POST-CRICOID CARCINOMA

By M. LEDERMAN (London)

In the absence of any agreed classification, it is still necessary to define the term "post-cricoid cancer", otherwise there can be no certainty that the same tumours are being discussed by different speakers. The term "post-cricoid" is time-honoured and widely used, but it refers not so much to a definite anatomical site or a single clinical form of cancer as to the region lying behind the larynx where neoplasms may occur and can be detected by mirror examination. The common tumours arising in this so-called post-cricoid region can be subdivided into three main groups:

(*a*) Cricopharyngeal.
(*b*) Pharyngo-œsophageal.
(*c*) Cervical œsophagus.

(1) Crico-pharyngeal Tumours

This group includes all the tumours arising from the regions usually designated "post-cricoid" or "mouth of the œsophagus". Tumours of these parts may arise anteriorly from the mucosa overlying the posterior surface of the cricoid or crico-arytenoid region, or posteriorly from the mucosa covering the cricopharyngeus; some lesions may arise laterally from the lowest part of the pharyngo-laryngeal grooves.

(2) Pharyngo-Œsophageal Tumours

This term can be applied to tumours arising from the region of the œsophagus just below the crico-pharyngeal sphincter. Characteristically, these tumours affect equally both the lower pharynx and upper œsophagus and the thyroid gland is also often invaded, the resulting clinical picture being frequently one of a patient who can neither swallow nor breathe.

(3) Cervical Œsophagus

Whilst it may seem somewhat out of place to include tumours of the cervical œsophagus in this discussion, such a step can be justified both on diagnostic and technical grounds. Advanced œsophageal lesions do present in the post-cricoid region and their true origin and extent may be overlooked in the absence of thorough clinical and radiological examination. As far as surgical or radiological treatment are concerned, the œsophagus cannot with safety be divorced from the lower pharynx and it is worth

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noting that a great deal of the surgical literature concerns itself as much with the "upper œsophagus"as with the "post-cricoid region". Jacobsson (1951) notes that two-thirds of the cancers affecting the lower pharynx extend into the œsophagus and 45 per cent. of the tumours are more than 5 cm. long.

Radiotherapy Technique (1956)

In discussing the technique of radiotherapy, the important point to establish is that 200 kV. X-radiation is the least desirable method of treatment, the harder quality gamma radiation from radium or cobalt, and supervoltage X-radiation being preferable. By the latter methods, higher doses can be given with less risk of complications and with the minimum of discomfort to the patient. Of far more importance to the radiotherapist than the possession of special radioactive isotopes or modern supervoltage equipment is his ability to use a laryngeal mirror and to individualize treatment. A standard tumour does not exist nor is there any special tumour dose, the administration of which is likely to be regularly successful. In these circumstances, the best chance of success does not lie in forcing the patient to do battle with a prescribed "lethal tumour dose" of radiation, but in individualizing treatment according to the patient's needs. To this end, regular and frequent examination of the patient by the radiotherapist is essential. The radiotherapist who cannot or will not examine the larynx regularly during the course of radiation treatment fails in his duty and may well reduce his patient's chances of success as well as add to the risks of treatment.

At the Royal Marsden Hospital there are two small telecurie therapy units; one, containing 12 gm. of radium, has been in constant use with variable quantities of radium for 21 years, and a second containing 10 curies of Cobalt 60 which has been available for the past 5 years. For all practical purposes, the radium and Cobalt 60 can be regarded as equivalent in their effects and uses.

The technique of treatment depends on the age, general condition of the patient and the site and extent of the tumour. The anæmic, dehydrated and emaciated patient is a poor subject for radiotherapy, but it is very rare to have to delay treatment on these grounds. Occasionally nasal feeding is necessary or even a gastrostomy may have to be performed but generally, if the patient's condition is so bad that a gastrostomy or tracheotomy is necessary, then it is often worthwhile offering radiotherapy. 20 per cent. of our patients had to have a gastrostomy, 10 per cent. a tracheotomy and 5 per cent. had both gastrostomy and tracheotomy.

As a general rule, telecurietherapy is used for the earlier cases, X-ray therapy being reserved for advanced cases requiring palliation. The treatment fields used depend on the part of the pharynx or œsophagus affected

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but in all cases a wide segment is irradiated and the appropriate lymph node areas must be routinely included in the treatment area.

The doses employed vary: using telecurietherapy the aim is to give 6,000-7,000 r in 6-8 weeks, and using 200 kV. X-rays, 4,500-5,500 r in the same time.

Material and Results

During the period 1933-1956, some 623 cases of laryngopharyngeal cancer have been seen at the Royal Marsden Hospital (Table I). Much of

TABLE I

CA. LARYNGOPHARYNX: 1933-1956

MATERIAL

Group	Number Seen	Previously Untreated	Recurrent or Post-operative	Not treated by Radiotherapy
Epilaryngeal	132	119	8	5
Sinus Pyriformis	234	208	16	10
Posterior and lateral walls ..	35	28	7	—
Post-Cricoid: Cricopharyngeal .. .. Pharyngo-œsophageal .. Cervical œsophagus ..	222	94 64 = 197 39	19	6
Total	623	552	50	21

this material has come during the last 8 years as a result of our co-operation scheme with the Royal National Throat, Nose and Ear Hospital, and more recently with the Metropolitan E.N.T. Hospital. Table II lists the post-cricoid cases in relation to site of origin and stage, the basis for staging being the condition of the lymph node areas of the neck and the presence or absence of laryngeal mobility (Lederman, 1954). At least two-thirds of the cases come into the advanced stages III and IV.

TABLE II

POST-CRICOID CANCER: 1933-1956

DISTRIBUTION ACCORDING TO SITE AND STAGE

Site	Stage				Total
	I	II	III	IV	
Cricopharyngeal	9 (10%)	23 (24%)	40 (43%)	22 (23%)	94 (48%)
Pharyngo-œsophageal ..	6 (9%)	12 (19%)	27 (42%)	19 (30%)	64 (32%)
Cervical œsophagus	4 (10%)	13 (33·3%)	9 (23%)	13 (33·3%)	39 (20%)
Total	19 (10%)	48 (24%)	76 (38%)	54 (27%)	197

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The results of treatment are notoriously bad and our results are no exception. From Table III the points of interest which emerge are:

(1) The Stage I cases which would be of most interest to the surgeon, form the one group which gives a worthwhile result following radiotherapy. It is salutary to reflect on the paucity of the really early case—19 in a 24-year period!

(2) The results obtained in selected cases of carcinoma of the cervical œsophagus merit special attention because of the particularly poor surgical results in this group.

(3) The results in the remaining groups are deplorable and are in fact the worst for all the laryngopharyngeal tumour sites.

TABLE III

POST-CRICOID CANCER: 1933-1956

RESULTS ACCORDING TO SITE AND STAGE

Site	5-year results: 1933-1951					3-year results: 1933-1953				
	I	II	III	IV	All	I	II	III	IV	All
Cricopharyngeal	2/7	0/10	2/24	1/15	5/57 (9%)	3/7	1/13	1/29	1/16	7/65 (11%)
Pharyngo-œsophageal ..	1/5	0/6	0/17	0/15	1/43 (2%)	2/6	0/9	2/20	0/15	4/50 (8%)
Cervical œsophagus ..	3/4	1/4	0/3	0/4	4/15 (27%)	3/4	2/5	0/6	0/8	5/23 (22%)
Total	6/16	1/20	2/44	1/34	10/115 (9%)	8/17	3/27	4/55	1/39	16/138 (12%)

No one can complacently accept results of this kind: in the search for future improvement there are the following possibilities to consider:

(1) Developments in radiotherapeutic apparatus and technique. There would appear to be an optimum range of energy of radiation (1-5 MeV) for the treatment of head and neck cancer. Many centres now have apparatus in routine use capable of providing radiant energy of this quality and there is, as yet, no evidence to show that either newer or more powerful equipment or the use of more esoteric techniques or isotopes will materially influence the prospects of the patient suffering from post-cricoid cancer. The reason for this pessimistic outlook rests on the fact that radiation is a non-specific remedy and therefore such sporadic radiocurable cases as are encountered should be curable by existing equipment and technical methods.

This same argument applies to :

(2) The possibility of developments in surgical technique. The natural

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history of the disease and the non-specificity of the remedy militate just as much against the surgeon as the radiotherapist. There is no lack of boldness or technical skill among present-day surgeons, yet as a rule the greater the surgical effort the less the reward. If the prospects for both surgery and radiotherapy used independently are admittedly poor, can (3) radiotherapy and surgery in combination offer more? As the results could scarcely be worse, this approach must be seriously considered. It is the writer's view that there may well be a place for some combination of surgery and radiotherapy in the treatment of post-cricoid cancer but the precise manner of combination is of vital importance.

It is natural that the surgical part of the treatment should be considered first since the patient is rapidly relieved of most of his neoplasm and the difficulties and complications of excision after radiotherapy are avoided: also a number of patients who receive radiotherapy first and improve, may well be tempted to refuse any subsequently proffered operation. In spite of this, however, the fundamental differences between pre- and post-operative radiotherapy must be appreciated and considered by both surgeon and radiotherapist before deciding on any particular combination of methods.

Where radiotherapy is employed *before* operation, its purpose is to assist the surgeon in his task and this is achieved by shrinkage of the tumour, diminution of sepsis and reduction in viability of tumour cells so that the likelihood of recurrence in the operative field is lessened. These benefits can be conferred by radiotherapy without necessarily employing full dosage or unduly delaying the operation.

The purpose of post-operative irradiation is entirely different since radiotherapy is of no prophylactic value in an immunological sense and, therefore, if a tumour has been completely removed its use is pointless since future recurrence or metastasis cannot be prevented by this means. If, however, removal has been incomplete, then the purpose of radiotherapy is to salvage the patient and a full course of treatment becomes necessary. In these circumstances, even when full doses have been used, radiotherapy is still not very effective since cancer cells present in scar tissue rarely respond satisfactorily and treatment as a rule proves only of palliative value.

In the writer's opinion, if surgery and radiotherapy are to be combined to the patient's advantage, radiotherapy should be employed first and then followed by surgery. Obviously each case would have to be considered individually: in the advanced, complicated case where a poor response to radiotherapy was shown, there would be little point in persevering beyond a dose of 2,000 r in 2-3 weeks. When, however, a favourable response is observed treatment could be continued and full dosage given in the hope of obtaining a cure by radiotherapy alone. Provided that hard quality radiation is used and repeated courses of treatment avoided, the problems

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of surgical removal and reconstruction, although aggravated by the previous course of radiation, need not prove insoluble.

Table IV lists the surgically treated cases in this series.

TABLE IV

POST-CRICOID CANCER

OPERATIONS 1933-1953	
No. performed	4
Lateral pharyngotomy and block dissection	1*
Pharyngo-laryngectomy	2
Transthyroid pharyngectomy	1

* Patient lived 5 years. Other patients died of disease within 2 years.

1954-1956 (INCLUSIVE)	
No. performed	5
Laryngopharyngectomy	2
Laryngopharyngectomy and block dissection	3

1 patient is alive for 1 year
4 patients died within 1 year

(4) Prevention

Logically, prevention would provide the only satisfactory solution to the problem of post-cricoid cancer—or any form of cancer for that matter. Fortunately a study of these cancers shows without doubt that certain of them possess features of such ætiological and clinical significance that the possibility of prophylaxis must be considered seriously. Thus:

Laryngopharyngeal (hypopharyngeal) cancer is common in most European countries but there is a remarkable geographical variation in the frequency with which the post-cricoid region is affected and the frequency with which women are the sufferers. In Table V the sex incidence of laryngopharyngeal cancer in different countries is well shown. It would

TABLE V

HYPOPHARYNGEAL (LARYNGOPHARYNGEAL) CANCER.
SEX INCIDENCE IN DIFFERENT COUNTRIES (AFTER JACOBSSON)

Country	Percentage of women
France (Baclesse)	1
Switzerland (Schinz & Senti)	9
U.S.A. (Martin)	15
Denmark (Videbaek)	20
England (Cade)	25
Finland (Sipila)	30
Ireland (Douglas)	40
Norway (Rennaes)	50
Scotland (Turner)	>55
Sweden (Radiumhemmet)	60
Royal Marsden Hospital	31

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seem that in the Latin countries and Switzerland (Jacobsson, 1951; Leroux-Robert, and Ennuyer, 1952; Agazzi, 1953), women rarely develop laryngopharyngeal cancer, men being the chief sufferers and the pyriform sinus the region usually affected. There is also a geographical variation in the frequency with which the post-cricoid region is affected (Table VI), the site being commonly affected in Scandinavia, whilst it is excessively uncommon in France and Italy and the Mediterranean countries generally (Leroux-Robert and Ennuyer, 1952; Agazzi, 1953).

TABLE VI

INCIDENCE OF POST-CRICOID TUMOURS RELATIVE TO OTHER LARYNGOPHARYNGEAL SITES (AFTER JACOBSSON)

Country	Per cent. Carcinoma of lower part of hypopharynx*
England	25
Finland	25
Ireland	35
Norway	40
Scotland	50
Sweden	75
Royal Marsden Hospital	30

* post-cricoid region.

It would appear, therefore, that in the Latin countries it is the male who develops laryngopharyngeal cancer, usually in the sinus pyriformis, whilst in the Scandinavian countries it is the female who develops this form of cancer and usually in the post-cricoid region. In the Anglo-Saxon countries the incidence seems to fall between these two extremes. It should also be noted that irrespective of country, when a woman develops laryngopharyngeal cancer it is the post-cricoid region that is most likely to be affected.

As an explanation of the extraordinarily high incidence of laryngopharyngeal cancer in women in Sweden, Ahlbom (1941) pointed out that 90 per cent. of these women showed signs of sideropenic dysphagia, i.e. the Plummer Vinson syndrome and simple achlorhydric anæmia. Apart from sideropenia, there may be other characteristic clinical features such as: rhagades at the corners of the mouth, atrophic changes of the buccal and lingual mucosae, and changes in the fingernails (Lindvall, 1953). The fully established picture originally described by Ahlbom has rarely been seen by the writer; instead, many patients show some, but not all, of these features to a greater or lesser degree.

In Table VII it can be seen that this syndrome is much less common in this country than in Sweden. Of 106 patients especially examined,

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TABLE VII

SIDEROPENIC DYSPHAGIA (AHLBOM'S SYNDROME)

Number of patients previously untreated ..			197
Changes noted		60	
Tongue smooth, mm. atrophic or smooth	3		
Fissures at corners of mouth, nail changes	4		
Tongue smooth, fissures at corners of mouth	12		
Fissures at corners of mouth	9		
Tongue smooth, nail changes	10		
Nail changes	8		
Tongue smooth	14		
No changes noted		46	
Not recorded		91	
		197	

BLOOD COUNT

Number of patients previously untreated ..		197	
Blood count within normal limits .. .. (Hb. less than 70 %)	127		
Low blood count (RBC less than 4,000,000) ..	14		
Not recorded	56		
	197		

DYSPHAGIA

Number of patients previously untreated ..			197
No. of patients with dysphagia as first symptom		139	
Dysphagia present over 1 year	28		
Dysphagia present over 5 years	17		

60 showed some changes of the tongue and oral mucosae and nails. Of 127 patients whose blood count is recorded, only 14 (11 per cent.) showed any significant change and of the 139 patients in whom dysphagia was the dominating symptom, only 17 (12 per cent.) had a long history that might be suggestive of Plummer Vinson's syndrome.

Bearing these facts in mind, a possible manner of prevention may well be along the following lines:

(1) Detection by mass survey. This could follow the example of other mass surveys for the detection of malignant disease, e.g. gynæcological cancer. The investigation could be restricted in the first instance to women in certain age groups who admit to symptoms suggesting anæmia, avitaminosis or difficulties in swallowing. The routine initial examination would include special attention to the state of the mucous membranes of the mouth and pharynx, the nails and teeth, and a blood examination. It should be possible to detect patients who present clinical features suggestive of Plummer Vinson syndrome or so-called sideropenic dysphagia

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even when present to a minor degree. On recognition, such individuals should be submitted to full investigation and any deficiency found corrected.

(2) The epidemiological aspects, with special reference to possible environmental, social and economic factors should be considered (Wynder and Bross, 1957), and finally.

(3) The purely experimental side of a problem of this kind also merits consideration. This would include the study of the lesions in the mucous membranes by modern methods of biopsy, cytochemistry and histochemistry, and experimental work on the effects of iron deficiency on the mucosae of the alimentary tract (Witts, 1956).

These comments and suggestions are, of course, largely speculative but it is my belief that more good will come from future research along these fundamental lines than will result from any further developments in surgery or radiotherapy.

REFERENCES

Agazzi, C. (1953) *Arch. ital. Otol.*, **64** (Supp. 14) 234.

Ahlbom, H. E. (1941) *Acta radiol (Stockh.)*, **22**, 155.

Jacobsson, F. (1951) *Acta radiol. (Stockh.)*, **35**, 1.

Lederman, M. (1956) *Indian med. J.*, **50**, 516.

——— (1954) *J. Laryng.*, **68**, 333.

Leroux-Robert, J. and Ennuyer, A. (1952) *Congr. Soc. franç. Oto-rhinolaryng.*, **59**, Pt. 1 (Rapport).

Lindvall, N. (1953) *Acta radiol. (Stockh.)*, **39**, 17.

Witts, L. J. (1956) Anæmia and the alimentary tract, Edinburgh.

Wynder, E. L., and Bross, I. J. (1957) *Brit. med. J.*, **1**, 1137.

https://doi.org/10.1017/S0022215100054086 Published online by Cambridge University Press