DYSPHAGIA AND ANÆMIA.

By DR MUNRO CAMERON.

THE present series consists of 25 typical examples of this syndrome, and I shall begin by summarising briefly the history and clinical condition of two:—

CASE I.—A married woman, aged 45, was admitted to hospital, and stated that she had always enjoyed moderately good health until five years before, when she began to have difficulty in swallowing.

At first there was inability to swallow pieces of meat and sometimes if she masticated crusts of bread carelessly a similar stoppage took place. Usually she could wash down the offending morsel with a draught of water, recently the water itself was regurgitated.

A week or two might pass in which deglutition proceeded normally, but she gradually got worse until, being afraid of choking at every meal, her diet had become reduced to fluids with softened bread and butter. Two years after the first onset of dysphagia she became pale, was weak, easily fatigued and breathless on very slight exertion.

On examination she appeared to be thin and the skin of her face showed a pallor not unlike that of pernicious anæmia. The lips were dry and pale, and a slight fissure extended downwards from the junction of the lips on the right side. The mucous membrane of the mouth was pale and dry, and the tongue smooth and devoid of papillæ. The pharyngeal wall had a similar dry or waxy appearance. Heart sounds were soft but pure. The spleen was palpated three finger-breadths below the ribs and extended to within 2 inches of the umbilicus. The liver was just apparent below the costal margin. Reflexes, deep and superficial, were found to be normal, and no alteration of the pupils or any of the special senses could be detected.

Blood Examination:—

Red blood corpuscles	2,800,000 per c.mm.
Hæmoglobin	15 per cent.
White blood corpuscles	5000

Differential Count:—

Polymorphonuclear corpuscles	50 per cent.
Lymphocytes	45 „
Eosinophiles	2·5 „
Hyaline	2·5 „

The red blood corpuscles were of normal size, stained evenly, showed slight poikilo cytosis but no nucleated forms. The Wassermann

https://doi.org/10.1017/S0022215100033296 Published online by Cambridge University Press

and Van den Bergh reactions were negative and no occult blood was present in the fæces. The urine was free from abnormal constituents.

Fractional Analysis of Stomach Contents:—

	¼ hr.	½ hr.	1 hr.	1½ hrs.	2 hrs.
Total acidity . .	10	15	20	35	40
Free HCl . . .	...	...	...	10	20
Starch . . .	plus	plus	plus	plus	plus
Bile	...	...	...	...	...

Blood was absent, mucin excessive; microscopic examination revealed nothing of any importance.

Bacteriological examination of the throat showed streptococci and some leptothrix filaments; blood cultures were negative.

In view of the atrophic changes in the mouth and pharynx the hydrogen-ion concentration of the saliva was estimated and pH was found to be 6.6—slightly on the acid side of normal, which is taken as 6.9.

Very little difficulty was experienced in passing the tube for gastric analysis, so that this is probably rather an example of non-relaxation than spasm of the sphincter such as was found in the second case.

Case II.—An unmarried woman, aged 42 years, was admitted complaining of severe dysphagia, pallor, general weakness and debility. She looked ill and it appeared that for some time she had been swallowing nothing but occasional fluids. She could not attribute her condition to any particular cause, and for six years she had been getting steadily worse.

The red blood corpuscles numbered 3,600,000 per c.mm. Hæmoglobin, 30 per cent. White blood corpuscles, 4000.

Differential Count:—

Polymorphonuclear	50 per cent.
Lymphocytes	48 „
Eosinophiles	2 „

Wassermann reaction negative. A fractional test meal could not be employed as she was unable to swallow the tube.

Bacteriological examination showed streptococci in the throat; blood cultures negative. The spleen was palpable but the enlargement was not excessive; the liver showed slight enlargement.

There was general and rather striking pallor of the face and of the mucous membranes of the eyelids and lips. There was atrophic glossitis and the mouth was dry and parched. pH of saliva, – 6.4.

No general anæsthetic was used for the endoscopic examination, and when the œsophagoscope entered the sphincter it was so tightly gripped that no further passage was possible.

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These two examples reveal very clearly the limits of the pharyngeal condition encountered in this syndrome. The blood changes, the splenomegaly, the slight enlargement of the liver are similar in both; but in one the Einhorn tube is passed relatively easily, the other resisted the passage of an œsophagoscope.

It is because of variations like these in the condition of the sphincter that so much confusion has arisen in describing this syndrome. The examples of non-relaxation are seen more often by physicians; the severe spasmodic cases by laryngologists. It is not therefore surprising that Plummer first called this condition hysterical dysphagia, and that Brown Kelly and D. R. Paterson described it as spasmodic contraction of the pharyngo-œsophageal junction. At first sight, indeed, we might easily imagine that the American and British observers were describing different conditions, or if the conditions were the same, that they were dealing with quite different aspects of it; for Plummer, and even more, Vinson, stresses the anæmia and splenomegaly, while the Scottish laryngologists describe in detail the atrophic changes in the buccal and pharyngeal mucous membranes and the frequently unyielding nature of the sphincteric spasm, although at the same time they draw attention to the pallor and anæmia, which they suggest is secondary to the deprivation of food rich in iron and other essentials.

Age and Sex Incidence and Social Condition.—In the present series of cases all the patients were women—15 married, 10 unmarried. The youngest was 41 years, the oldest 60; the average age was 47·1 years.

No one class of the community seems to be affected specially; some of the patients were poor and probably always undernourished, others were of good social standing, and no fault could be found either with their surroundings or mode of living.

Syphilis and alcoholic indulgence can be excluded as causative factors, and there appears to be no connection between this syndrome and the globus hystericus. Many of the sufferers are highly strung, nervous and easily worried, but they often state that their nervousness is due to fear of choking and only commenced with the onset of dysphagia.

Symptoms.—Dysphagia is referred to the level of the larynx, and the complaint is made that there is an unusual tightness of the throat or that something behind the larynx is gripping

https://doi.org/10.1017/S0022215100033296 Published online by Cambridge University Press

the food. Pain is not usually mentioned, as in ulcerated conditions, and in only one case (No. 22 in the Tables) was there referred pain. This patient stated that when the food was gripped she had pain in the neck, apparently quite definitely referred over the 5th and 6th cervical vertebræ. The symptoms are sometimes more exaggerated at night when she is tired than at the first meal of the day. The onset may be sudden, and she may remember having choked over a particular bolus of food; again it is insidious, and sudden attacks are separated by intervals of varying duration in which deglutition proceeds normally. It is seldom that a history is given of scalding or burning, though sometimes the disorder may be dated from the impaction of a fish-bone.

The result in the long run is the same, and food has to be masticated and swallowed with punctilious care. The diet inevitably becomes reduced and semi-solids washed down by tea or coffee become the daily fare.

In the milder cases, examination of the mouth and pharynx may reveal nothing beyond a pale and waxy-looking mucous membrane with the tongue smooth and devoid of papillæ.

Later there may be fissures extending outwards from the junctions of the lips and the pharyngeal mucosa is parchment-like, dry and atrophic, with a tendency to bleed on manipulation. In more severe or old-standing cases the endoscopic appearances, as described by Brown Kelly, are as follows:—"It is found that the deepest part of the hypopharynx does not present the usual sphincter-like appearance. Instead of rounded folds or cushions of mucous membrane forming a stellate arrangement, tense bands pass in various directions with their edges pressed tightly together. The entrance to the œsophagus appears as a pinhole or small irregular opening and not in the middle line. Sometimes it appears as an obliquely placed slit, again it would seem to be closed by a web passing from the cricoid."

Vinson, in his paper, while agreeing that the mucosa of the mouth and pharynx is often dry and atrophic, states that no œsophageal web was ever seen by him, and in this his colleagues Moersch and Conner concur, although the latter authors come nearer to Brown Kelly's opinion when they remark that, "while none of our patients complained of a lump in the throat they said that during the periods when they were able to eat they could feel something relax in the throat. Might it not be possible that due to some nervous strain such a spasm occurs,

https://doi.org/10.1017/S0022215100033296 Published online by Cambridge University Press

or is even brought on through an infection? In the final analysis the condition may be found to be on the same basis as cardiospasm."

Blood Changes.—With one or two exceptions the pallor of these patients was striking, and as distinctive as the facial appearance of pernicious anæmia; no degree of jaundice was ever found.

The blood changes were essentially these of chlorosis or

TABLE A.

Case.	Age.	Red Blood Corpuscles.	White.	Hb per cent.	Differential.
1	45	4,200,000	7,200	50	Normal.
2	60	3,500,000	5,600	40	Leucopenia.
3	50	3,800,000	6,600	50	Normal.
4	55	5,000,000	7,200	60	,,
5	45	3,850,000	6,400	50	,,
6	47	4,000,000	6,200	55	,,
7	50	3,820,000	6,100	55	,,
8	52	4,160,000	6,400	58	,,
9	45	3,840,000	6,800	60	,,
10	50	4,200,000	7,000	55	,,
11	46	4,400,000	6,600	52	,,
12	48	3,600,000	5,800	48	Leucopenia.
13	47	4,400,000	6,200	50	Normal.
14	46	3,920,000	6,800	48	,,
15	48	3,300,000	6,700	48	,,
16	44	4,100,000	8,200	50	,,
17	42	5,800,000	7,000	50	,,
18	45	3,200,000	5,600	30	Leucopenia.
19	45	2,800,000	3,000	15	,,
20	42	3,000,100	4,000	40	,,
21	50	3,500,000	6,000	50	Normal.
22	44	3,400,000	5,000	40	Leucopenia.
23	42	4,000,000	6,000	35	Normal.
24	45	4,200,000	7,500	40	,,
25	48	3,800,000	7,200	30	,,
Average .	47·6	3,972,000	6,270	47	

mild secondary anæmia with a constant and considerable reduction in the percentage of hæmoglobin. The red blood corpuscles were reduced but never to the same extent; the leucocytes, often slightly reduced, were not beyond normal limits. No alterations were found in the differential count apart from slight relative lymphocytosis.

The averages of the series are these:—

Red blood corpuscles . . . . . 3,972,000 per c.mm.
White „ „ 6270
Hæmoglobin . . . . . 47 per cent.

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Splenomegaly was present in eight patients, but in seven no examinations were made. Four also had slight enlargement of the liver. The increase in the size of the spleen is usually very definite if enlargement takes place, and it has been found to occupy nearly one quarter of the abdomen.

In every case in which the Einhorn tube could be passed, free HCl was present in the gastric contents. Bacteriological examination of the throat revealed—streptococci in 8 cases,

TABLE B.—*General Examination.*

Case.	Saliva *p*H.	Spleen.	Liver.	Free HCl.	Throat Swab.
1	6·4	Normal	N. E.	N. E.	Streptococcus and Leptothrix.
2	6·2	Enlarged	Enlarged	,,	Streptococcus : *M. catarrhalis.*
3	6·6	Normal	N. E.	,,	Streptococcus.
4	6·9	N. E.	,,	,,	N. E.
5	6·4	Normal	,,	,,	Pneumococcus + *Staph. aureus.*
6	6·6	,,	,,	,,	,, + ,,
7	N. E.	N. E.	,,	,,	N. E.
8	6·4	Normal	Normal	Present	Pneumococcus.
9	6·6	N. E.	N. E.	N. E.	N. E.
10	6·4	Normal	Normal	Present	,,
11	6·6	N. E.	N. E.	N. E.	Leptothrix filaments.
12	6·4	Normal	Normal	,,	Pneumococcus and Staphylococcus.
13	N. E.	N. E.	N. E.	,,	N. E.
14	6·9	Enlarged	Normal	Present	Streptococcus.
15	N. E.	,,	N. E.	N. E.	Pneumococcus.
16	,,	N. E.	N. E.	,,	N. E.
17	6·6	Normal	Normal	Present	*M. catarrhalis :* Staphylococcus.
18	6·4	Enlarged	Enlarged	,,	N. E.
19	6·4	,,	,,	,,	Streptococcus and Leptothrix.
20	6·4	,,	,,	,,	Streptococcus.
21	N. E.	,,	Normal	,,	Pneumococcus.
22	6·4	,,	,,	N. E.	Streptococcus.
23	6·6	N. E.	N. E.	,,	N. E.
24	N. E.	Normal	Normal	,,	Pneumococcus : Staph.: *catarrhalis.*
25	6·4	,,	,,	Present	Streptococcus.

N. E. = Not examined.

pneumococci in 7, and in 4 in which the experiment was tried the patient's serum did not agglutinate the organism isolated.

Differential Diagnosis.—Although in making a differential diagnosis consideration must necessarily be given to a wide variety of possible causes of dysphagia, paralysis following a central or cortical lesion, ulceration from tuberculous, syphilitic or other infection, the destructive effects of the ingestion of a corrosive fluid or the impaction of a foreign body, cardiospasm referred high up in the gullet, pulsion diverticula at the œsophageal entrance, pressure on the œsophagus from lymph-

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adenoma, aneurysm or mediastinal tumour—usually, as far as throat conditions are concerned it is only of importance to exclude malignant disease. In my experience it is with no other pharyngeal or œsophageal condition that confusion tends to arise but with the anæmias pernicious and secondary, and this is frequently not the fault of the examiner. In three of these examples no complaint of dysphagia was made until long after treatment for secondary anæmia had been instituted —even then it was found out accidentally. In one case when taxed with her omission to speak about her dysphagia the patient said that she was afraid to as she did not want an operation on her throat. Another was satisfied that she had suffered from a "small swallow" and looked upon it as a dispensation of Providence. The third was informed by someone that she had simply rheumatism of the muscles of the throat and from her experience of that ailment in the more mobile parts of her frame, was convinced that no amelioration was to be expected from treatment.

Treatment.—The treatment of the condition is fortunately simple and effective and consists in the passage of some form of dilator according to the resistance met with on examination. I have noticed that sometimes for days after the passage of a tube swallowing has been greatly improved.

It is essential too that the patient should be impressed that improvement will follow the passage of an instrument and, if she is in hospital, that she is seen to eat meat, vegetables, apples, walnuts and similar things which before were impossible.

A mixture of iron and arsenic is ordered or iron alone is given, and small doses of thyroid extract seem to hasten recovery. Very soon the hæmoglobin percentage begins to rise; the red cells come back to normal numbers and the spleen resumes its ordinary dimensions.

Etiology and Pathology.—Any attempt at elucidating the pathology of this syndrome is met at the very outset by the difficulty of determining whether the dysphagia precedes or is the result of the anæmia. In 15 of these patients dysphagia appeared to be the first symptom, and at periods varying from two months to a year thereafter, pallor was noticed by them or commented on by their relatives. In 5 it was difficult to ascertain the sequence of developments, and in the remaining 5, three thought that they had been pale before dysphagia began and two were positive that unusual pallor and weakness

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had for some months preceded any difficulty in swallowing. The Mayo Clinic observers have had precisely the same difficulty in settling this point.

When anæmia is the first change we must conclude that the alterations in the pharyngeal and oral mucous membranes are comparable to, if indeed they are not due to, the same cause as the glossitis of pernicious anæmia. More often, I think, dysphagia is the first indication of this trouble and anæmia develops from semi-starvation of essential foods, particularly iron. The obstruction takes place at the crico-pharyngeus muscle, the lower half of the inferior constrictor of the pharynx, and therefore it is technically pharyngeal. I only want here to mention four anatomical points, which are not often made clear in statements about this region, and I mention them without in any way suggesting that any or all of them may be of significance in explaining the ultimate development of non-relaxation or of spasm of this physiological sphincter.

1. The inferior constrictor is not continuous with the circular muscular coat of the œsophagus but with the longitudinal coat.

2. At the top of the œsophagus the striated muscle has no Auerbach's plexus between its layers.

3. The mucous glands very often show striking changes. Instead of or in addition to finding tubuloracemose glands, at the cricoid, glands identical with the cardiac glands of the stomach are found, which contain chief and oxyntic cells, presumably secrete acid, and therefore are called " upper cardiac glands."

4. In addition to its supply from the glossopharyngeal and vagus nerves, through the pharyngeal plexus, and the external laryngeal and recurrent branches, this muscle also receives through the plexus the ascending pharyngeal branch from the superior cervical ganglion.

How far this sympathetic supply may determine the onset of spasmodic contraction offers you room for conjecture.

My own impression is that the non-relaxation or spasm of the sphincter can be explained on simple lines.

With the atrophic changes in the pharyngeal mucosa the nerve-endings become involved, they may even be destroyed and the starting-point of the reflex arc is out of commission. At the same time there appears to be considerable atrophy

https://doi.org/10.1017/S0022215100033296 Published online by Cambridge University Press

of the mucous glands which normally facilitate swallowing, and as a combined result the swallowing reflex is not instantly initiated and completed. The result in the first instance is that the cricopharyngeal does not relax normally. When it does relax at all it probably only does so under the influence of unusual pressure applied to it directly or to its immediate surroundings. I believe that it is at this stage, when normal excitation is removed and contraction is evoked by pressure on the muscle substance or possibly through some unusual sympathetic stimulation, that spasm of this sphincter, or for that matter any sphincter, may develop.

It would be, however, illogical to lose sight of what, after all, are the principal factors in this syndrome—the age and sex of the patients; and no consideration of etiology can neglect the possibility of a vicious circle—a debility and anæmia associated with the climacteric, consequent changes in the pharyngeal mucosa, then dysphagia and limitation of food, with resulting accentuation of anæmia and splenomegaly. That I must confess is the view to which increasing experience of this disorder makes me personally incline. It is, too, a singular and suggestive fact that nearly 80 per cent. of the malignant affections of this site should occur in women about the same age. There is no known difference in the histological picture of the pharyngo-œsophageal junction in the two sexes, and certainly no greater liability to damage in women. Often too malignant disease appears to be a late development of the syndrome under discussion. So it may be that with the changes of the menopause there is at times a tendency to alterations in the mucous membranes of the pharynx and œsophagus which in one is manifested in disordered action of the pharyngo-œsophageal sphincter, and in another, and in greater severity leads to excessive or malignant proliferation.

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