INTRINSIC CANCER OF THE LARYNX:

USUAL SITE OF ORIGIN, AS DEMONSTRATED AT 50 LARYNGO-FISSURES, AND ITS INFLUENCE ON DIAGNOSIS, PROGNOSIS, AND TREATMENT.*

BY

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It has been well said by McBride that in investigations on cancer of the larynx, the "pearl of great price is early diagnosis, for upon this depends the curability of the fell disease."¹ I think it is evident that many of the failures which overtook early efforts at cure by laryngo-fissure were due to delayed diagnosis. Just as early diagnosis and improved technique have advanced, so has this operation progressed until it has succeeded in securing more lasting cures than can be claimed for cancer in any other internal region of the body. Earlier diagnosis has also led to a steady diminution of the number of cases for which complete laryngectomy is the only possibility.

Last year I gave the results of an investigation into impaired mobility of a cord as an indication in diagnosis and prognosis in intrinsic cancer of the larynx, showing that it was neither a necessary nor a frequent symptom, that it was only met with in a minority of cases, and that, though it was a valuable symptom when present, other signs must be relied on for an early diagnosis.²

This summer I submit a research on another point which has not been settled and has threatened to mislead us. I refer to the current view that malignant disease of the endolarynx is most commonly met with in the posterior third of the glottis.

Historical.

Fortunately, in our speciality, and in this country, we need not go very far back to discover a source of error. If we turn to Morell Mackenzie's *Textbook*, published in 1880, we can detect one source and, at the same time, appreciate the progress made in the study of laryngeal cancer in forty years. On page 338 he begins his description by saying that "pain, dyspnoea and dysphagia are generally present," symptoms which, nowadays, we can only regard as indicative of a late and generally inoperable stage of the disease. It is true that he says, later on, that hoarseness may be a very early symptom, and sometimes precedes all other symptoms by months or even years; but the much greater prominence he gives to haemorrhage, fetor and cachexia would only mislead a present-day student. It is evident that he knew little of intrinsic cancer as we see and know it, possibly because forty years ago patients did not present themselves early for a persistent hoarseness, and even at the present day we know that medical men may fail to recognize the danger of delay in getting an expert opinion on a case of "mere huskiness." Mackenzie also misled a generation by stating (p. 336) that "the site of the tumour is in most cases one of the ventricular bands"; he even gives a table of 53 cases in which the cords only appear as the site of origin in 7 cases, and he points out that in 28 cases (or 56.7 per cent.) one of the ventricular bands was the first part affected.

By 1899 progress in diagnosis had been made, as shown by Lennox Browne's greater appreciation of the difference between extrinsic and intrinsic cancer, and his recognition of the fact that in the latter type "hoarseness is the earliest symptom of the disease and may have existed a very long time before advice will have been sought."³ But he also is mistaken when he writes that "enlarged experience convinces me that this form of cancer frequently commences in the ventricle." This teaching, in these two leading textbooks, was retarding progress.

Recent Views.

There can be little doubt that, as claimed by McBride,⁴ it was Semon who altered this view by showing from his experience that the intrinsic form of laryngeal cancer was more common than the extrinsic, and that the cords were "by far the most frequently affected parts." Semon recorded this as early as 1896⁵; it has been

confirmed by Schmiegelow, Chevalier Jackson and myself, and, doubtless, it is now admitted by all laryngologists. It was a great step forward. But, coming next to the consideration of which part of the cord is most frequently the site of origin, we see that Semon's independent observation was dimmed by the teaching of Virchow. He writes as follows: "Virchow has taught us that benign growths, if occurring on the vocal cords, have a tendency to localize themselves on their front parts, and very frequently on the anterior commissure of the vocal cords. If, on the other hand, you find a papillomatous-looking growth on the posterior parts of a vocal cord, particularly if the patient be well advanced in years, that is primarily suspicious, and still more so if such a growth be seated in the interarytenoid fold where benign growths practically never occur."

McBride, in summarizing Semon's teaching on this subject, gives as the first point of most importance, a "tumour which may be very minute, and, while it may be found in any part of the cord, is most commonly situated on the posterior third." I must confess that, like others, I accepted this teaching, and also McBride's statement, that Semon's observations "still remain the last important word which has been said on the diagnosis of early laryngeal cancer."⁶

Material and Methods.

The results of my own observations, which are now considerably larger than Semon's, will, I feel sure, demonstrate to your satisfaction that intrinsic cancer does not show a preference for the posterior part of the vocal cord, and that the interarytenoid region must be rarely affected—for I have never seen a case.

My conclusions are founded on 50 cases, in which the diagnosis was based not only on the appearances reflected in the laryngeal mirror, but also on the direct inspection of the disease when the larynx was opened by a laryngo-fissure. In addition, confirmation was sought in every instance by microscopic examination of the growth; the pathologist confirmed the clinical diagnosis in every case. I have never opened the larynx for epithelioma and found it to be anything else than cancer, although I have twice thought, at first, from clinical inspection that the disease was tuberculosis, but later on altered my diagnosis in time to secure a successful laryngo-fissure.

It will indicate the greater precision we are now able to arrive at in diagnosis if I recall that Grünwald, in 1907, recorded that out of 93 radical operations undertaken for the cure of what was supposed to be laryngeal cancer, the diagnosis turned out to have been mistaken in no less than 17—that is, in nearly 20 per cent.⁷ Jobson Horne, about the same date, formed the opinion that tuberculous disease was not infrequently mistaken for epithelioma, as he had learned from the examination of tissues sent him after removal by the mouth, by laryngo-fissure, or even with the entire larynx.⁸

Statistics.

These 50 cases have been tabulated according to the invasion by the neoplasm of (a) the anterior third of the cord only, (b) the middle third only, (c) the posterior third only; or combined invasion of (d) the anterior and middle thirds, (e) the middle and posterior thirds; or (f) the whole cord. I have also the numbers of the cases where (g) the anterior commissure or (h) the posterior commissure was attacked, and, finally, the statistics as regards (i) the subglottic area.

The results, so far as figures can express them, are as follows:

TABLE A.—*Intrinsic Cancer.*

Site of invasion in 50 cases.

(a) Anterior third only of cord	...	3 cases
(b) Middle third only of cord	...	7 "
(c) Posterior third only of cord	...	0 "
(d) Anterior and middle thirds of cord	...	16 "
(e) Middle and posterior thirds of cord	...	3 "
(f) Whole cord	...	21 "
		50

TABLE B.—*Intrinsic Cancer.*

Extension in 50 cases to—

(g) Anterior commissure	...	6 cases
(h) Posterior commissure (that is, the interarytenoid region)	...	0 "
(i) Subglottic region	...	13 "

* A paper read before the Summer Congress of the Section of Laryngology, Royal Society of Medicine, London, June 2nd, 1921.

Putting it, as regards the cords, in another way, I find that the portion of cord invaded by the cancerous growth is as follows:

TABLE C.—*Intrinsic Cancer.*
Third of cord invaded in 50 cases.

Anterior third in	...	...	39 cases
Middle third in	...	...	47 "
Posterior third in	...	...	24 "

In no single case was the growth at operation found to grow from any other area surrounding the glottis except the vocal cords and subglottic region.

Subglottic Cancer.

To have found the growth in the subglottic area in 13 out of 50 cases may come as a surprise. I was not prepared to find it, or, at least, to have found it so extensive, in several cases. Neither direct nor indirect laryngoscopy will always reveal it, but we may be prepared to meet it when the mobility of the cord is interfered with, and particularly when that mobility is impaired out of proportion to the visible extent of the lesion. Another discovery has been that a subglottic growth is more common in the anterior than in the posterior segment of the larynx. The subglottic invasion was found in one case where the anterior third only of the cord was affected; in 6 cases where only the anterior and middle thirds were attacked; and in 6 cases where the whole cord was invaded. But even in these last 6 cases, I hasten to say, the subglottic part of the growth was much more marked anteriorly, and, in some, was limited to the anterior half of the subglottic area. Indeed, as will be presently shown by illustrations, the cancer, in certain cases, undoubtedly originated below the anterior half of the cord, which it only invaded slowly and after it had made, relatively speaking, considerable progress before causing any symptoms. Want of tension in one cord was, in some cases, the first and only sign. Immobility of the cord is much more common in the subglottic cases; thus, in the 13 cases, the cord was fixed in no less than 6—that is, in nearly half the cases. Whereas, in the remaining 37 cases impaired mobility was only noted in 11—that is, in about 30 per cent. of them.

Author's View.

We now see that these 50 cases—controlled by indirect laryngoscopy, by direct inspection at a laryngo-fissure and by histological examination—yield a conclusion which is in direct opposition to that of Virchow and Semon. In other words, intrinsic cancer of the larynx is much more apt to take its origin in the centre or anterior portion of the vocal cord, or in the anterior half of the subglottic area, than in the posterior third of the larynx.

Pathology.

It is interesting to note that this conclusion appears to me to confirm the previsions which Jobson Horne based on his histological and pathological investigations of the larynx. In 1898, and again in 1907, he pointed out that tuberculosis attacks, by preference, that area of the larynx which is covered with columnar epithelium and is richest in glandular structure; whereas epithelioma shows a preference for that part of the larynx which is clad with squamous epithelium and is relatively free from glands. The posterior half of the larynx supplies the former conditions; the anterior half, which I have just shown to be the favourite site of intrinsic cancer, is lined with pavement epithelium, and is almost void of glands.⁹

As regards prognosis in reference to the site of an intrinsic cancer, it need hardly be pointed out that growths found on the upper surface of the cord, and those of a projecting or even semi-pedunculated character, are the most favourable. The more limited the growth the better is the prospect of completely removing it with a good margin of healthy tissue all round—that is in front and behind, above and below the cord, and also in the depth away from the glottis and toward the thyroid ala. These conditions are most likely to be met with in a growth of the middle of the cord, or of the anterior two-thirds; fortunately, as a reference to my statistics will show, these are the most usual sites.

If the anterior commissure is invaded the prognosis is not quite so good, though complete extirpation can still be effected, although with some sacrifice of the anterior part

of the opposite cord. As the growth approaches the arytenoid region the prognosis becomes less promising, and if the arytenoid itself is undoubtedly invaded it is probable that a hemi-laryngectomy or complete laryngectomy is the more promising operation.

When an epithelioma originates on the inner—that is, the glottic—surface of the cord the prognosis becomes less favourable, partly because there is lymphatic tissue in this area into which the cancer cells spread more rapidly than they do into the elastic tissue of the cord itself, and partly because the growth is already fairly extensive before it has appeared on the surface of the cord in sufficient amount to cause noticeable hoarseness and to be recognized clinically. Doubtless it is for these same two reasons that subglottic cancer is even more unpromising, and also because, as it dips down inside the crico-thyroid membrane, it is less circumscribed than when it lies entirely within the limiting barrier of the thyroid ala. In two cases I had to divide the cricoid cartilage to get below the downward extension of a subglottic epithelioma.

This darker prognosis with subglottic growths is confirmed by a reference to my 13 such cases: 7, or more than 50 per cent. of them, have died of recurrence. It is also striking to note that of these 13 cases the mobility of the cord was impaired or abolished in no less than 6, and that 4 out of the 6 are amongst the recurrences. This confirms the conclusion I enunciated in my paper of a year ago—namely, that impaired mobility of a cord is an unfavourable symptom.¹⁰

Treatment.

As the naked eye is not sufficiently trustworthy as a judge of the extent of an infiltrating growth, the entire cord should always be removed. Thus in one of my cases (No. 25) the pathologist reported that "the growth appears to be in the anterior part of the cord and to have burrowed backwards in the tissues beneath the surface epithelium, which is still intact over a considerable area of the growth." (The patient remains free from recurrence at the age of 77, five years after operation.) In a subglottic case (No. 24) the report of the pathologist was: "Specimen presented a deeply ulcerated new growth in subglottic region, immediately beneath the left vocal cord. A typical epithelioma. Though the growth arises beneath the cord, and the actual mucous membrane of the cord is still intact, the growth has invaded the substance of the cord beneath the mucosa." (The patient died of recurrence.)

CONCLUSIONS.

As Regards Usual Site of Origin.

1. Intrinsic cancer of the larynx originates on the vocal cords or in the subglottic area.
2. It has never been found in the posterior commissure (interarytenoid region), nor originating from the ventricular bands or the ventricle of Morgagni, in 50 cases carefully examined both indirectly with the mirror and by direct inspection after splitting the larynx.
3. A malignant growth may originate on any part of a cord, but is more common in the central portion or anterior half than in the posterior area of the larynx.
4. As is now well known, an epithelioma originating in this region remains for a long time limited to the cord affected and the adjoining side of the larynx, but it may cross the anterior commissure, and, in later stages, it invades the arytenoid and the area to the outer side of it.
5. The inner surface of the cord may be affected primarily or by extension. The subglottic area may be invaded by a growth originating in a cord. But a cancer may also start below the level of the cords, in the subglottic area.
6. A subglottic cancer is much more common in the anterior than in the posterior half of the larynx.

As Regards Prognosis.

1. The superficial or projecting tumours of limited extent are the most favourable.
2. Those situated in the middle third or anterior half of the cord are more promising than those invading the anterior commissure in front or the arytenoid region behind.
3. Growths embedded in a cord, or extending into it below an intact mucosa are not so favourable.
4. An epithelioma extending along the inner margin of a cord is still less favourable.

5. Subglottic cancers are very unpromising as regards lasting cure by laryngo-fissure. They are frequently associated with impaired mobility or complete fixation of a cord.

As Regards Operation.

1. In every case, however limited the growth, the entire vocal cord should be excised from the anterior commissure up to and including the vocal process of the arytenoid.

2. The growth, with as wide a margin as possible of apparently healthy tissue all round it, should be removed in one mass; the excision should therefore go down to the lower edge of the subglottic area; above, it should pass through the healthy ventricular band; and externally it must include the perichondrium lining the thyroid ala.

3. To facilitate this the thyroid ala should be removed so that a laryngo-fissure is really a partial hemilaryngectomy.

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HAEMATURIA AS SEEN BY THE SURGEON.*

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THERE are certain general rules laid down by clinicians to enable the practitioner to make a shrewd guess as to the cause and origin of haematuria in a given case. These rules are useful, but, as I shall show, they cannot always be relied upon for accurate diagnosis.

The cystoscope, combined in many cases with radiography, is indispensable for the examination of cases of haematuria from kidney, ureter, bladder, or prostate, and the urethroscope for doubtful cases of urethral haemorrhage. Indiscriminate enthusiasm, however, must be deprecated. A cystoscope or a urethroscope is not to be used in every patient who complains of urinary symptoms. The cystoscope may prove to be a dangerous weapon in certain cases of tubercle, malignant disease, enlarged prostate, sepsis, and incipient or established uraemia. It is well to proceed as far as possible along the ordinary lines towards diagnosis. The cystoscope or urethroscope may then be used to complete the examination.

General Considerations.

When blood is intimately mixed with the urine it is probable that the source of the haemorrhage is the kidney. This rule is not absolute. All we can say with certainty is that the blood is shed in small or moderate quantity, allowing intimate mixture with the urine before clotting has had time to take place. The cystoscope in a renal case may show a red efflux, the smoky or dark colour of the voided specimen being due to the change of oxyhaemoglobin into methaemoglobin by admixture with the acid urine. The following cases exemplify the difficulties of diagnosis:

A male, aged 56, presented himself with haematuria. The specimen passed was dark in colour. The only other symptom was frequency of micturition. Cystoscopy showed a malignant ulcer on the base of the bladder.

A man, aged 74, complained of difficulty and frequency of micturition, especially at night. The stream was small and the urine dark red; no clots were present. Instead of the expected enlarged prostate the cystoscope showed renal haematuria from the left side.

A clergyman, aged 56, stated that after a chill in 1919 he passed blood intimately mixed with the urine. He passed no clots, had no pain nor any dysuria. He had intervals of freedom with clear urine; later, tiny clots began to appear. The symptoms suggested haematuria of renal origin. Cystoscopy showed a papilloma on the right lateral wall of the bladder.

I could multiply cases to show the fallacy of depending for a diagnosis upon the character of the urine alone.

The presence of frequency of micturition is strongly suggestive that the site of the haematuria is the bladder or prostate; but the second case just mentioned, in which the haemorrhage came from the left kidney, shows how little dependence can be placed on this symptom. Frequency and bleeding in an old man will at once suggest enlarged prostate. The bleeding, as in the case just mentioned, may be from the kidney, or it may be from an unsuspected tumour, as in the case of a man, aged 70, who had symptoms of enlarged prostate. About a month before I saw him he had haematuria with clots and complete retention. Operation discovered not only an enlarged prostate but a papilloma as well. The haematuria was due to the papilloma and his other symptoms to the enlarged prostate.

If frequency of micturition and haematuria are combined with pain in the glans penis, scalding, and urgency, and if, in addition, pus and mucus are present, the diagnosis of cystitis is justified, but malignant growths and calculus must be excluded by direct observation.

Pain in the lumbar region, whether or not it culminates in renal colic, suggests an affection of the renal region of that side, but our expectations were belied in the case of a man, aged 49 years, who had haematuria with left lumbar pain. The cystoscope showed blood issuing from the right ureteral orifice.

If the haematuria is initial—that is, at the beginning of micturition—it comes, probably, from the prostatic urethra, or possibly from the anterior urethra. Blood issuing from the urethra, independently of micturition, comes from a source distal to the compressor urethrae. A small quantity may lie in the urethra and form a cast of the canal, which is swept out by the next act of micturition. Haematuria with massive clotting is often of bladder origin. During the late war, however, one of the most formidable complications of gunshot wounds of the kidney was secondary haemorrhage,¹ and in some of the cases blood was poured out in such quantity that the bladder was distended by large clots difficult to evacuate. In civil injuries of the kidney produced by crushes or strains, clots may form in the bladder. Again, in tumours of the kidney large clots may be passed, as in the case of a man aged 53, who complained that he passed numerous blood clots, about the thickness of the little finger. Cystoscopy showed blood issuing from the right ureteral orifice. Operation revealed a hypernephroma of the right kidney.

The size and shape of the clots may be of assistance in diagnosis. A long cast of the ureter is sometimes passed. Its length and thickness indicate its origin. More frequently shorter lengths are passed. Casts formed in the urethra are thicker and often show constrictions corresponding to those normally present in this canal.

Microscopical examination of the urine, especially if it can be carried out in the intervals between the attacks of bleeding, may be helpful. Mention need only be made of the presence of renal casts, cells from the bladder, ureter, or kidney, portions of tumour, pus cells, crystals, micro-organisms, etc.

In the accompanying table I have grouped my cases according to the region affected; under each heading they are arranged in order of frequency. This has many disadvantages, but is convenient for my present purpose.

CASES OF HAEMATURIA.

Kidney.	Cases.
Tubercle of kidney (generally involving bladder secondarily)	100
Symptomless renal haematuria	47
Renal calculus	44
Pyelitis (including pyelitis and cystitis combined)	32
Renal tumours (including cysts)	21
Nephritis	19
Injury to kidney (excluding war injuries)	7
Renal colic (cause?)	5
Hydronephrosis	4
Pyonephrosis	4
Movable kidney	3
Horseshoe kidney	2
Oxaluria	2
Henoch's purpura	1
Accessory renal artery	1
Ureter.	
Ureteral calculus	9
Injury to ureter (excluding war injuries)	1

* Abstract of remarks opening a discussion on haematuria at the Ulster Medical Society, January, 1921.