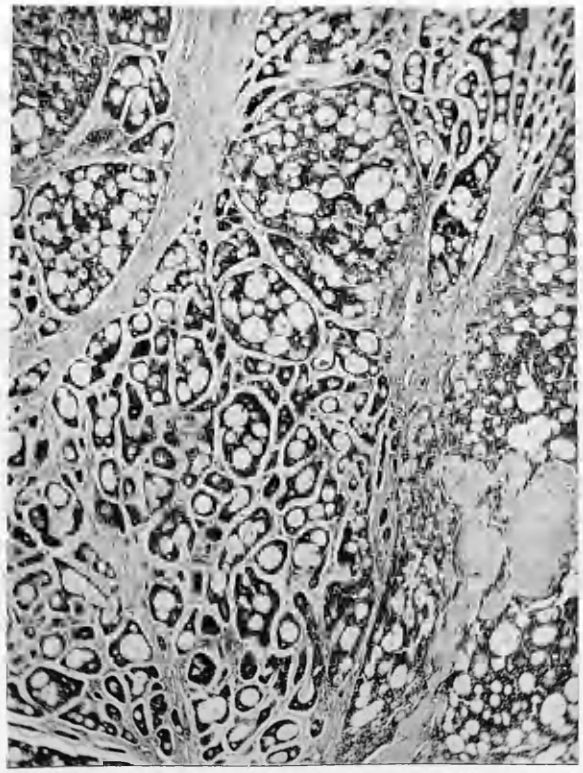


Fig. 17.
Cribriform pattern.
(H. & E. x 50).

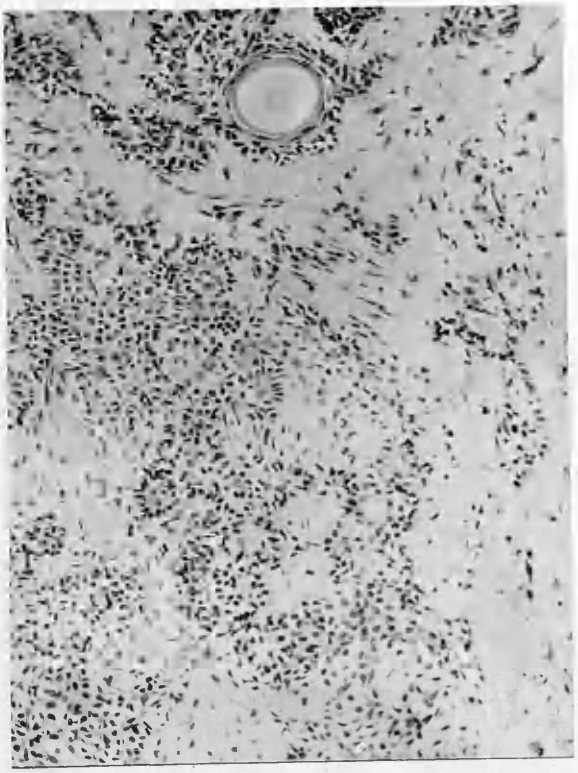


Fig. 18.
Showing squamous metaplasia.
(H. & E. x 70).

e). Cornifying squamous metaplasia.

Commonly in parts of these growths squamous metaplasia is seen (Fig. 18) and is comparable with that seen in adenocarcinoma of other glandular organs.

f). Variations in the proportions of the epithelial elements and the matrix.

The proportions of the epithelial elements to the matrix is very variable, in some (Fig. 19) a predominance of matrix with few epithelial elements is seen;

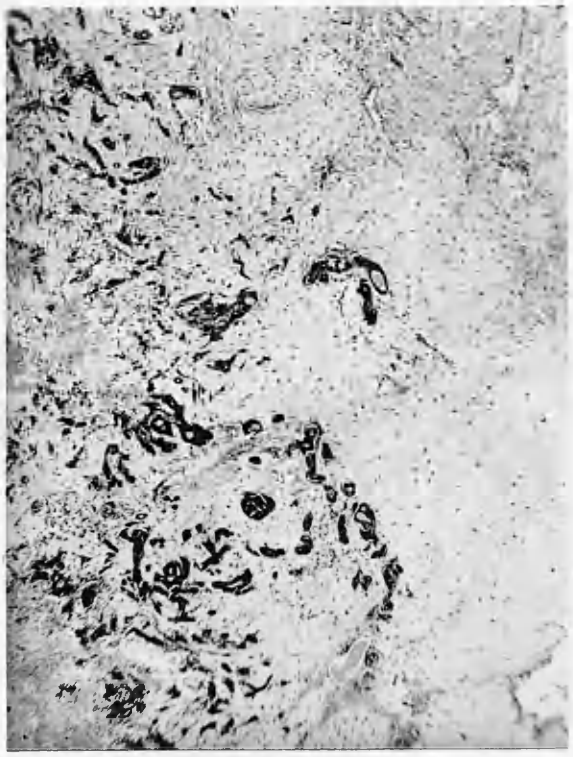


Fig. 19.
Predominantly matrix.
(H. & E. x 50).

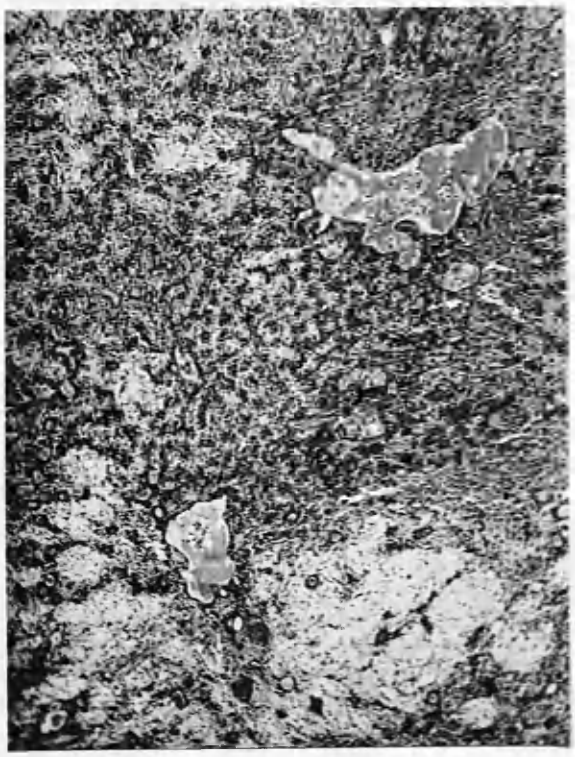


Fig. 20.
Mainly epithelial.
(H. & E. x 50).

another will be mainly epithelial (Fig.20); another (Fig. 21) where the elements are in approximately equal proportions and yet another (Fig. 22) showing a rather

spindle-shaped growth with scanty matrix. This meshwork

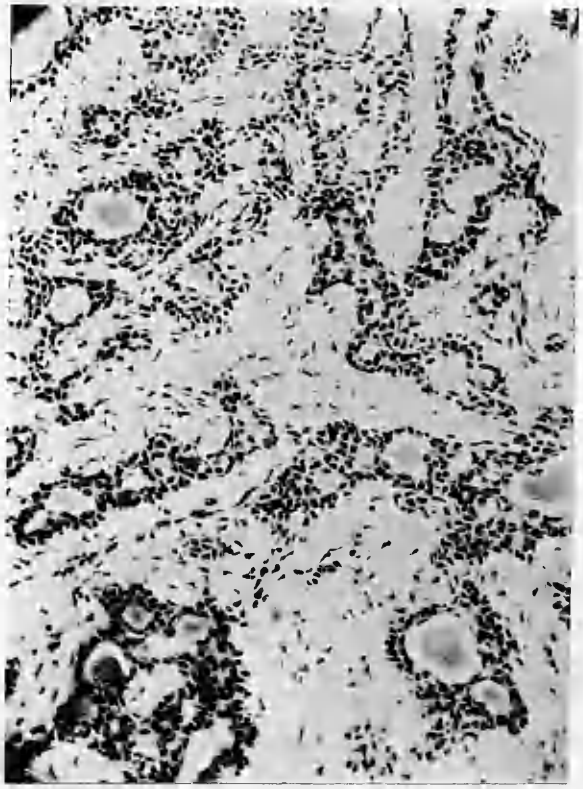


Fig. 21.
In equal proportions.
(H. & E. x 100)

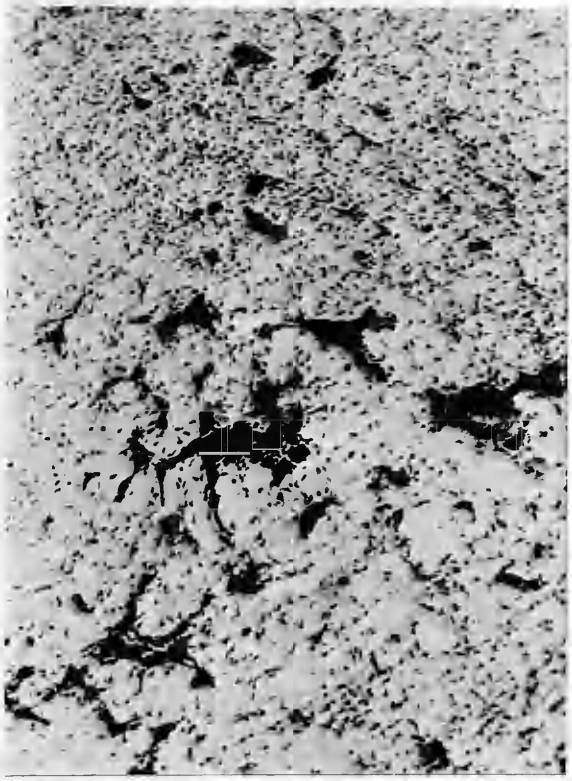


Fig. 22.
Spindle-shaped growth.
(H. & E. x 100).

suspended in the mucinous matrix is the type of structure which was previously described as "myxo-chondroid" where the matrix reveals its looseness with stellate cells as seen in Fig. 23.

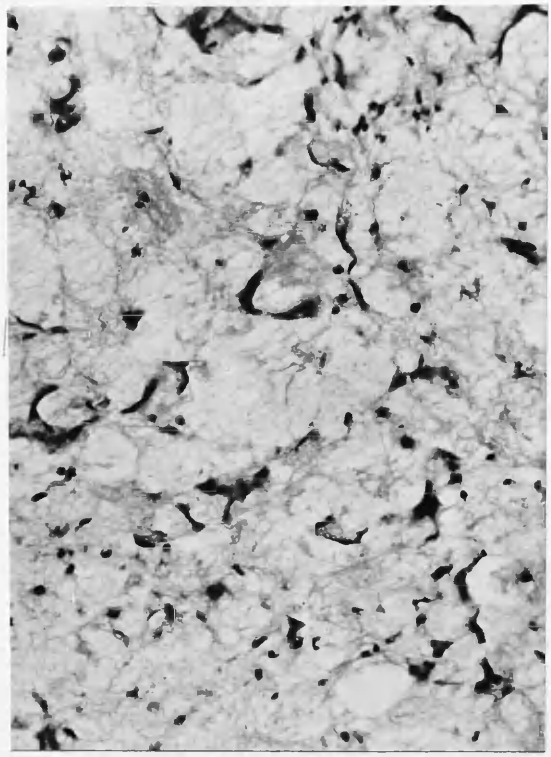


Fig. 23.
Shows stellate cells in a loose matrix.
(H.& E. x 250).

g). Areas of pseudo-cartilage.

A frequent finding in many tumours is the presence of areas of pseudo-cartilage (Figs.24,25,26) and in rare cases even bone (Allan, 1940; Yates & Paget, 1952). The "retraction spaces" around isolated

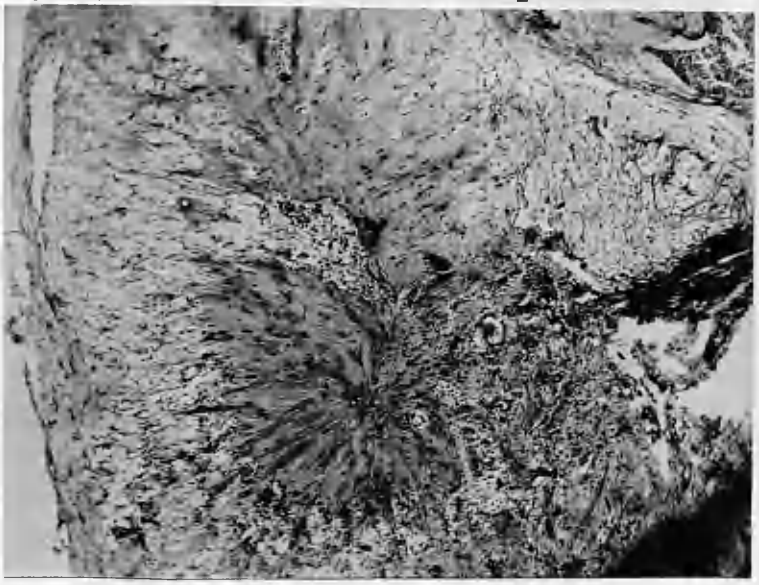
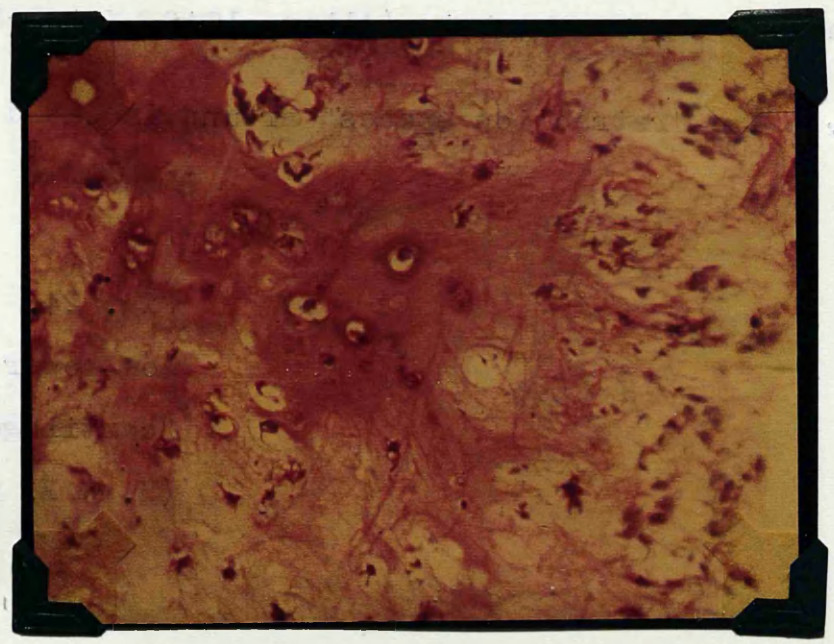


Fig. 24.
Low-power view of "cartilage".
(H. & E. x 50).



epithelial cells as reported by Harvey et al (1938) are clearly seen in Fig. 26. It is the belief of the author that cartilage and even bone do occur in pleomorphic adenomata on occasions, although probably not as frequently as the pseudo-cartilage so commonly talked about.

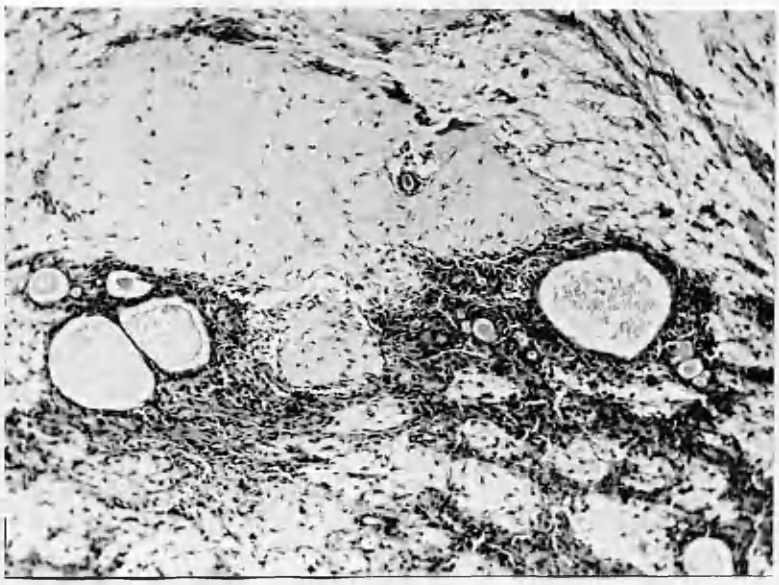


Fig. 25.
A slightly higher-power. (H.& E. x 60).

Fig. 26.
A high-power view in colour. (P.A.S. x 250).

The histological study of salivary carcinomata presents little difficulty in diagnosis as the tumours are invasive from the start. A typical carcinoma of salivary origin is shown in Fig. 27., where it arose in the parotid gland, and Fig. 28., arising on this occasion in the tongue.

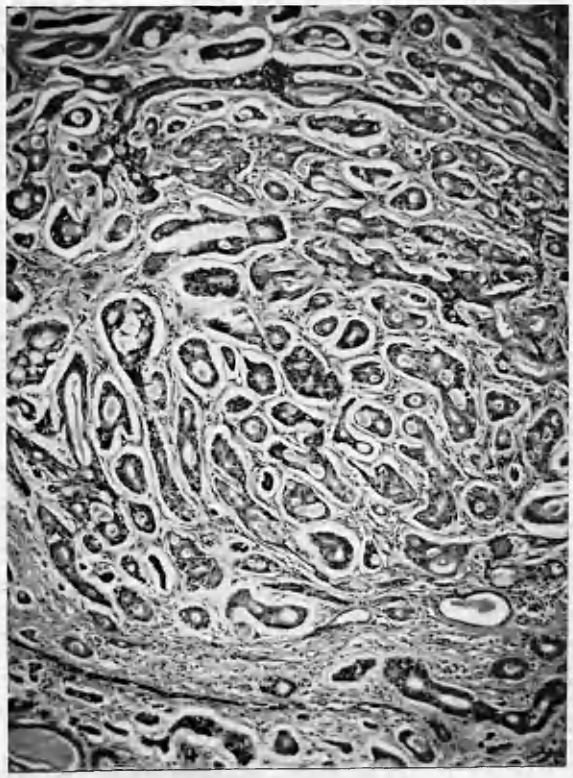


Fig. 27.
Salivary Carcinoma of the Parotid gland.
(H. & E. x 75).

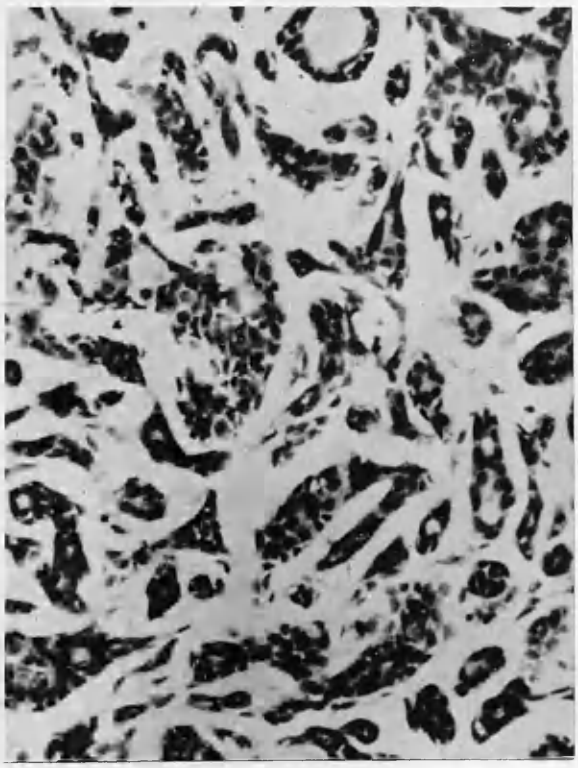


Fig. 28.
Salivary Carcinoma arising in the tongue.
(H. & E. x 100).

The histological pattern of salivary adenolymphomata is characteristic; the epithelium having a pale pink staining reaction, resembling closely the ductal epithelium. The tumours are frequently cystic in appearance (as in Fig. 29) and show branching papillary

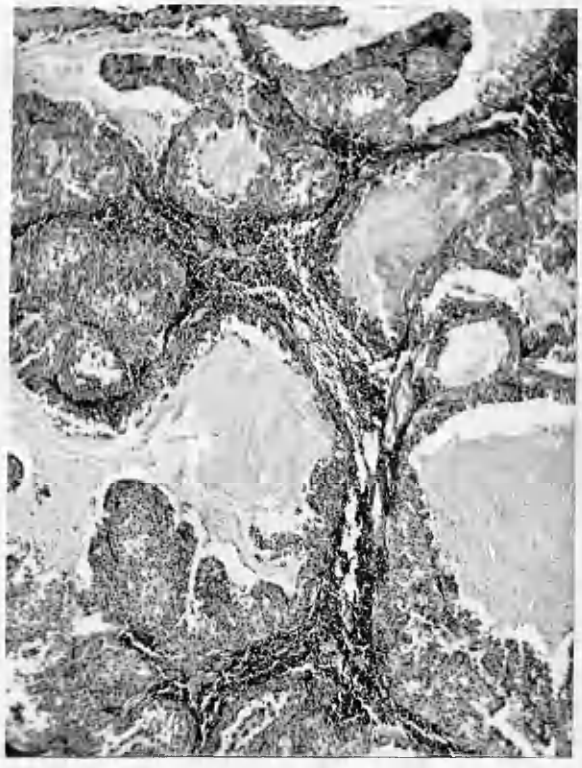
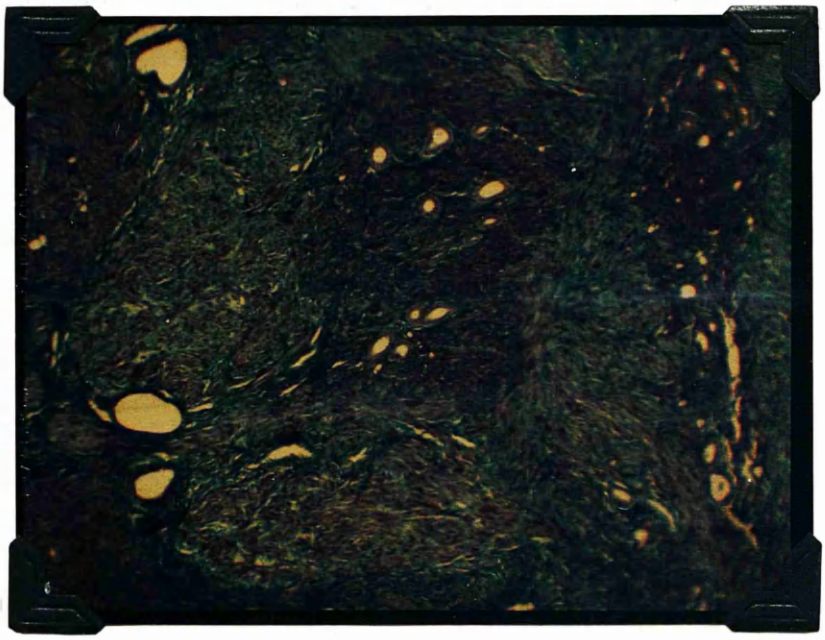


Fig. 29.
Adenolymphoma, rather cystic in appearance.
(H. & E. x 50).

Fig. 30.
Adenolymphoma in more glandular tissue.
(H. & E. x 50).

structure with intervening collections of small lymphocytes.



Of the miscellaneous group of tumours arising in salivary tissue, only the leiomyosarcoma, which arose within the substance of the parotid gland, is shown here (Fig. 31).

Fig. 31. Photomicrograph in colour of a leiomyosarcoma occurring in a parotid gland. (Masson's light green. x 50).

Blood groups in tumours of salivary tissue.

The idea that blood groups may be associated with a predisposition to particular kinds of disease is not new (Roberts,1957), but the evidence was unconvincing until Aird et al (1953) described the distribution of ABO blood groups in patients with gastric cancer - group A being more common than in a comparable control series. From such recent investigations into the relationship between disease and the ABO blood groups, it appears that these groups are associated with a susceptability to some disorders and relative immunity to others.

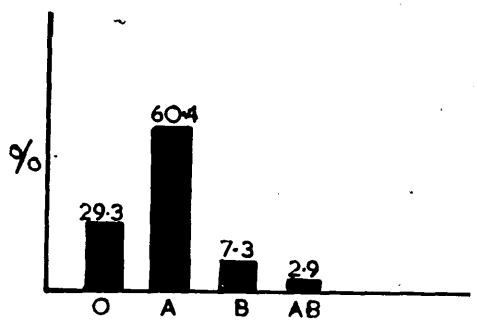
The incidence of group A has been shown to be unduly high in patients with pernicious anaemia (Buchanan & Higley, 1921); bronchopneumonia of infancy (Struthers,1951); carcinoma of the stomach (Aird et al,1953); diabetes melitus (Craig & Wang,1955; and McConnell et al,1956) and in portal cirrhosis (Billington,1956).

Group O occurs with excessive frequency in persons with

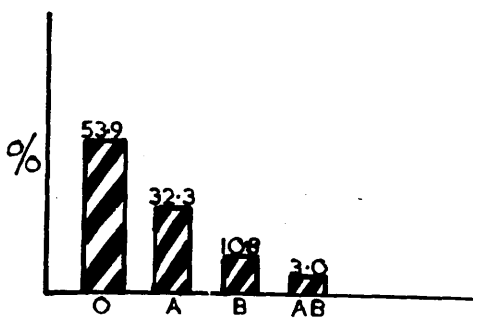
peptic ulceration (Aird et al,1954; and Brown et al,1956), and Clarke et al (1955) pointed out that the group O excess is confined to patients with duodenal ulceration. A high incidence of group O is also noted in cases of pituitary adenomata (Mayr et al,1956).

Because of this increasing evidence, the blood groups of patients with tumours of salivary tissue were acertained during the past three years from this series. Of 395 such patients the blood group is now known in 341 cases.

SALIVARY TUMOURS
(341 CASES)



CONTROL SERIES
(5,898 CASES)



The above figure (Fig.32) shows the general results side by side with those obtained in a control series of 5898 consecutive new registrations of blood-donors at the regional blood transfusion centre in Glasgow in 1952-55. Statistically the preponderance of group A in the tumour

TABLE [illegible] - SALIVARY TUMOURS - BLOOD GROUPS

BLOOD Gp.	Control Series		Pleomorphic Ad.		Carcinoma		Adenolymphoma		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
A	1906	32.3	170	57.8	29	82.9	7	58.3	206	60.4
B	637	10.8	23	7.8	1	2.8	1	8.3	25	7.3
O	3177	53.9	92	31.3	5	14.3	3	25.0	100	29.3
AB	178	3.0	9	3.1	–	–	1	8.3	10	2.9
All Groups	5898	100	294	100	35	100	12	99.9	341	99.9
Not Grouped	–	–	21	–	29	–	4	–	54	–

series is highly significant. It will be seen that the gain in this group is at the expense of group O. Table XVIII provides more detailed information about the blood

groups of the patients in the various types of salivary tumour and in the control. It will be seen that, in all three types, there is a striking preponderance of group A and a corresponding rarity of group O compared with the controls.

In analysing the figures, as groups B and AB are relatively constant throughout, group O has been compared with groups A, B, and AB combined together, and the results compared with the controls are as follows:-

a). Pleomorphic adenomata ($X^2 = 57.3$) shows a highly significant percentage, with group O significantly higher for the controls as against pleomorphic adenoma.

b). Carcinomata ($X^2 = 21.9$) again show a highly significant percentage, with group O significantly higher for the controls.

c). Adenolymphomata do not show a significantly lower percentage of group O ($X^2 = 2.94$). The indications however, are that, if the number of patients were increased, significance would be established.

d). All types of salivary tumours were finally taken and considered together, and, as would be expected, there was a highly significant (X^2 = 77.9) percentage, with group O significantly higher for the controls.

These findings, fully explained in Appendix I, provide convincing statistical evidence of an unusually high incidence of group A in this series of patients with tumours of salivary tissue. This is all the more striking because in Scotland group A is found in a smaller proportion of the population than in England.

The selection of a control series presents a well recognised difficulty (Allan,1954). As a proportion have diseases known to be associated with certain blood groups, hospital patients are unsuitable. Thanks are due therefore to Dr. J. Wallace, Regional Blood Transfusion Centre, Glasgow for the data concerning the consecutive donor registrations.

It is the usual practice, when showing such a high

incidence of a blood group and a disease, to compare the blood group distribution with carcinomata of other organs.

BLOOD GROUPS IN CARCINOMATA.

SITE	O	A	B	AB	TOTAL
Salivary.	100	206	25	10	341
Large Intestine.	73	54	17	2	146
Stomach.	109	82	27	11	229
Breast.	76	56	13	7	152
Bladder.	60	52	6	5	123
Pancreas.	15	15	3	1	34
Oesophagus.	16	8	4	2	30

Assistance in compiling the above table was given by Dr. Davies, Department of Pathology, Victoria Infirmary, Glasgow.

Much work has been done recently on the fate of radioactive sulphur given as sulphate ion to mammals; but only on a very few occasions has it been administered to man (Borsook et al, 1957), and h re the rate of excretion is high. The results help to explain the apparent specificity of the autoradiographic method for mucopolysaccharides. In autoradiographs, sulphur-35, given as the sulphate ion, is "fixed" only in the sulphated mucopolysaccharides of the tissues, and is present in particularly high concentration within the cytoplasm of the cells producing them. In view of the specific nature of the location of the $^{35}SO_4$ ion within the cytoplasm of the cells forming mucopoly-saccharides; fibroblasts do form and secrete mucopoly-saccharides into the surrounding tissues during collagen formation (Meyer, 1957; Curran & Kennedy, 1955a). Bunting & Bunting (1953) reviewed much of the evidence

for the source of the mucopolysaccharide in fibroplasia and came to the conclusion that an origin from "fibrocytes" seemed probable but not conclusive.

The fraction of ^{35}S sulphate retained by various tissues has been shown by chemical extraction to be present in an esterified form, such as chondroitin sulphate - in skeletal cartilage and intestinal tract (Dziewiatkowski, 1952, 3,4); skin (Boström & Gardell, 1953); connective tissue ground substance and collagen (Layton, 1951); aorta, spleen, kidney, tibia, red marrow, heart and skeletal muscle of chick embryos (Layton, 1952); and in the healing wound in the hen (Layton, 1950,1952). The presence of sulphur -35 in these tissues is confirmed by Curran & Kennedy (1955b) who show the invariable association with mucopolysaccharides, and clearly demonstrate that the highest activity is within the cells forming mucopolysaccharide. Fibroblasts also appear to show this (Curran & Kennedy, 1955a) and recent

observers (Gibson et al, 1955; Curran & Gibson, 1956), on uptake of ^{35}S in vitro by human cartilage cells, show activity is largely confined to cartilage cells.

It was, therefore, considered worthwhile to examine, in vitro, human salivary tumour tissue to see whether the "cartilage" takes up the radioactive sulphur.

Materials and Methods.

Technique.

Immediately following the excision of a human salivary tumour, a slice of tumour ½mm in thickness was removed under aseptic non-touch technique and placed in a sterile test-tube containing 2ml of buffered Tyrode's solution. The isotope used was ^{35}S, which has a half-life of 87.1 days and releases β particles of energy 0.167 MeV. Into each tube was therefore injected 10μc of carrier free sulphate (^{35}S) and 500 units of Crystalline Penicillin, and the tubes incubated for 48 hours at 37°C. Thereafter the tissue was fixed in Bouin's fluid and

and paraffin sections cut at 5-6μ. Autoradiographs were prepared from these by stripping-film technique, using coarse - and fine - grain films. Adjacent sections were stained by haemalum and eosin and also by the per-iodic acid-Schiff methods.

Materials.

From 10 consecutive human salivary tumours subjected to surgery, specimens were taken from each and were treated by the technique described above.

Results.

No.	Histological Type	Comments.
1.	Pleomorphic adenoma.	Negative
2.	Pleomorphic adenoma.	Negative
3.	Mixed - tubular in type.	Very light uptake.
4.	Mixed - glandular in type.	Very light uptake.
5.	Pleomorphic adenoma.	Spoiled.
6.	Carcinoma.	Negative.
7.	Pleomorphic adenoma.	Negative.
8.	Adenolymphoma.	Negative.
9.	Pleomorphic adenoma.	Negative.
10.	Pleomorphic adenoma.	Negative.

From the above table it will be seen that 8 failed to show any uptake of sulphur-35 at all, while 2 showed only a very light uptake. In neither case was the material photogenic. In the first case to show any uptake (Case 3) the histological pattern was that of a tubular pleomorphic adenoma, and the uptake was over the epithelial cells; whilst in the other case (Case 4) which was of the glandular pleomorphic adenomatous type, the uptake was over "stromal" fibroblasts and over cells similar to chondrocytes.

No definite conclusions can be reached with these results of such a small series, and it would appear that rather than being a help to distinguish "pseudocartilage" from true cartilage, sulphur-35 used in the above technique is just another staining method.

PART III.

Experimental Study.

Experimental Study.

"..... but why think, - why not try the experiment ?"

John Hunter (1775)

Letter to Edward Jenner.

As an extension of this study of tumours of human salivary tissue, attempts were made to produce such growths in rats, mice, guinea pigs and in dogs. In general, these attempts have been as unsuccessful as have those of previous investigators. According to Steiner (1940, 1942, 1956) no "mixed" tumours of the salivary gland type have been produced experimentally in animals.

Since 1915, when Yamagiwa & Ichikawa succeeded in producing tar cancers experimentally, considerable progress has been made towards the elucidation of the chemical nature of the substances capable of inciting malignant changes in cells (Shear, 1936).

Tumours induced in the salivary glands of animals have been reported. Lowenstein (1910) injected Scharlach red oil into the parotid ducts of rabbits and caused inflammatory changes which were claimed to resemble human cylindromas. Steiner (1939) described epidermoid cyst, squamous cell carcinoma and carcino-sarcoma induced in rats and mice with 3.4 benzpyrene and 20.methylcholanthrene. Benecke & Schroder (1939) injected benzpyrene in olive oil into the parotid glands of 53 rats and 55 mice, obtaining positive results in the form of sarcomas in only 2 rats. Rusch et al (1940) surgically exposed the submaxillary glands of mice and introduced 1.2.5.6.dibenzanthracene and 3.4benzpryrene with resulting sarcoma and squamous cell carcinoma in a few animals. Franseen et al (1941) produced "abscesses" and squamous cell carcinoma in rats by the introduction of methylcholanthrene and 1.2.5.6.dibenzanthracene into the salivary glands of rats and mice. Steiner (1942)

extended his experiments to the use of other carcinogens and to other animals - mice, guinea pigs and rabbits, apart from rats. Although tumours of the type originally sought were never produced, a wide variety of cell changes ranging from metaplasia to neoplasia were induced. The types of epithelial neoplasm were epidermoid cyst, squamous cell carcinoma and adenocarcinoma. The type of connective tissue neoplasm were spindle cell and mixed cell sarcoma. Three blood vessel tumours, called hemangiosarcomas, were also seen. From his observations on mice, Steiner (1942), considered that the submaxillary salivary gland was more susceptable to neoplasia than the other salivary glands. Similar histological changes were seen later by Bauer & Byrne (1950) where the majority of mouse tumours produced were adeno-acanthomas. Adenocarcinomas of rat submaxillary glands were produced by feeding with 2.acetylaminofluorine (Heiman & Meisel, 1946), although some years earlier Wilson et al (1941)

had failed to do so. Viruses have also been claimed to produce salivary tumours experimentally in animals; Bauer & Grand (1954) thought various viruses had an oncolytic effect on methylcholanthrene - produced neoplasms, while Gross (1955) following the innoculation of an Ak leukaemic extract into new born C_3H mice showed typical salivary gland carcinoma developing in the parotids of some of the innoculated mice. These tumours were microscopically adenocarcinomas becoming sarcomatous later.

Materials and Methods.

Following the advice of Steiner (1956) unnecessarily large doses of carcinogens were avoided, as otherwise the chemical may slough out, spread to expose unwanted sites and cells, produce a direct caustic, non-specific, injurious chemical reaction. With this in mind, attempts were made to produce salivary tumours in white rats, C_3H and $C_3H(f)$ strains

of mice, guinea pigs and in dogs. The carcinogens used were 20.methylcholanthrene and 9.10.dimethyl 1.2. benzanthracene.

Experiment I.

In the first experiment two batches of 24 white rats were used. In the first series 20.methylcholanthrene was injected under direct vision into the submaxillary gland; while in the second series an excised portion of submaxillary tissue containing a crystal of 20.methylcholanthrene was implanted into the subcutaneous tissue on the back of the donor animal. All experiments were performed under ether anaesthesia and a strict aseptic technique was used throughout.

Experiment 2.

The animals used in this experiment were mice of the C_3H and $C_3H(f)$ strain; no case of salivary gland tumour developing spontaneously in any of the non-treated

mice was noted. The technique used was a modification (Appendix II) of that recommended by Rous & Smith on numerous occasions (1945a & b, 1946, 1947, 1949, 1950). Using this technique 35 adult male mice were treated.

In a second series of mice, portions of autogenous excised salivary tissue containing a crystal of 20. methylcholanthrene were implanted in the backs of 12 adult male $C_3H(f)$ mice.

Experiment 3.

The third experiment was limited to 3 guinea pigs and 9.10.dimethyl 1.2.benzanthracene. The carcinogen was implanted under direct vision into the submaxillary gland, again using ether anaesthesia and an aseptic technique.

Experiment 4.

Finally, implants of 20.methylcholanthrene were made into both parotid glands of 10 dogs. These

These operations were performed under thiopentone induced general anaesthesia, and each dog was given 1×10^6 units of Penicillin post-operatively.

Results.

Experiment I.

In no case was there any evidence of tumour formation. In six cases chronic interstitial inflammatory change with intense lymphocytic infiltration was noted.

Experiment 2.

In 24 of the 35 adult male C_3H mice, treated by the modification of the method described by Rous & Smith, developed massive tumours after 10 weeks (Fig. 33 and 34). It was hoped that one of these,

Fig. 33.
Photograph of the mouse at autopsy.

Fig. 34.
X-ray of the animal prior to autopsy.

at least, might prove to be of salivary origin but histologically they all appeared to have the general characteristics of a highly cellular anaplastic spindle cell sarcoma, probably a variety of "myosarcoma" (Fig.35).

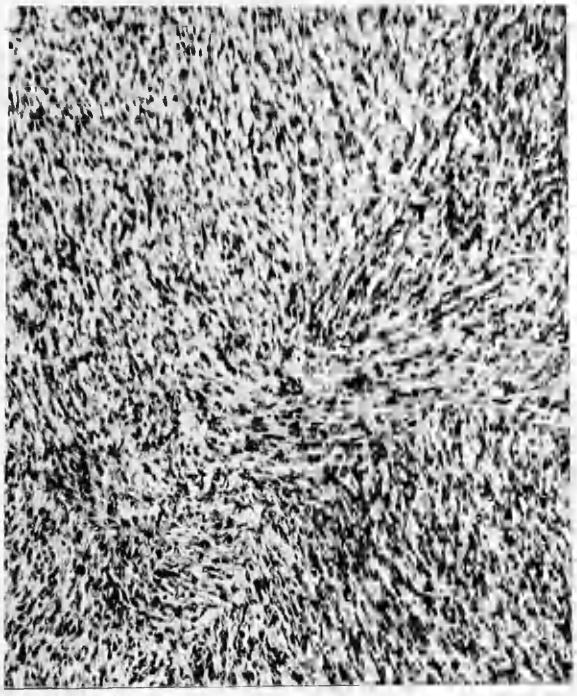


Fig. 35.

Photomicrograph of a "myo-sarcoma" produced. (H. & E. x 80).

The tissue transplanted, together with the carcinogen, into the back of the donor animal survived in only 5 cases, and in 2 of these the salivary epithelium had disappeared, or had suffered a squamoid type of change. It was scattered in a disorganised way in a cellular stroma. There was in addition much inflammatory and foreign body reaction; some of the injected foreign material could still be seen in fat-laden phagocytes. The epithelial picture (Fig. 36) in certain respects

resembled that of a squamous epithelioma and was not unlike a picture occasionally found in parts of human pleomorphic salivary adenoma or carcinoma. It would obviously, however, be stretching evidence unreasonably to regard this as histological evidence of artificial production of a mixed salivary gland tumour.

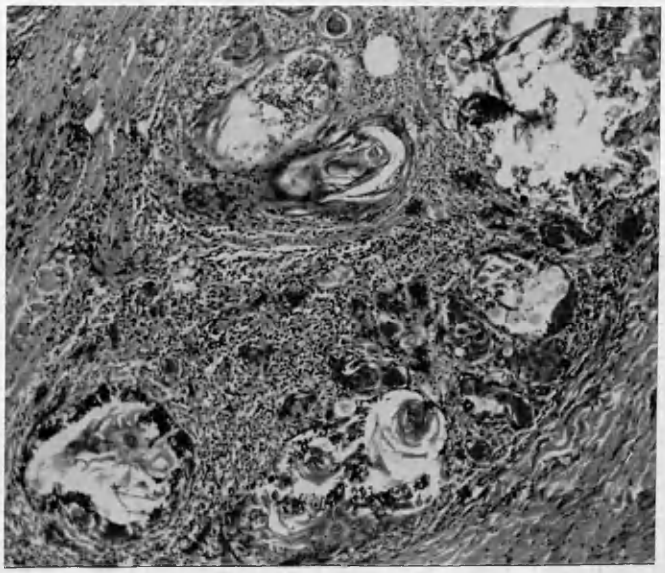


Fig. 36.

Photomicrograph of the epithelial picture described above. (H. & E. x 100).

Experiment 3.

After 3 months there was a palpable and visible enlargement of the submaxillary glands in the 3 guinea pigs, but histological examination only showed chronic inflamatory change with abscess formation. There was

no evidence of tumour formation.

Experiment 4.

At autopsy 6 to 60 weeks later 7 of the 10 showed visible and palpable enlargement of the gland. Histologically, however, there was only a vigorous inflammatory reaction, marked fibrous and in places squamoid change in the epithelium. In other parts there was some proliferation of the acinar epithelium. These

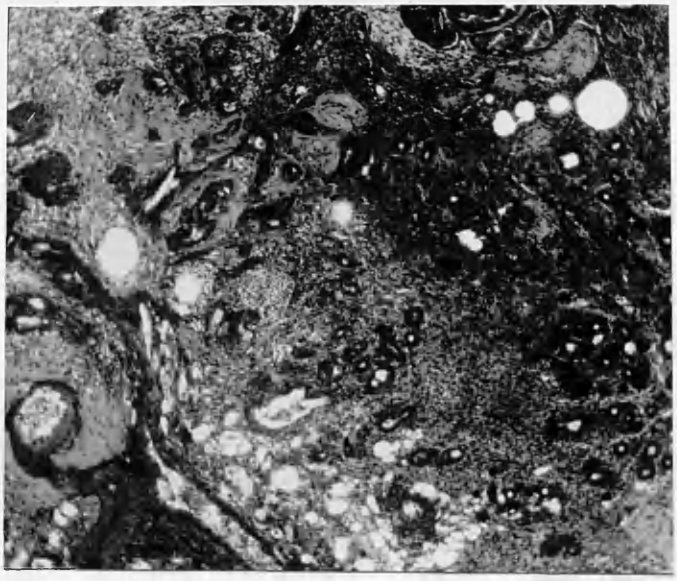


Fig. 37.

Photomicrograph of tissue from dog parotid showing changes described in text. (H. & E. x 100).

changes show some similarity to those referred to earlier in the mouse implants, but in none was a true tumour of salivary tissue produced.

Therefore, attempts to reproduce experimentally in animals anything resembling a salivary tumour, let alone a "mixed salivary tumour" have failed.

PART IV

Conclusions and Summary.

CONCLUSIONS

A clinico-pathological and experimental study of tumours of salivary tissue has been made. A series of 401 clinical cases have been investigated and the results reported. From this survey it would appear that it is only necessary to classify such tumours as:-

a). Pleomorphic adenoma,

b). Carcinoma, and

c). Adenolymphoma.

The type previously classified as Simple Adenoma is only a variety of pleomorphic adenoma, and so does not need a separate classification. Also the miscellaneous group of tumours hardly enter the survey as they are only rarities and can occur in almost any organ. Working on this basis the survey will be discussed.

a). Pleomorphic adenoma.

Of the 80% of pleomorphic adenomata occurring in the parotid gland there was a slight preference for the right

side; it was also observed that 60% occurred before the age of 40 years and 90% before the age of 60 years. It is agreed that such tumours show a slow intermittent growth and that they can reach gigantic size (Case No. 221). The recurrence rate of almost 30% is due to the following reasons:-

i. general habit of such tumours.

ii. subjected to operation before being fully investigated, and before all the nodules of tumour tissue have joined together, that is in keeping with the multicentric origin theory.

iii. surgery not radical enough; all such tumours should be looked upon as potentially malignant and radical excision undertaken.

In this series there was noted on 3 occasions a familial incidence, a fact which had apparently not been reported on before in the literature. In the first family there is histological proof; in the second, clinical observations must be relied upon; and in the third family the evidence is so circumstantial as to be almost certainly valid.

As previous workers have already described, there is

correlation between the histological pattern and the clinical course of the tumour, but one cannot agree with McFarland (1926) when he stated that, "nothing of prognostic value results from the microscopic study of a mixed tumour". In cases which recurred the histological picture was more often than not similar to the original material, but in some cases it was more cellular. There was, however, no tendency towards a more truly malignant pattern. In other words, a malignant tumour is mainly malignant from the onset and does not develop from a pleomorphic adenoma.

Histologically there are many variations of pleomorphic adenomata, and many or all the possible variations of structure may be found in close juxtaposition with all gradiations between them; while in others, one or another structural variant predominates. Much has been written on the presence of areas of "pseudo-cartilage", and many deny the possibility of

such a finding. In spite of having been unable to prove or disprove this theory by in vitro tests with radioactive sulphur (S^{35}) on slices of human salivary tumour, there would appear to be no reason why cartilage, or even bone on rare occasions, should not be seen on histological section. Whether the cartilage is present from the onset of the tumour, or that it arises by metaplastic change will be, for some time to come, a matter for research.

b). Carcinoma.

Carcinomata of salivary tissue is usually heralded by a tumour showing a rapid increase in size with associated pain and/or paralysis in a patient in a slightly older age group. The sex incidence as with side, is not convincing statistically. As would be expected the recurrence rate is high, and the death rate equally raised. As the tumours are invasive from the start, the histological study presents little difficulty in diagnosis

usually.

c). Adenolymphoma.

Only 4% of the tumours in this series were classified as such, and all but one occurred in the parotid glands. The outsider arose in the tonsil. On four occasions the adenolymphomata were bilateral, and the sex ratio was equal in this series. Such tumours have a characteristic histological pattern.

Blood-groups in salivary tumours.

A statistical preponderance of group-A in the tumour series over the control is clearly demonstrated and that the gain is at the expense of group-O. It is shown that in all 3 types of salivary tumours the preponderance of group-A and a corresponding rarity of group-O compared with the control series is striking. Although in the case of Adenolymphomata significance is not established, the indications are that if the numbers were increased, significance would be established.

It is hoped that it will be possible to determine the secretor status of some of the sample in the future, in order to determine whether secretion of group specific substances comes into it (Fraser Roberts, 1958).

Experimental study.

Attempts were made to produce salivary tumours in animals experimentally, using carcinogens. But like previous workers, tumours resembling the human mixed salivary tumour did not result. In rats and guinea-pigs only acute and chronic inflammatory changes were produced, while in mice numerous tumours were produced in the hind-leg following the technique described in Appendix II. All of these tumours showed a highly cellular anaplastic spindle cell sarcoma. In the same strain of mice and in some dogs there was a vigorous inflammatory reaction with much fibrosis and some squamoid change in the epithelium and also some proliferation of the acinar epithelium.

This, however, cannot be regarded as histological evidence of artificial production of a mixed salivary tumour.

SUMMARY.

i. A clinical study has been made of 401 cases of tumours of salivary tissue and the results reported; familial incidence being noted on 3 occasions.

ii. A histological study has been made of those cases seen at the Southern General Hospital, Glasgow. Attempts were made to clarify the presence or absence of "cartilage" in pleomorphic adenomata using Sulphur-35 with no result.

iii. Blood-grouping was carried out in 341 patients from this series, and a highly significant preponderance of group-A was noted as compared with the control series. This preponderance was also present in the separate types of salivary tumours as well as in salivary tumours in general.

iv. The results of attempts to produce salivary tumours experimentally in animals is discussed.

v. The literature is reviewed in all parts of the thesis.

ACKNOWLEDGEMENTS.

"The gratitude of men is but a secret
desire to receive greater benefits."

La Rochefoucauld - Reflections No.298.

The page who sings in "As You Like It" that, "hawking or spitting, or saying we are hoarse" speaks the truth; and books, like songs, should be their own interpreters. It is rare, however, that one unaided person can write, print, illustrate and publish them. Debts alone may justify an acknowledgement, and mine are many.

Dr. A. Dick, Department of Pathology, Southern General Hospital, Glasgow, was the first to introduce me to the subject of Salivary Tumours, and he has been an invaluable help and source of encouragement at every stage of the work. To Professor W. A. Mackey and all members

of his staff must go my heartwarm thanks; to Professor T. Symington and the staff of his department, I venture to express my gratitude. I am indebted to Dr. J. Wallace, Regional Blood Transfusion Service, Glasgow, for considerable help and to Dr. R. A. Robb, Department of Mathematics, Glasgow University, who gave his expert assistance with the statistical analysis; also Dr. Davis, Department of Pathology, Victoria Infirmary for giving assistance in compiling Table XIX.

Dr. P. Peacock and Dr. B. Pullinger, Royal Beatson Memorial Hospital, Glasgow, together with Professor Paul E. Steiner, Chicago University, have kindly offered suggestions and criticisms of my attempts to produce such tumours experimentally in animals. To them, and to Professor W. L. Weipers and his staff at the Glasgow University Veterinary Hospital, particularly Mr. D. Lawson, must go my sincere thanks.

Mr. W. Masson, Department of Pathology, Royal Hospital

for Sick Children, Glasgow, and Mr. P. Towler, Department of Surgical Photography, Glasgow Royal Infirmary have given much assistance with their photographic prowess.

To the Medical Superintendents of the Southern General Hospital, Western Infirmary and the Glasgow Royal Infirmary; and to all the surgeons and general practitioners who have assisted me throughout the investigations must go my sincere thanks.

Finally Miss Hamilton and Miss Orr for carrying out the secretarial duties so deftly deserve special thanks.

BIBLIOGRAPHY.

1. Ackerman, L.V., (1943) Oncocytoma of the Parotid gland. Arch. Path., 36.508-511.

2. Ahlbom, H.E., (1935) Mucous and Salivary gland tumours. A clinical study with special reference to radiotherapy, based on 254 cases treated at Radiumhemmet, Stockholm. Acta. radiol., Suppl.XXIII 1-452.

3. Aird, I., Bentall, H.H., & Roberts, J.A.F., (1953) A relationship between cancer of stomach and the ABO blood groups. B.M.J. 1.799-801.

4. _____, _____, Mehigan, J.A., & Roberts, J.A.F., (1954) The blood groups in relation to peptic ulceration and carcinoma of colon, rectum, breast and bronchus. An association between the ABO groups and peptic ulceration. B.M.J. 2.315-321.

5. Albrecht, H. & Arzt, L., (1910) Beiträge zur Frage der Gewebsverirrung. I. Papilläre Cystadenome in lymphdrusen.

Frankf. Ztschr. f. Path., 4.47-69.

6. Allan, T.M., (1954)

Blood groups and disease.

B.M.J. 2.644.

7. Allen, A.C., (1940) So called mixed tumour of mammary gland of dog and man with special reference to general problems of cartilage and bone formation.

Arch. Path., 29.589-624.

8. Bailey, H., (1941) The treatment of tumours of the parotid gland; with special reference to total parotidectomy.

B.J.S. 28.337-346.

9. Balme, H., (1912) An enormous parotid tumour in a Chinese woman.

B.M.J. 1.1292.

10. Bauer, W.H., & Fox, R.A., (1945) Adenomyo-epithelioma (cylindroma) of palatal mucous glands.

Arch. Path. 39.96-102.

11. _____, & Byrne, J.J., (1950) Induced tumors of the parotid gland.
Cancer Res., 10.755-761.

12. _____, & Grand, N.G., (1954) Interaction of a salivary gland virus and experimentally produced carcinomas of the mouse salivary gland.
Ibid. 14.768-784.

13. Benecke, E., & Schröder, J., (1939) Über experimentelle Geschwülstezengung in Speicheldrüsen.
Ztschr. f. Krebsforsch 49.505-514.
Abs. Am.J.Cancer 39.255 (1940).

14. Benedict, E.B. & Meigs, J.V., (1930) Tumors of the Parotid gland. Surg., Gyn., & Obstet. 51.626-647

15. Berard, A., (1841) Des operations que reclament les tumeurs developes dans la region parotidienne.
Thèse du Conc. de Med. operat. Paris.

16. Bernier, J.L., (1946) Mixed tumors of lip.
J.Oral Surg.. 4.193-202.

17. Billington, B.P., (1956) A note on the distribution of ABO blood groups in bronchiectasis and portal cirrhosis.
Aust. Ann. Med. 5.20-22.

18. Billroth, T., (1859) Beobachtungen über Geschwulste der Speicheldrusen.
Virchow's Arch. path. Anat. 17.357.

19. Birsch-Hirschfield, (1894) Lehrbuch der pathologischen Anatomie. Bel 2. S. 604. Leipzig.

20. Blady, J.F., & Hocker, A.F., (1938) Sialography, its technique and application in roentgen study of neoplasms of the parotid gland.
Surg., Gyn., & Obstet., 67.777-787.

21. _____, _____, (1939) Application of sialography in non-neoplastic diseases of the parotid gland.
Radiology, 32.131-140.

22. Bland-Sutton, J., (1906) Tumors - Innocent and Malignant.

4th. Edit., Cassell. London p.97.

23. Borsook, H., Keighley, G., Yost, D.M., & McMillan, E., (1937). Urinary excretion of ingested radioactive sulfur.

Science. 86. 525.

24. Boström, H., & Gardell, S. (1953) The uptake of sulphates in mucopolysaccharides esterified with sulphuric acid in the skin of adult rat after intraperitoneal injection of S^{35} - labelled sodium sulphate.

Acta. Chem., Scand. 7.216-222.

25. Böttner, O., (1921) Das sezernierende Epitheliom (die sogenannte Mischgeschwülste) der Mundspeicheldrüsen.

Beitr. z. Pathol. Anat. u. Allg. Pathol. 68.364.

26. Boyd, P.L., (1938) Mixed tumors of the parotid type. With a report of 3 cases.

Am.J.Surg., 39.641-645.

27. Brown, D.A.P., Melrose, A.G., & Wallace, J., (1956) The blood groups in peptic ulceration.

B.M.J., 2.135.

28. Buchanan, J.A., & Higley, E.T., (1921) The relationship of blood-groups to disease.
Brit.J.Exp.Path., 2.247-255.

29. Bunting, C.H., & Bunting, H., (1953) Acid mucopolysaccharides of the aorta.
Arch.Path., 55.257-264.

30. Byars, L.T., Ackerman, L.V., & Peacock, E., (1957) Tumors of salivary gland origin in children.
Ann.Surg., 146.40-51.

31. Cade, I.S., (1954) Mixed parotid tumour.
Proc. R. Soc. Med., 47.513.

32. Carmichael, R., Davie, T.B., & Stewart, M.J., (1935) Adenolymphoma of the salivary glands.
J.Path. & Bact., 40.601-615.

33. Chevassu, M., (1910) Tumeurs de la glande sous-maxillaire.
Rev. de Chir., 41.450.

34. Clarke, C.A., Cowan, W.K., Edwards, J.W., Howel-Evans, A.W., McConnell, R.B., Woodrow, J.C., & Sheppard, P.M., (1955). The relationship of the ABO blood groups to duodenal and gastric ulceration. B.M.J., 1.643.

35. Cohnheim, J., (1876) Einfacher Gallertkropf mit Metastasen. Virchow's Arch. 68.547.

36. Cooray, G.H., et al (1950) Glandular tumours of oral., nasal and orbital cavities. Ceylon J.Med. Sc. 7.73-83

37. Cotterill, J.M., (1907) A case of mixed parotid tumour. Scot. Med. & Surg. J., 20.526.

38. Craig, J., & Wang, I., (1955) Blood-groups in diabetes mellitus. Glas. Med. J., 36.261-266.

39. Cuneo, B., & Veau, V., (1900) Sur l'origine bronchiale

des tumeurs mixtes cervicofaciales.

Congrés. internat. Med. Paris (1900) Sect.10.Chir. gén., pp.278-281. Cited by Zymbal (1933).

40. Curran,R.C., & Kennedy,J.S.,(1955a) Utilization of sulphate ion by fibroblasts in the Quartz focus. Nature 175.435.

41. _____, _____,(1955b) The distribution of the sulphated mucopolysaccharides in the mouse. J.Bath. & Bact., 70.449-457.

42. _____, & Gibson,T.,(1956) The uptake of labelled sulphate by human cartilage cells and its use as a test for viability. Proc. Roy. Soc. B. 144.572-576

43. D'Aunoy,R.,(1930) Mixed tumors of the palate. Am.J. Path.6.137-145.

44. Davidson,J.,(1910)

Mixed tumour of the parotid.

India Med. Gaz., 44.292.

45. Davis,L.J.,(1935) Mixed tumours of the palate - a report of four cases.
J. Path. & Bact. 41.289-292.

46. De,M.N., & Tribedi,B.P.,(1939) A mixed epidermoid and mucus-secreting carcinoma of the parotid gland.
J. Path. & Bact., 49.429-433.

47. Delaney,P.A.,(1931) Mixed tumor of the scalp.
Arch.Path., 12.145.

48. Dick,A.,(1954) Carcinoma in newborn- report of a case.
Am. J. Surg., 87.673-675.

49. Dockerty,M.B., & Mayo,C.W.,(1942) Primary tumors of submaxillary gland with special reference to mixed tumors.
Surg., Gyn., & Obstet., 74.1033-1045.

50. Dunlop,J.,(1879) Adenoid tumour of the parotid.
Glas. Med. J. 11.308.

51. Du Plessis,D.J.,(1957a) Some features in the

development, structure and function of the parotid salivary glands.

S.A. Med.J., 31.773-781.

52. _____,(1957b) Disorders of the parotid lymph glands simulating diseases of the parotid salivary glands.

Medicine in S.A.,(1957) 9.18.

53. Dziewiatkowski,D.D.,(1952) The radioautographic studies of sulphate-sulfur (S^{35}) metabolism in the articular cartilage and bone of suckling rats.

J.Exp.Med., 95.489 - 495.

54. _____,(1953) The sulphate-sulfur metabolism in rat fetus as indicated by Sulfur-35.

Ibid., 98.119-127

55. _____,(1954) Utilization of sulphate sulfur in the rat for the synthesis of cystine.

J.Biol.Chem., 207.181-186.

56. Edwards,A.O.,(1958) Non-malignant teratoma of neck

in newborn baby.

Nursing Mirror, Vol.106 10th January, 1958.

57. Eggers,H.E.,(1928) Mixed tumors of the palate.

Arch.Path. 6.378-395

58. Ewing,J.,(1940) Neoplastic Disease.

p.793 Saunders, Philadelphia.

59. Fick,J.,(1909) Zur Kenntnis der sog. Mischgesch-

wülste der Parotisgegend und zur Endotheliomfrage.

Virchow's Arch., 197.472.

60. Fitzgibbon,G.M.,(1953) in "Discussion on the surgical

treatment of parotid tumours."

Proc. Roy.Soc. Med., 46.1016-1018.

61. Foote,F.W.,jr. & Frazell,E.L.,(1953) Tumors of the

major salivary glands.

Cancer, 6.1065-1133.

62. _____, _____,(1954) Atlas of Tomor

Pathology. - Sect.IV.,Fasc.,II.. Armed Forces

Inst. Path., Washington, D.C.

63. Forgue, E., & Massabuau, G., (1908) Comment se pose actuellement le problème des tumeurs branchiogènes du can?

Rev. d. Chir., 60.181

64. Forman, J., & Warren, J.H., (1918) The so-called "mixed tumors" of the salivary glands, with a possible explanation of the morphological behaviour of the tumor cells.

Ann. Surg., 67.67 - 70.

65. Franseen, C.C., Aub, J.C., & Simpson, C.L., (1941) Experimental tumors in lymph nodes and in endocrine and salivary glands.

Cancer Res., 1.489-493.

66. Fraser, A., (1918) Mixed tumors of the salivary glands. A study based on the experimental production of neoplasm in the submaxillary gland of the dog.

Surg., Gyn., & Obstet., 27.19-39.

67. Frazell, E.L., (1954) Clinical aspects of tumors of the major salivary glands.

Cancer, 7.637-659.

68. Fry, R.M., (1929) The structure and origin of the "mixed" tumours of the salivary glands.
B.J.S., 15.291-306.

69. Furstenberg, A.C., (1941) The parotid gland. Its common disorders.
J.A.M.A., 117.1594-1598.

70. Gaston, E.A., & Tedeschi, C.G., (1946) Adenolymphoma of the parotid and submaxillary glands.
Ann. Surg., 123.1074-1089.

71. Gibson, T., Curran, R.C., & Kennedy, J.S., (1955) An in vitro test for cartilage cells.
Transplant Bull., 2.44.

72. Gilis, & Godlewski, (1905) Sarcome mélanique bilatéral de la région sous-maxillaire.
Soc. de Sc. Méd. Montpellier.

73. Gross, L., (1955) Mouse leukaemia: an egg-borne virus disease (with a note on mouse salivary gland carcinoma)

Acta Haemat., 13.13-29.

74. Haggard, ,(1919) Melanotic sarcoma of parotid. J.Ten.Med.Ass. Cited by Dunet,C.,&Crysel,J.,(1933) Cancer des glandes salivaires, Paris. G. Doin et Cie.

75. Halpert,B.,(1935) Salivary gland tumors in rare sites. Yale J. Biol. & Med., 5.469-471.

76. _____,(1946) Salivary gland tumors, adamantinomas and craniopharyngiomas. Cancer Res., 6.504.

77. Hamperl,H.,(1931) Onkocytes und geschwülste der speicheldrüsen. Virchows Arch.f.Path.Anat., 282.724-736.

78. Harris,P.N.,(1937) Adenocystoma lymphomatosum of the salivary glands. Am. J. Path., 13.81-87.

79. Hartz,P.H.,(1946) Development of sebaceous glands from intralobular ducts of the parotid gland. Arch. Path., 41.651

80. Harvey, W.F., Dawson, E.K., & Innes, J.R.M., (1938) Debatable tumours in human and animal pathology. IV. "Mixed tumours" of the salivary glands. Edin. Med. J., 45.275-284.

81. Heiman, J., & Meisel, D., (1946) Tumors of salivary and parathyroid glands in rats fed with 2-acetylaminofluorine. Cancer Res., 6.617-619.

82. Heineke, H., (1913) Die geschwülste der speicheldrüsen, Ergebn. d. Chir. n. Orthop., 6.239.

83. Heister, L., (1739) A general system of surgery, Helmstadt (1739) Translated and published in England in 1768(8th Edit).

84. Hemplemann, L.H., jr., & Womack, N.A., (1942) The pathogenesis of mixed tumors of the salivary gland type. Ann. Surg., 116.34-42.

85. Hevenor, E.P., & Clark, C.E., (1950) Adenolymphoma

(papillary cystadenoma lymphomatosum).

Surg., Gyn., & Obstet., 90.746-751.

86. Hickey, B.B., (1957) Pleomorphic adenomata of the palate and tongue.

B.J.S. 44.483

87. Hindelbrandt, O., (1898) Über angeborene epitheliale cysten un fisteln des halses.

Arch.klin.Chir., 49.167-192.

Cited by Kraissl, G.T., & Stout, A.P., (1933).

88. Hinsberg, V., (1899) Beiträge zur Entwicklungsgesch und Natur der Mundspeichel-drüsen geschwülste ichte.

Deutsche. Zeitschr. f. Chir., 51.281.

89. Holmberg, R.E., & Glover, D.M., (1951) Papillary cystadenoma lymphomatosum of the parotid gland.

Surgery, 29.240-248.

90. Jaffé, R.H., (1932) Adenolymphoma (Onkocytoma) of the parotid gland.

Am. J. Cancer. 16.1415-1423.

91. Janes, R.M., (1940) The treatment of tumours of the salivary glands by radical excision. Canad. med. Ass. J., 43.554-559.

92. _____, (1943) Surgical treatment of tumors of the salivary glands. Surg. Clin.N.Amer., 23.1429-1439.

93. _____, (1957) Tumours of the Parotid gland. Ann.R. Coll. Surg., Engl. 21.1-20.

94. Kaufmann, E., (1929) Pathology p.603. Reimann's translation, Philadelphia.

95. Keen, W.W., (1904) Enormous mixed tumor of the parotid region; reaching to the clavicle and weighing about 7 pounds; operation; recovery. J.A.M.A., 42.1138-1141.

96. Kennon, R., (1921) Tumours of the salivary glands with their after history. B.J.S., 9.76-86.

97. Kraissl, G.T., & Stout, A.P., (1933) "Orbital inclusion"

cysts and cystadenomas of the parotid salivary glands.

Arch. Surg., 26.485-499.

98. Krompecher, E., (1908) Zur Histogenese und Morphologie der Mischgeschwülste der Haut sowie der Speichel- und Schleimdrüsen.

Beitr. path. Anat., 44.51-88.

99. Kux, E., (1931) Zur histogenese der sogenaunten Mischgeschwülste der Speicheldrüsen.

Virchow's Arch. f. path. Anat., 280.175.

100. Lawrence, H.C., & Procita, L., (1948) Papillary cystadenoma lymphomatosum. Bilateral involvement.

Am. J. Surg., 76.440-442.

101. Layton, L.L., (1950) In vitro sulfate fixation by granulation tissue and injured muscle tissue from healing wounds.

Proc.Soc.Exp.Biol. & Med., 73.570-572.

102. _____, (1951) The anabolic metabolism of

radioactive sulfate by animal tissues in vitro and in vivo.

Cancer, 4.198-201.

103. _____,(1952) Effect of cortisone upon the tissue synthesis of acid mucopolysaccharides.

Bull. Schweiz. Acad. med Wiss., 8.74-78.

104. Lebert & Broca (1850) Tumeur encéphaloide de la parotide accessoire.

Bull d. Soc. Anat. d. Paris.

105. Lederman, M.,(1943) Adenolymphoma of the parotid salivary gland.

Brit. J. Radiol., 16.383-385.

106. Lennox, B., Everson Pearse, A.G., & Richards, H.G.H., (1952) Mixed salivary tumours of skin.

J. Path. & Bact., 64.865

107. Lepp, H., (1939) Zur Kenntnis des papillär wachsenden Schleimigen. Cystadenokarzinoms der Mundhöhle. (Eine morphogenetishce Studie).

Beitr. path. Anat., 102.164-186.

108. Leriche, R., (1935) D'une voie nouvelle, cervicale, predigastrique, pour enlever les tumeurs énucléables du prolongument pharyngien de la parotide.
Pr. méd., 43.1449

109. Linell, F., (1948) Mucus-secreting and cystic epidermoid carcinomas of mucous and salivary glands.
Acta. Path. Microbiol. Scand., 25.801-828.

110. Lloyd, O.C., (1946) Salivary adenoma and adenolymphoma.
J.Path. & Bact., 58.699-710.

111. Löwenstein, C., (1910) Über atypische epithelwucherungen und tumoren der Speicheldrüsen, besonders der parotis.
Frankf. Ztschr. f. Path., 4.187-202.

112. McConnell, R.B., Pyke, D.A., & Roberts, J.A.F., (1956) Blood groups in diabetes mellitus.
B.M.J., 1.772-776.

113. McFarland, J., (1926) Ninety tumors of the parotid

region; in all of which the post-operative history was traced.

Am. J. Med. Sc., 172.804-848.

114. _____, (1927) Adenoma of the salivary glands with a report of a probable case.

Ibid., 174.362-378.

115. _____, (1933) Tumors of the parotid region; studies of 135 cases.

Surg., Gyn., & Obstet., 57.104-114.

116. _____, (1936) 300 mixed tumors of the salivary glands of which 69 recurred.

Ibid., 63.457-468.

117. _____, (1942) The histopathologic prognosis of salivary gland mixed tumors.

Am. J. Med. Sc., 203,502-519.

118. _____, (1943) The mysterious mixed tumor of the salivary glands.

Surg., Gyn., & Obstet., 76.23-34.

119. McGregor, A.N., & Wartman, C., (1906) A large teratoma of the neck successfully removed from an infant 3 weeks old.
Lancet, 1.433-435

120. Marchand, , (1910) Verhandl de Ges deutscher. Naturforch u. Ärzte.
Bel 82. Tl1. S17.

121. Martin, H., & Ehrlich, H.E., (1944) Papillary cystadenoma lymphomatosum (Warthin's tumor) of the parotid salivary gland.
Surg., Gyn., & Obstet., 76.611-623.

122. Martini, E., (1907) Über Mischtumoren endothelialen Ursprungs der Speicheldrüsen.
Virchow's Arch., 189.337-414.

123. Mayr, E., Diamond, L.K., Levine, R.P., & Mayr.M., (1956). Suspected corelation between blood-group frequency and pituitary adenomas.
Science, 124.932-933

124. Meyer, K., (1947) The biological significance of hyaluronic acid and hyaluronidase. Physiol. Rev., 27.335-257.

125. Meza-Chávez, L., (1949) Oxyphilic granular cell adenomas of the parotid gland (oncocytoma); report of 5 cases and study of oxyphilic granular cells (oncocytes) in normal parotid glands. Am. J. Path., 25.523-547.

126. Minssen, , (1874) Über gemischte Geschwülste der Parotis. Inaug. Diss. Göttingen.

127. Montella, G., & Fontana, P.F., (1956) I tumori delle ghiandole salivari. Ann. ital. chir. 33.619.

128. Moyse, P., (1955) A propos de 200 tumeurs parotidiennes operees. Mém. Acad. Chir., 81.999-1007.

129. Muir, R., (1941) Textbook of Pathology, Arnold, London. p.258.

130. Nangle, E.J., & Symmers, W.StC., (1956) Pleomorphic sweat gland adenoma of foot.
Brit.J.Bone & Jt.Surg. 32.70.

131. Nasse, D., (1892) Die Geschwülste der Speicheldrüsen und verwandte Tumoren des Kopfes.
Arch.f.klin.chir., 44.233.

132. Nicholson, G.W., (1923) Studies on tumour formation. V. The importance of congenital malformations in tumour formation.
Guys Hosp. Rep., 73.37.

133. Ñino, F.L., (1940) Cistoadenolinfomas papiliferos del cuello.
Bol. d. Inst. clín. quit., 16.271.
Univ. de Buenos Aires.

134. Oughterson, A.W., (1941) Quoted by Plaut, J.A., (1942)

135. Paget, J., (1853) Lectures on Tumours. Longmans, London.

136. Paget, S., (1886) Tumors of Palate. St.Barth.Hosp.Rep. 22.315.

137. Pailler, ,(1903) Les épithéliomas polyformas de la parotide.

Thèse de Paris (1903).

138. Patey,D.H.,(1931) The mixed tumours of the salivary glands.

B.J.S., 18.241-258.

139. _____,(1940) The treatment of mixed tumours of the parotid gland.

Ibid., 28.29-38.

140. _____, & Thackeray,A.C.,(1954) Tuberculous disease of the parotid.

Arch. Middsex. Hosp., 4.256-262.

141. _____, _____,(1957) The pathological anatomy and treatment of parotid tumours with retropharyngeal extension (Dumb Bell tumours). With a report of 4 personal cases.

B.J.S., 44.352-358.

142. Pitance, ,(1897) Etude sur les tumeurs mixtes

du voile du palais.

Thèse de Paris.(1897)

143. Plaut,J.A.,(1942) Adenolymphoma of the parotid gland.

Ann. Surg., 116.43-53.

144. Proby,H.,(1924) Les tumeurs mixtes du prolongement pharyngien de la parotide.

Arch. int. laryng., 3.302.

145. Prudden,T.M.,(1883) Rhabdomyoma of the parotid gland.

Am. J. Med. Sc., 85.438-443.

146. Quattelbaum,F.W., Dockerty,M.B., & Mayo,C.W.,(1946) Adenocarcinoma, cylindroma type, of the parotid gland; a clinical and pathologic study of 21 cases.

Surg.,Gyn., & Obstet., 82.342-347.

147. Ramage,J.S., Binnie,G.G., & McCall,A.J.,(1943) Bilateral adenolymphoma of the parotid glands.

B.J.S. 31.189-192.

148. Rawson, A.J., & Horn, R.C., (1950) Sebaceous glands and sebaceous gland-containing tumors of the parotid salivary gland, with a consideration of the histogenesis of papillary cystadenoma lymphomatosum. Surgery, 27.93-101.

149. Redon, H., (1953) in "Discussion on the surgical treatment of parotid tumours." Proc. Roy. Soc. Med., 46.1013-1016.

150. _____, & Belcour, J., (1955) Chirurgie des glandes salivaires. Mém. Acad. Chir., 81.991.

151. Roberts, J.A.F., (1957) Blood groups and susceptability to disease. Brit. J. prev. soc. Med., 11.107-125.

152. _____, (1958) Personal communication.

153. Robinson, D.W., & Harless, M., (1943) Papillary cystadenoma lymphomatosum of the parotid gland. Surg., Gyn., & Obstet., 76.449-452.

154. Rodriquez, , (1889-90) Contribution à l'étude du

sarcome pur de la parotide.

Thèse de Paris (1890).

155. Ross, D.E., (1955) Salivary gland tumors.

Springfield, Illinois.

156. Rous, P., & Smith, W.E., (1945) The neoplastic potentialities of mouse embryo tissue.

I. The findings with skin of C-strain embryos transplanted to adult animals.

J.Exp.Med., 81.597-620.

157. Rouville, G.de., & Martin, J., (1904) Tumeur mixte de la parotide d'un volume remarquable.

Bull. et mem. Soc.Anat. de Paris, 79.659-690.

158. Rusch, H.P., Baumann, C.A., & Maison, G.L., (1940) Production of internal tumors with chemical carcinogens.

Arch. Path., 29.8-19.

159. Schilling, F., (1921) Beitrag zur Kenntis der Parotisgeschwülste.

Ziegler's Beitr. z. path. Anat.n.z.allg.Pathol.,

68.139.

160. Schreiner, , & Mattick, ,(1929) Tumors of the salivary glands. Based on a study of 66 cases. Am. J. Roentgenol. a. Rad. Ther., 21.541.

161. Schulenburg,C.A.R.,(1954) Salivary gland tumours. A report of 105 cases. S.A. Med. J., 28.910-914.

162. Schutz,C.B.,(1926) Adenoma of the salivary gland. Am. J. Path., 2.153-157.

163. Shear,M.J.,(1936) Studies in carcinogenesis. I. The production of tumours in mice with hydrocarbons. Am. J. Cancer, 26.322-332.

164. Short,D.W., & Puller,P.,(1956) Giant parotid tumours with report of a case. J. Roy.Col.Surg.,Edin., 1.240-248.

165. Siebold,C.G.,(1793) Dissertatio de squirrho parotides. Arburg. Cited by Dunet,C.,& Crysel, J.,(1933) Cancer des glandes salivaires. Paris G. Doin et Cie. (1933).

166. Siebold,J.P.,(1797) Historia systematis salivalis physiologica et pathologica considerata accessoria ex eadem doctrina corrollaries chirungica. Jena.

Cited by Dunet,C., & Crysel,J.,(1933).

167. Simard,L.C.,(1938) Tumors of palm.

Am. J. Cancer, 33.182.

168. Sirsat, ,(1953) Salivary gland tumour. Review of 121 cases.

India J. Surg., 15.65-73.

169. Skorpil,F.,(1940) Über das Speicheldrüsenadenom.

Virchow's Arch., 306.714-736.

170. Slaughter,D.P., Southwick,H.W., & Walter,L.,(1953). The fate of recurrent or persistent parotid tumors.

Surg.,Gyn., & Obstet., 96.535-540.

171. Smith,W.E., & Rous,P.,(1945) The neoplastic potentialities of mouse embryo tissues. II. Contributory experiments; results with the skin

of C^3H and Webster-Swiss embryos; general considerations.

J. Exp. Med., 81.621-646.

172. _____, _____, (1946) The neoplastic potentialities of transplanted embryo tissue; the gastric and pulmonary tumors induced with methylcholanthrene.

Cancer Res., 6.500

173. _____, (1947) The neoplastic potentialities of mouse embryo tissues. III. The tumors elicited from gastric epithelium.

J. Exp. Med., 85.459-478.

174. _____, (1949) The tissue transplant technic as a means of testing materials for carcinogenic action.

Cancer Res., 9.712-723.

175. _____, (1950) The neoplastic potentialities of mouse embryo tissues. V. The tumors elicited with methylcholanthrene from pulmonary

epithelium.

J. Exp. Med., 91.87-104.

176. Spence,J.,(1863) Case of enormous deep-seated tumour of the face and neck, successfully removed by operation.

Dublin Quarterly J. Med Sc., 36.272-283.

177. Ssobolew,L.M.,(1912) Zur kauistik der branchiome.

Frankf. Ztschr. f. Path., 11.462-465.

178. Stein,I., & Geschickter,C.F.,(1934) Tumors of the parotid gland. Arch. Surg., 28.492-526.

179. Steiner,P.E.,(1939) in Program of the Third International Cancer Congress, Atlantic City, Sept. 11th - 16th., 1939. p.138.

180. _____,(1940) Induced tumors of the salivary glands.

Acta de l'union Internationale Contre le Cancer, 5.70-72.

181. _____,(1942) Comparitive pathology of

induced tumors of the salivary glands.

Arch. Path., 34.613-624.

182. _____,(1956) Personal communication.

183. Stewart,F.W., Foote,F.W., & Becker,W.F.,(1945) Mucoepidermoid tumors of the salivary glands.

Ann. Surg., 122.820-844;

184. Stobie,H.,(1935) A mixed salivary tumour of the palate.

Proc. Roy. Soc. Med., 28.739.

185. Stöhr,F., & Risak,E.,(1926) Zur Klinik und Anatomie der Parotisgeschwülste.

Arch. f. klin. Chir., 143.609-648.

186. Street,A.,(1913) A series of cases of parotid tumours.

B.M.J., 1.1047

187. Struthers,D.,(1951) ABO groups of infants and children dying in the West of Scotland (1949-1951).

Brit.J.soc.Med., 5.223-228.

188. Thomas,H.O.,(1957) Cervical teratoma.

B.J.S., 44.625-627.

189. Thomson, A.S., & Bryant, H.C.jr., (1950) Histogenesis of Papillary cystadenoma lymphomatosum (Warthin's tumor) of the parotid salivary gland.

Am. J. Path., 26.807-849.

190. Verhoeff, F.H., (1904) The mixed tumors of the lachrymal and salivary glands.

J.Med.Res., 13.319-340.

191. Virchow, R., (1863) Die krankhaften geschwülste.

Sechzehnte vorlesprung, 1.502.

192. Volkmann, R., (1895) Über endotheliale Geschwülste Zugleich ein Beitrag zu den Speicheldrüsen und Gaumentumeren.

Deutsche. Ztschr. f. Chir., 41.107.

193. Von Hansemann, D., (1910) Beitrag zur Histogenese der Parotistumoren.

Ztschr. f. Krebsforsch., 9.379.

194. Warthin, A.S., (1929) Papillary cystadenoma lymphamatosum; a rare teratoid of the parotid

region.

J. Cancer Res., 13.116-125.

195. Wartmann, A.H., (1879) Recherches sur l'enchondrome.

Inaug. Diss. Genève et Bâle. Strasburg (1880).

196. Wheelock, M.C., & Madden, T.J., (1949) Uncommon

tumors of the salivary glands.

Surg., Gyn., & Obstet., 88.776-782.

197, Willis, R.A., (1953) Pathology of Tumours.

Butterworth, London.

198. Wilms, , (1899) Die Mischegeschwulste. Leipzig.

199. Wilson, L.B., & Willis, B.C., (1912) The so called

mixed tumors of the salivary glands.

Am.J.Med.Sc., 143.656.

200. Wilson, R.H., De Eds, F., & Cox, A.J.jr., (1941) The

toxicity and carcinogenic activity of 2.acetylamino-

fluorine.

Cancer Res., 1.595-608.

201. Wood, F.C., (1904) The mixed tumors of the salivary

glands; summary of the clinical course and general morphology of the tumors.

Ann. Surg., 39.207-339.

202. Yamagiwa,K., & Ichikawa,K.,(1915-16) Experimentelle Studie über die Pathogenese der Epithelialgeschwülste.

Mitt. med. Facultat. kaiser. Universitat Tokyo 15.295-344.

203. Yates,P.O., & Paget,G.E.,(1952) Mixed tumour of salivary gland showing bone formation.

J.Path. & Bact., 64.881.

204. Yen,F.C.,(1915) A case of fibroma of the parotid.

J.A.M.A., 64.1238.

205. Zymbal,W.E.,(1933) Histologische und experimentelle Untersuchungen über die Geschwülste der Speicheldrüsen.

Beitr. z. Pathol. Anat., 91.113-175.

APPENDIX I.

Statistical analysis of blood groups in Salivary Tumours.

All the various types of salivary tumours were compared with the controls. The only one which does not show a significantly lower percentage of group O is in Adenolymphomata where only 12 patients are considered. The indications are, however, that if the number of patients is increased then significance will be established. All types were also tested taken together, although in view of the significance established for two of the varieties of salivary tumours, I do not think that this test was necessary.

a). Pleomorphic Adenomata.

Blood-group.	Control.	Pleomorphic Adenomata.	Total.
O	3177	92	3269
Non-O	2721	202	2923
Total	5898	294	6192

$$X^2 = \frac{(3177 \times 202 - 2721 \times 92)^2 \, 6192}{5898 \times 294 \times 3269 \times 2923}$$

$$= \frac{153,211,182,084}{2,809,254,378} \times 1.049847$$

$$= 57.3$$

This is a highly significant percentage with group O significantly higher for the controls as against pleomorphic adenomata.

b). Salivary carcinomata.

Blood-group.	Control.	Carcinoma.	Total.
O	3177	5	3182
Non-O	2721	30	2751
Total	5898	35	5933

$$X^2 = \frac{(3177 \times 30 - 2721 \times 5)^2 \, 5933}{5898 \times 35 \times 3182 \times 2751}$$

$$= \frac{6,675,707,025}{306,378,870} \times 1.0059342$$

$$= 21.7891 \times 1.0059342$$

$$= 21.9$$

This is again a highly significant percentage with group O significantly higher for the controls.

c). Adenolymphomata.

Blood-group	Control.	Adenolymphomata.	Total.
O	3177	3	3180
Non-O	2721	9	2730
Total	5898	12	5910

$$X^2 = \frac{(3177 \times 9 - 2721 \times 3 - 2955)^2 \, 5910}{5898 \times 12 \times 3180 \times 2730}$$

$$= \frac{305,375,625}{104,176,800} \times 1.0020346$$

$$= 2.93132 \times 1.00203$$

$$= 2.94$$

As has been stated this is NOT significant.

d). All types together.

Blood-group.	Control	All types.	Total.
0	3177	100	3277
Non-O	2721	241	2962
Total	5898	341	6239

$$X^2 = \frac{243,598,512,249 \times 1.0578162}{3,309,907,634}$$

$$= 77.9$$

As would be expected this percentage is highly significant.

All these figures have been checked by Dr. R.A. Robb, Mathematics Department, Glasgow University and to whom I am indebted.

APPENDIX II.

Technique used in Experiment 2.

The technique used was a modification of that described by Rous & Smith on numerous occasions (1945a & b, 1946, 1947, 1949, 1950).

i. Newly born mice were killed with coal gas and washed in Locke's solution.

ii. Using the dissecting microscope the salivary tissue was removed as aseptically as possible.

iii. With Locke's solution a suspension of salivary tissue was made.

iv. A 0.25ml. Luer syringe was taken and 0.05ml. of the suspension of salivary tissue drawn up; followed by 0.05ml. of a 1% suspension of 20.methylocholanthrene in olive oil.

v. After cleaning the right thigh of the adult male C_3H mouse, a 16 gauge needle was fitted to the syringe and the contents injected into the thigh.

vi. The thigh was not palpated for 2 weeks.

APPENDIX III.

Clinical Material.

i. Pleomorphic adenoma.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist. No.	Sit.	Side.	Hosp.	Blood group.
1.	M.	37	40	-	1578/49	P	L	G.R.I.	O.
2.	F.	49	52	-	A5379/55	P	L	G.R.I.	B.
3.	F.	39	42	+	C3009/56	P	L	G.R.I.	A. +
4.	M.	39	51	+	/45	P	R	G.R.I.	O. +
5.	F.	28	48	-	C 5/49	P	L	G.R.I.	A.
6.	M.	32	57	+	1086/39	P	R	G.R.I.	O. -
7.	M.	29	32	-	1313/56	P	L	G.R.I.	A.
8.	M.	68	70	+	Law /	P	R	G.R.I.	A. +
9.	M.	44	45	-	869/45	P	R	G.R.I.	A.
10.	F.	46	49	-	219/53	P	L	G.R.I.	A.
11.	M.	39	59	-	/57	Sx	L	G.R.I.	O. +
12.	M.	49	52	-	C1299/42	P	R	G.R.I.	A. +

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist. No.	Site.	Side.	Hosp.	Blood group.
13.	M.	34	36	+	1186/43	P	R	G.R.I.	B.
14.	M.	37	48	-	1441/43	P	L	G.R.I.	A. +
15.	F.	58	65	-	1890/42	P	L	G.R.I.	-
16.	M.	56	62	-	P0733/56	P	L	G.R.I.	O.
17.	F.	59	59	-	2671/53	Lip	-	G.R.I.	B.
18.	F.	30	35	+	4109/53	P	R	G.R.I.	A.
19.	F.	31	35	+	1419/44	P	R	G.R.I.	A.
20.	M.	43	43	-	C /56	Pal	-	G.R.I.	O. +
21.	F.	9	14	-	51	P	R	G.R.I.	A. +
22.	M.	13	15	+	1840/44	P	R	G.R.I.	O. +
23.	F.	68	69	-	St /54	P	L	G.R.I.	A. +
24.	F.	19	20	+	814/41	P	R	G.R.I.	O. +
25.	F.	60	65	+	-	P	L	G.R.I.	O.
26.	M.	51	52	-	1376/56	P	R	G.R.I.	O. -
27.	F.	3	42	+	860/43	Cheek	-	G.R.I.	O.
28.	F.	20	21	+	1932/45 I402	P	R	G.R.I.	O.

No.	Sex.	Age at onset	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
29.	M.	58	68	-	1333/39	P	R	G.R.I.	-
30.	F.	24	28	-	4715/54	P	L	G.R.I.	A. +
31.	F.	42	62	+	St3951/51	P	R	G.R.I.	O.
32.	M.	46	49	-	3247/56	P	L	G.R.I.	B. -
33.	M.	36	36	-	311/52	P	R	G.R.I.	O.
34.	M.	68	77	-	1339/50	P	L	G.R.I.	A. +
35.	M.	17	29	-	Oban	P	L	G.R.I.	A. +
36.	F.	53	57	-	4992/54	P	R	G.R.I.	AB.
37.	M.	35	43	+	431/50	P	R	G.R.I.	O.
38.	F.	44	48	+	2272/54	P	R	G.R.I.	O. +
39.	F.	41	45	-	C5470/55	Sx	R	G.R.I.	O.
40.	F.	26	28	+	4374/54	P	L	G.R.I.	O.
41.	F.	35	50	-	2000/42	P	L	G.R.I.	A.
42.	F.	18	19	+	1429/43	Sx	L	G.R.I.	A.
43.	M.	47	52	-	2262/48	P	L	G.R.I.	A.
44.	M.	39	43	-	58/44	P	R	G.R.I.	A +

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
45.	M.	37	42	-	1199/45	P	R	G.R.I.	AB.
46.	M.	56	57	-	1220/38	P	L	G.R.I.	-
47.	F.	55	56	+	1764/42	P	L	G.R.I.	B.
48.	F.	16	18	-	L2767/50	P	R	G.R.I.	A. +
49.	M.	57	59	-	170/39	P	R	G.R.I.	A. +
50.	F.	30	38	-	2879/51	P	L	G.R.I.	O.
51.	M.	14	15	+	2017/38	P	L	G.R.I.	A.
52.	F.	29	36	-	744/44	P	R	G.R.I.	A.
53.	F.	67	75	-	2744/48	P	L	G.R.I.	A.
54.	M.	22	23	-	1776/46	Lip	-	G.R.I.	A. +
55.	M.	35	36	+	2010/47	P	R	G.R.I.	A. +
56.	F.	65	77	+	4090/50	P	R	G.R.I.	O.
57.	F.	49	53	-	1893/43	P	L	G.R.I.	A. +
58.	M.	30	50	-	2517/48	Sx	R	G.R.I.	O. +
59.	F.	49	52	-	1790/37	P	R	G.R.I.	-
60.	M.	30	45	-	V2044/53	Pal.	-	G.R.I.	O. -

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
61.	F.	26	29	-	V 81/53	Pal	-	G.R.I.	A. +
62.	F.	51	52	-	982/55	P	R	G.R.I.	O. -
63.	M.	37	38	-	752/38	P	L	G.R.I.	A.
64.	F.	42	44	+	-	P	L	G.R.I.	A.
65.	M.	44	45	+	1251/53	Lip	-	G.R.I.	AB.
66.	M.	52	62	+	82/46	P	L	G.R.I.	A.
67.	F.	46	49	+	St /45	P	L	G.R.I.	A. +
68.	F.	29	30	-	C1756/55	Lip	-	G.R.I.	A.
69.	M.	36	37	+	G /47	P	R	G.R.I.	A.
70.	F.	52	52	+	280/49	P	L	G.R.I.	A. +
71.	F.	18	26	+	Bristol/43	P	L	G.R.I.	A.
72.	F.	33	34	-	1128/56	P	R	G.R.I.	O. +
73.	M.	36	46	+	4101/56	P	L	G.R.I.	A.
74.	M.	44	46	-	2868/55	P	R	G.R.I.	B.
75.	F.	43	57	-	3878/50	P	L	G.R.I.	A.
76.	F.	23	26	-	2044/55	P	R	G.R.I.	O. +

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
77.	F.	29	42	+	-	P	L	G.R.I.	O.
78.	F.	38	40	+	-	P	R	G.R.I.	O.
79.	F.	18	19	-	410/55	P	R	G.R.I.	O.
80.	M.	73	74	-	-	P	L	G.R.I.	A. +
81.	F.	38	39	+	1757/52	Pharynx		G.R.I.	B.
82.	F.	39	43	-	1659/53	P	R	G.R.I.	O.
83.	F.	26	35	-	702/39	P	R	G.R.I.	B.
84.	M.	37	40	-	K	P	R	G.R.I.	B.
85.	M.	47	48	-	539/51	P	L	G.R.I.	A.
86.	F.	42	57	-	561/39	P	L	G.R.I.	A.
87.	F.	22	30	+	1902/51	P	L	G.R.I.	O.
88.	F.	9	13	-	1265/53	P	R	G.R.I.	A.
89.	M.	28	30	-	1055/47	P	L	G.R.I.	AB.
90.	M.	37	38	-	2267/49	P	R	G.R.I.	A.
91.	F.	39	40	-	398/56	P	L	G.R.I.	O. +
92.	F.	25	28	-	790/52	P	L	G.R.I.	A.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.	
93.	F.	24	29	+	St4377/53	P	R	G.R.I.	A.	
94.	F.	66	67	-	2434/48	P	L	G.R.I.	A.	-
95.	F.	62	64	-	5603/54	P	R	G.R.I.	A.	+
96.	F.	20	24	+	/49	P	R	G.R.I.	A.	
97.	M.	12	15	-	1872/43	Lip	-	G.R.I.	A.	-
98.	M.	38	43	-	1550/45	P	R	G.R.I.	A.	+
99.	F.	50	56	-	2941/56	P	R	G.R.I.	O.	
100.	F.	12	18	-	C 91/49	P	R	G.R.I.	-	
101.	M.	34	40	+	875/36	P	R	G.R.I.	O.	
102.	M.	33	35	+	-	P	L	G.R.I.	O.	
103.	F.	37	39	-	3040/50	P	R	G.R.I.	A.	
104.	F.	29	31	-	435/51	P	R	G.R.I.	A.	
105.	F.	51	54	-	2950/55	P	R	G.R.I.	A	+
106.	F.	33	35	-	-	P	L	G.R.I.	A.	+
107.	M.	28	29	-	Law	P	R	G.R.I.	A.	+
108.	M.	19	23	+	273/36	P	L	G.R.I.	O.	+

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
109.	F.	23	27	+	1930/39	P	L	G.R.I.	A.
110.	F.	58	73	-	-	P	L	G.R.I.	A.
111.	F.	38	42	-	79/55	Sx	L	G.R.I.	O. +
112.	M.	24	27	-	507/55	P	L	G.R.I.	A. +
113.	F.	23	26	-	E3202/50	P	L	G.R.I.	A.
114.	M.	26	28	+	1922/	P	R	G.R.I.	A.
115.	F.	46	52	+	-	P	L	G.R.I.	A.
116.	F.	48	49	+	Ayr	P	R	G.R.I.	B. +
117.	F.	26	30	-	P1963/53	P	R	G.R.I.	O.
118.	F.	30	31	+	1936	P	L	G.R.I.	O.
119.	F.	49	54	-	1219/38	P	L	G.R.I.	O.
120.	M.	36	41	+	G /52	P	R	G.R.I.	A. -
121.	F.	31	51	+	1929	Pal.	-	G.R.I.	A. -
122.	F.	43	46	+	1934	Sx	R	G.R.I.	-
123.	F.	37	38	-	699/49	P	R	G.R.I.	B.
124.	M.	28	30	-	V1522/51	Pal.	-	G.R.I.	A.

No.	Sex.	Age at onset.	Age at lst. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
125.	F.	39	42	-	168/46	Pharynx.		G.R.I.	A.
126.	M.	67	68	-	613/44	P	R	G.R.I.	-
127.	F.	45	48	-	676/43	P	L	G.R.I.	-
128.	F.	27	47	-	1137/42	P	R	G.R.I.	B.
129.	F.	23	33	-	1017/39	P	R	G.R.I.	O.
130.	M.	28	29	-	3653/51	P	L	G.R.I.	A.
131.	F.	71	72	-	1883/53	P	R	G.R.I.	A. +
132.	F.	27	30	-	G /53	P	L	G.R.I.	A. -
133.	F.	39	40	-	V1348/45	Sx	L	G.R.I.	O.
134.	M.	22	40	+	1940	P	L	G.R.I.	A. +
135.	M.	42	43	-	2526/52	Lip	-	G.R.I.	A.
136.	M.	70	80	-	St3986/55	P	R	G.R.I.	A.
137.	F.	61	63	-	402/43	Lip	-	G.R.I.	O.
138.	M.	36	40	+	2257/47	P	R	G.R.I.	O.
139.	M.	59	70	-	1853/45	P	R	G.R.I.	A.
140.	M.	13	40	-	221/48	P	R	G.R.I.	O.
141.	F.	55	75	-	I /51	P	R	G.R.I.	A.+

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
142.	M.	34.	38	-	1428/43	P	L	G.R.I.	A.
143.	F.	52	54	-	Oban/56	P	R	G.R.I.	O. +
144.	M.	44	48	-	Hel /42	P	R	G.R.I.	A.
145.	M.	9	12	+	2047/52	P	R	G.R.I.	A. +
146.	F.	41	45	-	1299/45	P	L	G.R.I.	B.
147.	F.	20	22	-	V2840/52	Pal.	-	G.R.I.	AB.
148.	F.	53	54	-	V1435/51	Pal.	-	G.R.I.	A.
149.	F.	15	27	-	A4240/53	Tonsil	-	G.R.I.	O.
150.	M.	44	45	-	317/45	P	L	G.R.I.	A.
151.	F.	71	74	-	Ayr /55	P	R	G.R.I.	A. +
152.	F.	23	26	+	2657/52	P	R	G.R.I.	O.
153.	F.	54	59	-	892/38	P	R	G.R.I.	-
154.	M.	37	67	+	593/52	P	R	G.R.I.	O.
155.	M.	18	21	+	222/44	P	L	G.R.I.	A.
156.	F.	40	50	+	1952	Pal	-	G.R.I.	A. -
157.	M.	79	80	-	1268/41	P	L	G.R.I.	-

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
158.	M.	14	17	-	1750/38	P	R	G.R.I.	A.
159.	F.	34	36	-	951/39	P	R	G.R.I.	-
160.	M.	48	49	-	499/50	P	L	G.R.I.	A.
161.	M.	52	53	-	1935/55	Sx	L	G.R.I.	AB. -
162.	M.	24	25	-	1484/47	Pal.	-	G.R.I.	B.
163.	M.	30	35	-	1182/47	P	L	G.R.I.	O.
164.	F.	58	59	-	1085/47	P	L	G.R.I.	A. +
165.	M.	57	58	-	-	P	R	G.R.I.	A.
166.	M.	50	59	-	259/50	P	L	G.R.I.	A. +
167.	M.	18	19	-	1653/38	Pal.	-	G.R.I.	-.
168.	F.	59	68	-	663/44	P	L	G.R.I.	-.
169.	M.	37	40	+	/40	P	L	G.R.I.	A.
170.	M.	37	47	-	1212/38	P	L	G.R.I.	-.
171.	F.	19	21	-	514/45	P	R	G.R.I.	O.
172.	M.	18	19	+	1855/45	P	L	G.R.I.	O.
173.	F.	33	38	-	1145/47	P	R	G.R.I.	O.
174.	F.	19	22	-	G /55	P	L	G.R.I.	A. +

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist. No.	Site.	Side.	Hosp.	Blood group.
175.	F.	36	42	-	Lewis/55	P	R	G.R.I.	A.
176.	F.	35	50	+	2761/49	P	R	G.R.I.	A. +
177.	F.	52	55	+	1286/42	P	L	G.R.I.	A. +
178.	F.	29	31	+	/44	P	R	G.R.I.	O.
179.	F.	50	54	-	3488/53	Lip	-	G.R.I.	A.
180.	M.	69	70	+	A /35	Sx	R	G.R.I.	-.
181.	M.	77	78	-	A4909/52	Lip	-	G.R.I.	A. -
182.	M.	70	75	-	/55	Pal.	-	G.R.I.	A. +
183.	F.	32	34	-	3137/52	P	R	G.R.I.	A.
184.	M.	59	63	-	1160/45	P	L.	G.R.I.	A. +
185.	F.	59	59	+	KP1878/53	Cheek	-	G.R.I.	O.
186.	F.	35	37	-	1737/43	P	R	G.R.I.	A.
187.	F.	56	63	-	5725/54	P	R	G.R.I.	A. +
188.	M.	17	18	-	St1760/55	P	L	G.R.I.	O. -
189.	F.	52	53	-	4089/55	P	R	G.R.I.	A.
190.	F.	31	37	+	1890/51	P	L	G.R.I.	O. +
191.	F.	53	54	-	C449/50	P	R	G.R.I.	A.

No.	Sec.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
192.	M.	33	43	-	St /47	P	L	G.R.I.	A. +
193.	M.	32	33	-	2415/48	P	L	G.R.I.	O.
194.	F.	29	37	-	3037/52	P	L	G.R.I.	A. +
195.	F.	50	55	-	822/48	P	R	G.R.I.	B.
196.	F.	35	41	+	/32	P	R	G.R.I.	O. -
197.	F.	64	65	-	5238/53	P	L	G.R.I.	A. +
198.	M.	37	38	+	1583/51	Chin	-	G.R.I.	O.
199.	F.	51	52	-	872/46	P	R	G.R.I.	A.
200.	F.	35	40	-	1094/40	P	R	G.R.I.	AB.
201.	F.	34	36	-	2255/48	Sx	L	G.R.I.	A. -
202.	F.	68	74	-	2057/55	P	L	G.R.I.	O.
203.	F.	65	66	-	27/55	P	R	G.R.I.	A. +
204.	F.	45	75	-	L2521/50	P	R	G.R.I.	-
205.	F.	44	54	-	1659/42	P	L	G.R.I.	O. +
206.	M.	14	15	+	365/53	P	L	G.R.I.	O.
207.	F.	20	22	+	Bal	P	R	G.R.I.	O.
208.	F.	65	69	-	E3062/56	P	R	G.R.I.	A. +

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
209.	F.	12	42	-	4957/53	P	L	G.R.I.	O.
210.	M.	12	14	+	C 79/49	P	R	G.R.I.	A.
211.	M.	46	58	-	-	P	R	G.R.I.	A.
212.	F.	25	30	-	V3155/50	Pal.	-	G.R.I.	A.
213.	M.	21	22	-	2127/50	P	R	G.R.I.	O.
214.	F.	21	22	±	1187/43	P	L	G.R.I.	O.
215.	F.	28	30	-	1533/37	P	R	G.R.I.	B.
216.	F.	42	43	-	2054/48	P	L	G.R.I.	O.
217.	F.	23	27	+	252/48	P	L	G.R.I.	O.
218.	F.	48	58	-	149/46	P	L	G.R.I.	A.
219.	F.	44	45	-	4809/55	P	L	G.R.I.	A. +
220.	F.	39	45	-	1744/46	P	R	G.R.I.	A. +
221.	F.	34	35	+	/38	P	R	G.R.I.	O. +
222.	M.	63	65	+	2443/49	Sx	L	G.R.I.	A.
223.	F.	63	70	-	-	P	R	G.R.I.	A. -
224.	F.	32	52	-	P 373/56	P	L	G.R.I.	A.
225.	M.	33	41	-	1015/45	P	L	G.R.I.	A.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
226.	F.	47	52	-	1277/45	P	R	G.R.I.	A. +
227.	F.	23	25	-	682/47	P	L	G.R.I.	O. -
228.	F.	16	18	-	Eng/	P	L	Eng.	O. -
229.	F.	64	65	+	St /50	P	L	G.R.I.	A. +
230.	F.	22	23	+	350/49	P	L	G.R.I.	A. +
231.	M.	25	35	-	369/48	P	R	G.R.I.	AB.
232.	F.	39	42	-	2825/53	P	R	G.R.I.	A.
233.	F.	16	19	+	2179/47	P	L	G.R.I.	B.
234.	M.	90	91	+	-	P	L	G.R.I.	- .
235.	F.	39	40	-	2190/46	P	L	G.R.I.	O.
236.	M.	70	72.	-	1162/46	P	L	G.R.I.	A. +
237.	M.	76	77	-	-	P	L	G.R.I.	A. +
238.	M.	48	56	-	Bal.	P	R	G.R.I.	O. +
239.	F.	21	22	+	1307/41	P	R	G.R.I.	A.
240.	M.	46	48	-	G /46	P	R	G.R.I.	-.
241.	M.	43.	46	-	130/53	Sx	R	G.R.I.	A.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
242.	F.	49	58	-	C 97/49	P	R	G.R.I.	A.
243.	F.	25	40	-	1472/53	P	R	S.G.H.	O.
244.	F.	40	41	-	P553659	P	R	W.I.G.	O.
245.	F.	70	76	-	-	P	L	S.G.H.	O.
246.	M.	51	61	-	882/50	P	R	S.G.H.	O.
247.	F.	49	59	-	21579/54	P	L	W.I.G.	A.
248.	F.	43	45	-	HR523551	P	R	W.I.G.	-.
249.	F.	37	52	-	1308/52	P	R	S.G.H.	A.
250.	F.	47	48	+	1789/52	P	R	S.G.H.	A.
251.	F.	46	59	+	/41	P	L	W.I.G.	A.
252.	F.	39	57	+	881/41	P	L	W.I.G.	A.
253.	F.	33	35	-	429/55	P	R	S.G.H.	A. -
254.	F.	49	52	-	1750/50	P	R	S.G.H.	B.
255.	F.	52	55	-	W.I.G./54	P	R	W.I.G.	A.
256.	M.	32	33	-	HR500704	P	L	W.I.G.	B.
257.	F.	43	44	-	69 C/52	P	R	S.G.H.	A.
258.	M.	59	60	+	-	P	R	G.R.I.	O.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
259.	M.	20	25	+	HR480796	P	L	W.I.G.	O.
260.	F.	28	51	+	HR501274	P	L	W.I.G.	A.
261.	F.	26	41	-	HR522525	P	R	W.I.G.	A.
262.	F.	54	56	-	HR540971	Pal.	-	W.I.G.	A.
263.	M.	30	37	-	HR511384	P	R	W.I.G.	O.
264.	F.	42	43	-	HR523594	P	L	W.I.G.	A.
265.	M.	39	40	-	HR533457	P	L	W.I.G.	A.
266.	F.	35	37	-	HR543876	Tonsil		W.I.G.	O.
267.	F.	39	49	-	HR501526	Sx	R	W.I.G.	A.
268.	M.	34	39	-	P554609	P	R	W.I.G.	O.
269.	M.	50	51	+	1571/53	Sx	L	S.G.H.	A. +
270.	M.	19	21	-	549/53	P	L	S.G.H.	A. +
271.	F.	19	21	-	/55	P	R	S.G.H.	A. +
272.	M.	37	45	+	62/50	P	L	S.G.H.	A.
273.	F.	20	23	-	1166/50	P	L	S.G.H.	-.
274.	F.	30	42	-	HR531252	P	R	W.I.G.	A.
275.	F.	26	56	-	HR530621	P	R	W.I.G.	A.

No.	Sex.	Age at onset.	Age at lst. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
276.	M.	24	39	+	HR501436	P	L	W.I.G.	B.
277.	M.	40	50	-	1611/52	P	L	S.G.H.	B.
278.	F.	40	45	-	1875/53	P	R	S.G.H.	O.
279.	F.	42	43	-	HR522409	P	L	W.I.G.	A.
280.	M.	26	31	+	2224/54	Sx	L	S.G.H.	A.
281.	F.	84	85	-	HR542203	P	R	W.I.G.	O.
282.	M.	42	48	-	HR510782	P	L	W.I.G.	O.
283.	F.	30	32	+	/50	P	L	W.I.G.	A.
284.	F.	18.	22	-	/56	Sx	R	S.G.H.	B.
285.	F.	39	54	-	675/55	P	R	S.G.H.	O.
286.	M.	48	53	-	32/54	Pa.	-	S.G.H.	O.
287.	M.	20	22	-	1559/55	P	R	S.G.H.	A. +
288.	M.	54	62	±	HR523880	P	L	W.I.G.	A.
289.	F.	43	53	-	HR501638	P	R	W.I.G.	A. +
290.	F.	20	21	-	/55	P	R	W.I.G.	O.
291.	F.	23	31	-	504/51	P	L	S.G.H.	-.
292.	F	43	55	-	1218/51	P	L	S.G.H..	A.B.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
293.	F.	22	42	-	HR543976	Sx	L	W.I.G.	O.
294.	F.	54	59	-	HR500573	P	L	W.I.G.	O.
295.	F.	46	52	-	565/56	P	R	S.G.H.	O.
296.	M.	29	40	-	/53	P	R	W.I.G.	A.
297.	F.	440	43	-	Falkirk/54	P	R	Falkirk	A.
298.	F.	33	59	-	HR550398	P	R	W.I.G.	A.
299.	F.	58	62	+	HR543913	Sx	R	W.I.G.	A.
300.	M.	59	60	-	1368/55	Sx	L	S.G.H.	A.
301.	F.	13	21	+	1889/54	P	R	S.G.H.	A.
302.	F.	38	39	+	P554396	P	R	W.I.G.	A.
303.	M.	71	72	-	1384/52	P	L	S.G.H.	B.
304.	F.	34	54	-	/54	P	R	W.I.G.	A.
305.	F.	48	56	-	242/52	P	R	S.G.H.	A.
306.	M.	45	50	+	/49	P	L	W.I.G.	O.
307.	F.	39	44	-	P551280	P	L	W.I.G.	A.
308.	M.	52	53	+	HR482426	Sl.	L	W.I.G.	A.
309.	M.	18	30	-, I57.	E2148/56	P	R	G.R.I.	A.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
310.	F.	28	35	+	680/50	P	R	G.R.I.	A.
311.	F.	47	48	+	814/39	P	R	G.R.I.	A.
312.	F.	32	34	-	2106/47	P	R.	G.R.I.	A.
313.	F.	58	60	-	233/47	P	L	G.R.I.	A.-
314.	M.	26	27	-	1034/53	P	R	G.R.I.	A.
315.	F.	38	40	-	1610/47	P	L	G.R.I.	A.

ii. Carcinoma.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
316.	M.	21	39	+	2342/56	P	L	G.R.I.	A.-
317.	M.	64	64	+	HR533512	Pal.	-	W.I.G.	A.+
318.	F.	60	62	+	HR503560	Sl.	L	W.I.G.	O.
319.	M.	16	26	+	K496/54	P	R	G.R.I.	A.-
320.	F.	72	73	+	Law.	P	L	G.R.I.	A.
321.	F.	44	74	+	G550336	P	R	W.I.G.	A.-

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group.
322.	F.	65	66	-	C1536/44	P	L	G.R.I.	A.+
323.	M.	60	60	+	K421	P	R	G.R.I.	O.
324.	M.	20	32	+	V1935/53	Pal.	-	G.R.I.	A.
325.	F.	57	57	+	/54	Tongue		S.G.H.	A.
326.	F.	60	60	+	Stranraer	P	L	G.R.I.	A.
327.	M.	47	57	+	HR482135	Sx	L	W.I.G.	A.
328.	M.	75	78	+	Law/54	P	R	G.R.I.	A.+
329.	F.	66	68	+	987/36	P	L	G.R.I.	-
330.	M.	20	60	-	1789/37	P	L	G.R.I.	-
331.	M.	48	48	+	4072/54	P	L	G.R.I.	A
332.	F.	72	72	+	1913/48	P	L	G.R.I.	A.
333.	F.	63	63	-	1105/41	P	R	G.R.I.	-
334.	M.	60	62	+	742/38	Sx	L	G.R.I.	-
335.	M.	28	48	+	P551572	P	L	W.I.G.	A.+
336.	F.	43	66	+	1455/35	P	R	G.R.I.	-
337.	F.	29	73	+	V2517/50	Lip	-	G.R.I.	-
338.	M.	71	71	+	1452/41	Pal.	-	G.R.I.	-

No.	Sex.	onset.	1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	group
339.	F.	62	62	+	3236/51	P	R	G.R.I.	A.
340.	M.	53	53	-	610/39	Sx	R	G.R.I.	-
341.	F.	48	49	+	V227/52	Pal.	-	G.R.I.	-
342.	M.	79	79	+	1165/50	P	R.	G.R.I.	-
343.	M.	55	55	+	K/50	Pal.	-	G.R.I.	A.
344.	M.	52	52	+	HR532050	P	L	W,I.G.	-
345.	M.	64	64	+	1036/48	P	L	G.R.I.	-
346.	M.	48	63	+	Edin/48	P	L	G.R.I.	O.
347.	F.	10	11	+	HR493167	P	L	W.I.G.	A.
348.	F.	20	20	+	1361/38	P	L	G.R.I.	A.+
349.	F.	51	52	+	1850/35	P	L	G.R.I.	-
350.	M.	10	11	-	1368/43	P	R	G.R.I.	O.
351.	M.	73	74	+	1320/38	P	R	G.R.I.	-
352.	F.	61	66	+	HR523149	P	R	W.I.G.	-
353.	M.	55	59	+	1564/40	Nose		G.R.I.	-
354.	F.	74	78	+	HR542544	P	R	W.I.G.	A.
355.	M.	53	53	+	1352/48	Sx	R	G.R.I.	-

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group
356.	M.	49	50	+	Law/50	P	L	G.R.I.	A.
357.	F.	66	69	+	873/41	P	R	G.R.I.	-.
358.	M.	73	73	+	L1679/50	P	L	G.R.I.	-.
359.	F.	52	52	+	586/40	P	R	G.R.I.	-.
360.	M.	47	48	+	C54/46	P	R	G.R.I.	B.
361.	F.	70	71	+	/40	P	R	G.R.I.	-.
362.	F.	62	63	-	262/55	P	L	G.R.I.	A. +
363.	F.	30	31	-	HR544212	Sx	L	W.I.G.	A.
364.	M.	69	70	+	A1738/53	P	L	G.R.I.	-.
365.	M.	46	52	+	1796/38	P	L	G.R.I.	A. +
366.	M.	76	76	+	P551573	P	R	W.I.G.	O.
367.	F.	27	31	+	586/40	P	R	G.R.I.	A.
368.	M.	64	67	+	Law/42	Sx	L	G.R.I.	-.
369.	M.	62	65	+	/39	P	L	G.R.I.	-.
370.	F.	50	52	+	830/52	P	R	G.R.I.	-.
371.	M.	51	53	+	B /54	Pal.	-	G.R.I.	A.

No.	Sex.	Age at onset.	Age at 1st. op.	Rec.	Hist.No.	Site.	Side.	Hosp.	Blood group;
384.	F.	72	73	-	Law/45	Parotids.		G.R.I.	A.
385.	M.	47	49	-	HR512367	P	L	W.I.G.	O.
386.	F.	35	39	-	HR501848	Parotids.		W.I.G.	A.
387.	M.	76	77	-	K /54	Tonsil	R	G.R.I.	A. +
388.	M.	62	64	-	1495/41	P	L	G.R.I.	-
389.	F.	58	62	-	HR500586	P	R	W.I.G.	A.
390.	M.	70	72	-	Law/44	Parotids.		G.R.I.	-.
391.	M.	80	84	-	S.G.H./55	P	R	S.G.H.	A. +
392.	F.	38	41	-	H / 44	Parotids.		G.R.I.	A. +
393.	F.	60	62	-	HR523861	P	L	W.I.G.	AB.
394.	F.	71	71	-	C2385/56	P	L	G.R.I.	O.
395.	M.	60	61	-	3770/56	P	L	G.R.I.	A.

iv. Miscellaneous group.

See over.

No.	Sex.	onset.	1st. op.	Rec.	Hist.No. & Type.	Site.	Side.	Hosp.
396.	M.	52	58	+	878/50 Leiomyosarc.	P	R	S.G.H.
397.	M.	70	70	+	261/49 Retic. sarc.	P	R	G.R.I.
398.	M.	59	63	-	1037/46 Fibroma.	P	R	G.R.I.
399.	F.	70	72	+	1820/53 Retic. Sarc.	Sx	R	G.R.I.
400.	M.	52	52	+	1767/51 Melanoma.	P	R	G.R.I.
401.	F.	55	57	+	1602/44 Melanoma.	P	L	G.R.I.

APPENDIX IV.

Own reprint on this work already published.

Lancet, 1.239-240 (1958)

Blood-groups in tumours of salivary tissue.
