Recurrent swellings of the parotid gland, sialectasis and Mikulicz's syndrome[1]

John Maynard MS FRCS
Guy's Hospital, London SE1 9RT

Recurrent parotitis has been a confused subject for many years. In 1892 Mikulicz described a case of lacrimal gland, submandibular gland and parotid gland swelling in a 42-year-old Prussian farmer. Biopsy of the parotid showed a 'uniformly arranged tissue consisting of small round cells'. In 1925 Gougerot (a French dermatologist) described patients with progressive atrophy of the salivary glands, lacrimal, nasal, laryngeal and vulval glands. In 1933, Sjögren described similar cases and was particularly interested in keratoconjunctivitis sicca. In 1953 Morgan & Castleman for the first time linked Mikulicz's syndrome and Sjögren's disease as probably the same disease process. Godwin (1952) described 10 cases with benign lympho-epithelial lesions which were histologically identical with the findings in Sjögren's and Mikulicz's disease.

This collection of diseases has now been recognized to have an autoimmune basis. Antibiotics to salivary-duct epithelium have been demonstrated and serum protein studies have shown characteristic abnormalities associated with autoimmune disease. Amidst this collection of diseases there appears to be a group of patients with recurrent swelling of the parotid glands, who have no associated keratoconjunctivitis sicca or associated arthritis and no abnormality of their serum protein suggestive of an autoimmune process. Although this group is recognized it has been thought by some authors to represent an incomplete form of Sjögren's disease (Shearn 1971).

Nearly 300 of such patients have been collected, treated and followed up over the last fifteen years. The initial investigation started in 1963 (Maynard 1965) and consisted of a study of the natural history, an investigation of the aetiology and an attempt to find an alternative to parotidectomy as treatment for patients with severe symptoms.

Natural history

Seventy-three patients were studied retrospectively (Table 1). Seven patients were diagnosed as having Sjögren's disease because of associated xerostomia and a positive Schirmer test, coincidental arthritis and the presence of abnormal serum proteins, suggestive of autoimmune disease (Table 2). The remainder of the patients had unilateral or bilateral parotid swellings and no other symptoms. The swellings were often related to eating, sometimes painful, and persisted for a few minutes to a few days. The frequency of the swelling ranged from daily to yearly and the length of history ranged from one year to twenty years; 20% of the adults of this series of patients had undergone spontaneous remission and had been symptom free for two years or more.

Table 1. Patients studied in retrospective series (Maynard 1965)

	Male	Female	Total
Children up to age 14	2	5	7
Young adults (15–40 years)	6	11	17
Adults (41 years and above)	20	29	49
Total	28	45	73

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Table 2. Analysis of 73 patients studied (Maynard 1965)

	No.	
Development of symptoms before puberty:		
(a) Pre-puberty at investigation	7	
(b) Post-puberty at investigation	5	(80% of adults)
Adults with present disease	42	
Adults whose symptoms spontaneously ceased	12	(20% of adults)
Adults with Sjögren's disease	7	

Table 3. Culture of saliva from parotids of patients and controls

	Sterile	Infected		Total
Patients	60	15		75
		Streptococcus viridans	(7)	
		Escherichia coli	(3)	
		Neisseria catarrhalis	(2)	
		Pneumococci	(2)	
		Streptococcus faecalis	(1)	
Controls	15	7		22
		Staphylococcus viridans	(2)	
		Neisseria catarrhalis	(2)	
		Escherichia coli	(1)	
		Staphylococcus albus	(1)	
		Diphtheroid	(1)	

Aetiology

In the past those authors who had distinguished such a group of patients from those with autoimmune diseases or who found no clinical evidence of Sjögren's disease had suggested the following aetiological theories: infection (Rose 1954), allergy (Pearson 1961), congenital anatomical abnormality (Bailey 1945), or duct orifice stenosis due to dental trauma (Payne 1938). These theories were investigated.

Saliva was collected by means of a cannula incorporated in a collecting cup (Figure 1). The results of culture of saliva from patients and controls is shown in Table 3. There seemed little difference between patients and controls, since no less than 60 collections of saliva from affected parotids were sterile. Persistent infection seemed an unlikely cause of the swellings. It has also been suggested that deficiency of lysozyme in the saliva in these patients permits the growth of bacteria which have contaminated the duct by retrograde spread from the mouth (Thompson 1940, McEwen & Kimura 1955). Therefore, the lysozyme content of the saliva was measured in units of egg white lysozyme by estimating light transference through mixtures of saliva and suspensions of the bacteria *Micrococcus lysodeikticus*. There was no evidence of

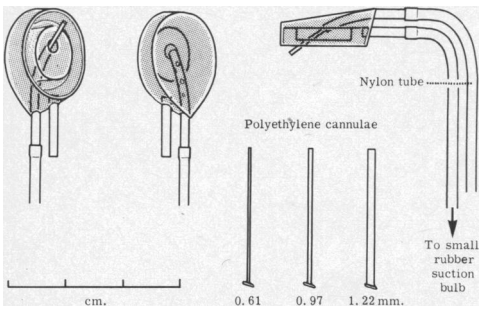

Figure 1. Suction cup for holding cannulae in position in parotid duct.
(Reproduced from Maynard 1965, by kind permission)

Table 4. Salivary lysozyme in parotids of controls and patients, measured in μg/ml of egg white lysozyme

	Controls	Patients
Number of parotids	55	96
Mean salivary lysozyme (μg/ml)	9.1	9.7

Table 5. Salivary lysozyme in right and left parotids of patients with Sjögren's disease, measured in μg/ml of egg white lysozyme

	Salivary lysozyme (μg/ml)	
	Right	Left
Suspected Sjögren's	11	15
	4	8
	20	20
Clinically conclusive Sjögren's	?0	—
	5	3

decreased lysozyme content in comparison with the controls (Table 4), nor was there any significant change in those patients with suspected Sjögren's disease (Table 5).

Hamilton Bailey (1945) has suggested a congenital abnormality of the parotid in children, named sialectasis, as a cause of symptoms and this is discussed below. There was no evidence of allergy as a cause. Duct orifice stenosis was not found in any of the patients. Most patients required a 0.97 mm cannula for successful intubation and a small proportion required the large 1.22 mm cannula (Figure 1).

A theory of aetiology was evolved based on the following hypothesis. On the assumption that acute parotitis was the result of retrograde spread of infection from the mouth in dehydrated patients, it was suggested that a similar retrograde spread of infection occurred in patients with Sjögren's disease and relative xerostomia. Patients with the latter disease occasionally suffer recurring swellings of the parotid glands, but not necessarily acute parotitis. It was suggested that retrograde infection, involving the ducts of the gland, resulted in mucous

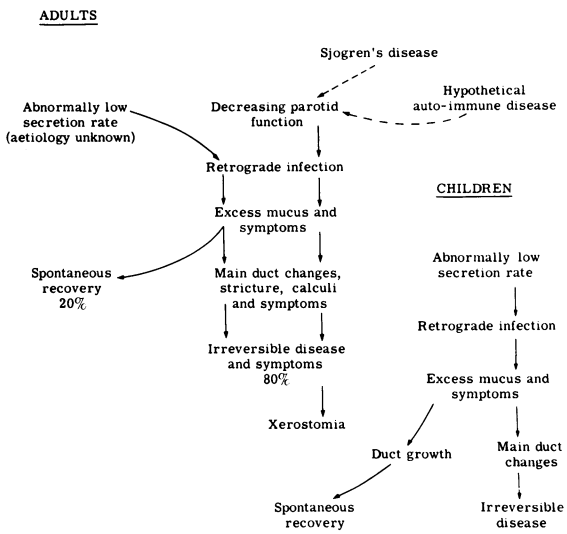

Figure 2. Theory of aetiology of recurrent swellings of parotid glands in patients with no autoimmune disease

metaplasia of the normal columnar epithelium and that the recurrent swellings were the result of mucus obstruction in a damaged and possibly strictured duct. There is histological evidence of metaplasia of duct epithelium to mucus-secreting cells in patients with recurrent swellings and no evidence of Sjögren's disease (Patey & Thackray 1955). It was therefore suggested that an abnormally low secretion rate in patients without Sjögren's disease resulted in similar retrograde spread of infection, in duct epithelial metaplasia, mucus production and hence recurrent obstructions (Figure 2).

The theory was investigated by measuring the stimulated secretion rates in controls and patients in this series. The parotid ducts were cannulated (Figure 1) and stimulation achieved by instructing the patients to suck an 'acid drop' so that they were constantly aware of the taste.

The results of repeated cannulation of one young adult control suggested that the method of measurement was reliable and reproducible (Table 6). Comparison of controls' and patients' stimulated secretion rate showed a significantly low secretion rate from patients' parotids (Table 7). This might be expected as a result of repeated obstruction of the diseased parotids. The control values were very similar to those of Patey's (1965) series where a different method of stimulation was used (Table 7). In those patients with unilateral disease, comparison of the secretion rates of the 53 affected parotids with those of the 30 symptomless parotids (Table 8) showed a significant difference which again might be expected: $t = 3.525$ at 81 d.f., $P < 0.0005$. However, comparison of the 30 symptomless parotids with the 33 control parotids showed also a highly significant difference: $t = 4.005$ at 61 d.f., $P < 0.0005$.

It seems possible, therefore, that the hypothesis is valid and these patients have an abnormally low secretion rate. It has been suggested (Shearn 1971) that such patients will ultimately develop an obvious autoimmune disease: Sjögren's. However, this series has been followed up since 1965 and Sjögren's disease has not developed in any of those successfully traced.

Table 6. Stimulated parotid secretion rate in one young adult

	Right parotid (g/min)	Left parotid (g/min)
Mean	1.10	1.12
Range	0.98–1.12	1.01–1.23

Table 7. Stimulated parotid secretion rates in controls and patients (Maynard 1965)

	Controls	Patients	Patey (1965) controls
Number of parotids	33	94	31
Stimulated secretion rate (g/min):			
Mean●	1.29	0.68	—
Range	0.60–2.42	0–1.88	0.60–2.60 (2 of 3.4 and 3.6)
s.d.	0.47	0.44	—

● Comparison of controls and patients: $t = 6.625$ at 125 d.f., $P < 0.0005$

Table 8. Stimulated parotid secretion rates in controls and in patients with unilateral disease (Maynard 1965)

	Controls	Affected parotids	Symptomless parotids
Number of parotids	33	53	30
Mean secretion rate (g/min)	1.29	0.56	0.89

All the patients in this series had bilateral sialograms. The X-rays were analysed in comparison with the length of history, severity of disease and depression of secretion rate. The changes found on X-ray were arranged in an order of what appears to be progressive structural damage when compared with the length of history and secretion rate: minor duct changes (Figure 3); sialectasis (Figure 4); coarse sialectasis and main duct dilatation (Figure 5); and gross main duct dilatation and strictures (Figure 6). The secretion rates in each group were compared with the sialographic changes (Table 9). The significant feature appeared to be main duct dilatation, almost always associated with a low secretion rate and irreversible disease. Fine sialectasis, however, was often associated with a normal secretion rate and frequently found in children and apparently reversible. Originally considered to be congenital in origin (Bailey 1945) it is now much more likely to be the result of extravasation of radio-opaque material into the interstitial tissue (Thackray 1955).

Treatment

In the past the following methods of treatment have been suggested: low-dose radiotherapy (Dorrance 1935, Smith 1953); avulsion of the auricular temporal nerve (Wakeley 1948); tympanic neurectomy (Golding-Wood 1962); duct ligation (Diamant 1958) and parotid-

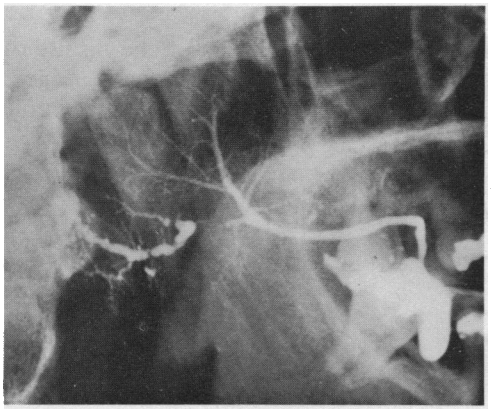

Figure 3. Dilatation of branch duct due to local obstruction

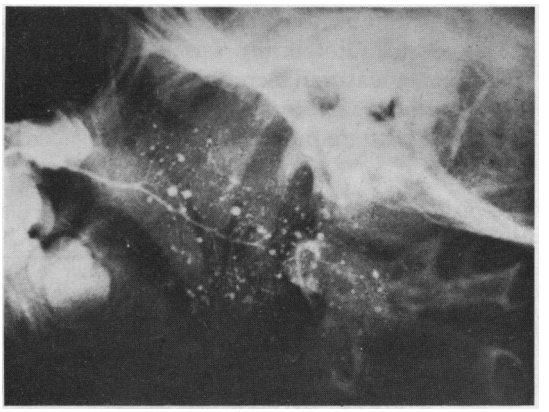

Figure 4. Sialectasis

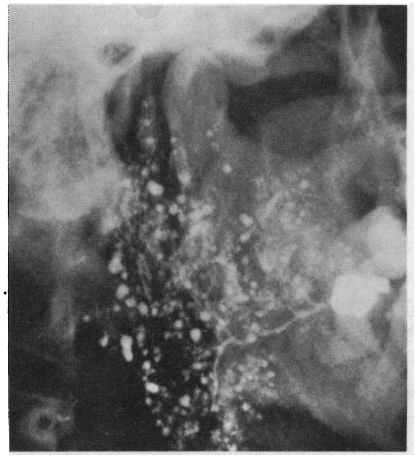

Figure 5. Coarse sialectasis and main duct dilatation

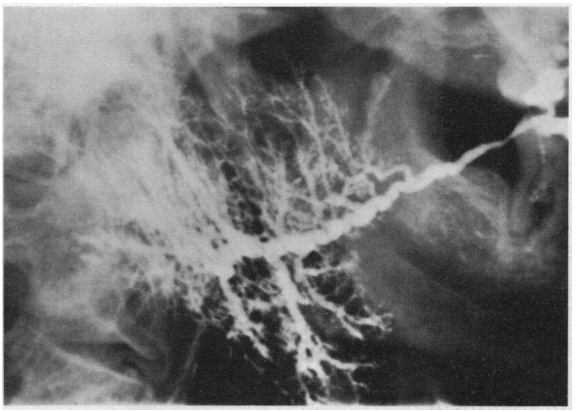

Figure 6. Main and branch duct dilatation

Table 9. Relation of stimulated secretion rates to sialographic appearances in 53 parotids showing symptoms (Maynard 1965)

	No. of parotids	Mean secretion rate (g/min)
Normal X-rays	20	0.83
Minor duct changes	7	0.77
Sialectasis and minor duct changes	10	1.09
Sialectasis and main duct changes	3	0.51
Main duct changes	11	0.52
Complete glandular disorganization	2	0

echtomy (Beahrs *et al.* 1961). In order to find a successful and less hazardous method of treatment than parotidectomy, the described methods were evaluated and a regime developed.

Avulsion of the auricular temporal nerve was performed on 4 patients without complication, but with no effect at all on the stimulated secretion rate or the recurrent obstruction. It was not thought justifiable to continue this trial.

Low-dose radiotherapy was used in 2 patients (Table 10) and in view of the results of subsequent measured secretion rates and a continuation of symptoms, this too was abandoned.

Tympanic neurectomy was not investigated. Duct ligation was found to be a simple procedure with no morbidity and some success.

Table 10. Effect of 600 rad on parotid stimulated secretion rate in two patients

		Stimulated secretion rate (g/min)	
	Date	Right parotid	Left parotid
Patient 1	14.5.64	0.35	1.48
	17.6.64	600 rad to right parotid	
	20.6.64	0.50	0.92
	23.6.64	0.57	1.15
	26.6.64	0.50	0.88
	29.6.64	0.56	0.96
Patient 2	1.5.63	1.04	1.10
	29.6.63	600 rad to right parotid	
	3.7.63	0.34	0.90
	10.7.63	0.40	1.16
			0.93

A regime of treatment was evolved, based on the sialographic findings and the severity of the symptoms. It was hoped that the figure of 20% spontaneous recovery found in the original series (Maynard 1965) might be increased by stimulating parotid secretion in patients without gross structural changes on X-ray. Chewing and taste both being effective in stimulation, patients on conservative treatment were asked to chew 3–4 raw apples a day. Duct ligation, seeming to be a safe alternative procedure to parotidectomy, was practised on those patients with severe symptoms, main duct dilatation and a low secretion rate. Figure 7 sets out the plan of treatment.

Patients have been followed up every five years and the last follow up was analysed in 1973. The results are shown in Tables 11 and 12 and 150 patients were included in the follow up.

Table 11. Results of conservative treatment on adults and treatment by duct ligation

	Conservative treatment on adults No. (%)	Duct ligation No. (%)
Total	90	46
Symptomless	48 (53%)	19 (41%)
Improved	29 (32%)	6 (13%)
Unchanged	13 (14%)	21 (45%)
Symptomless or improved	77 (85%)	25 (54%)

Table 12. Indications for superficial parotidectomy

	No.
Failed duct ligation	11
Severe symptoms in grossly infected gland	4
Abscess	7
Calculus	4
Cyst	1
Total	27

Discussion

In 1963 a retrospective review of untreated patients (Maynard 1965) suggested that the natural history of the condition led to spontaneous permanent remission of symptoms in 20%. Conservative management during the last ten years, in which the only treatment was stimulation of salivary secretion, resulted in a permanent remission in 53% of the patients. In a further 32% the symptoms were so much improved that they were of little concern to the patient. Thus 85% of conservatively-managed patients were cured or improved (Table 11).

Destructive surgery was employed only when the symptoms and X-ray appearances justified it, and after a trial of conservative treatment had failed. Duct ligation failed in approximately 45% of the patients on whom it was attempted (Table 11). Such results are unsatisfactory, but as the alternative of parotidectomy carries such a risk of damage to the facial nerve it seems justifiable to continue employing such a minor procedure. Although the failure rate of duct ligation is high, there seem to be no complications other than the establishment of an intra-oral fistula with a recurrence of symptoms; the situation can then be retrieved by parotidectomy.

Calculus obstruction in this series has been more frequent than is often stated. Conservative surgery with simple incision of the duct and ennucleation of the calculus seem justified whenever possible. Once again the situation can always be retrieved by parotidectomy if minor surgery fails.

When, in the final resort, parotidectomy is attempted, careful dissection can achieve resection of the superficial part of the parotid without permanent facial nerve damage. Total parotidectomy means a greater risk of facial nerve damage and seems an unnecessary procedure. In this series only superficial parotidectomy was performed and has been successful in all patients (Table 12).

Finally, conservative treatment only is indicated in the care of children with this condition. Those occasional patients whose symptoms persist into adult life may eventually need destructive surgery, but in this series of personal patients surgical procedures in children have never been necessary.

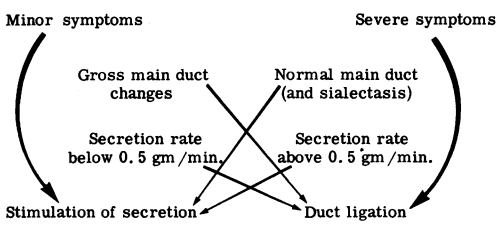

Figure 7. Plan of treatment

Summary

Autoimmune disease affecting the parotid and lacrimal glands is now well recognized and is usually named Sjögren's disease. Patients, including children, with repeated obstruction of their parotid glands and no other stigmata of Sjögren's disease, fall into a different clinical group, unrelated to an autoimmune process. Over 300 such patients have been seen over the last fifteen years and the natural history of a group of them has been studied. The aetiology was investigated and a plan of management developed. The results of treatment are reported.

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