

EARLY SIGNS OF MEDIASTINAL TUMOURS.¹

BY J. LLOYD ROBERTS, B.A., B.Sc., M.D., B.S. LOND.,
M.R.C.P. LOND., F.R.C.S. ENG.,

HONORARY PHYSICIAN, ROYAL SOUTHERN HOSPITAL, LIVERPOOL;
LECTURER ON CLINICAL MEDICINE, AND INTERNAL EXAMINER
IN CLINICAL MEDICINE, UNIVERSITY OF LIVERPOOL.

MEDIASTINAL tumours are usually classed among the uncommon diseases, but their occurrence is far from being rare. Under this title are included malignant growths involving any of the mediastinal structures, enlargement of the intrathoracic lymphatic glands from any other cause, and inflammatory swellings. Closely allied to them in the resulting symptoms are many cases of thoracic aneurysms, to which, however, I do not propose to allude in this communication, and also tumours originating in the substance of the lungs. All these tumours manifest themselves by symptoms due to pressure on adjacent structures. The rate at which symptoms develop varies considerably, for in some rapidly growing glandular tumours and in some inflammatory affections evidence of pressure on several organs may manifest themselves in the course of a few days, whereas in slowly growing tumours symptoms may be limited to irritation of a single organ for many weeks. By "early signs" I therefore mean those which are "early" in time, and not in degree.

For the purpose of this paper I have based my remarks on 36 cases with evidence of intrathoracic pressure which I have met with during recent years. Of these, 14 were cases of malignant growths of glands or lung, 8 were cases of malignant disease of the œsophagus subsequently affecting the surrounding structures, 3 were cases of enlarged tubercular glands, and 4 of non-tubercular lymphatic affections, 3 were cases of mediastinitis, and 4 were syphilitic in character. The symptoms met with in these cases were pain, dyspnoea, cough, dysphagia, wasting, anasarca, vomiting, hiccough, and palpitation. Wasting was, of course, common to all the malignant cases, and dysphagia was almost, but not altogether, limited to cases of disease of the œsophagus. The relative frequency of the remaining symptoms may be inferred from the fact that pain was the most prominent symptom in 11 cases, cough in 8, dyspnoea in 7, anasarca in 6, vomiting in 2, and hiccough in 1.

If the relative frequency of the causes in my cases is a fair average, seeing that 22 out of my 36 cases were malignant in character, it follows that the prognosis of mediastinal tumour, speaking generally, must be very bad. Of my remaining cases, one died from mediastino-pericarditis and two from lymphadenoma, but the remaining 11 cases recovered more or less completely from their symptoms, and the degree of recovery seemed to vary inversely with the length of time during which the patient had been affected. It follows, therefore, that early diagnosis of the presence and cause of intrathoracic pressure is particularly important in those cases where therapeutic treatment may be possible—i.e., when the cause is specific, inflammatory, or tubercular in nature. For this reason it seemed to me that a consideration of the signs of the disease—as far as can be undertaken within the limits of a short paper—as they were discovered in my cases on their first examination might not be without interest. In order to economise time I propose to confine my remarks to a few points bearing upon (1) obstruction to the venous circulation; (2) obstruction in the respiratory tract; (3) referred pains; and (4) effect upon the pericardium.

1. *Venous obstruction.*—This is, of course, one of the classical symptoms of mediastinal tumour. The dilated veins of the skin of the thorax, upper arms, and abdominal walls, as well as the œdema often associated with them, are familiar to all. But under this heading I wish to refer only to one particular vein which is less frequently affected and is apt to be overlooked in this connexion—viz., the vena azygos major. Pressure upon this vein is interesting for more than one reason. I was first led to take an interest in it by a case of mediastino-pericarditis which I met with some years ago in a young boy. This boy was sent

into hospital as a case of acute Bright's disease, and upon a superficial inspection the diagnosis seemed fully justified. The patient had marked general anasarca—over his abdomen, loins, legs, thorax, arms, and face—as well as effusion into his pleural and peritoneal cavities. But examination of the urine showed it to be perfectly normal, without albumin, deposit, or casts, so that it was clear that his dropsy was not due to renal trouble. That being so, the heart was examined as the next most probable seat of trouble. This organ, however, showed no sign of abnormality, and was beating slowly and regularly, without any suspicion of a murmur. From these facts it became possible to deduce that the dropsy was due to a mechanical obstruction to the circulation, and by consideration of the veins obstructed it was possible to locate the trouble in the thorax, pressing upon the superior vena cava and the right auricle.

There was, however, one symptom about this boy which impressed me—viz., that the effusion into the peritoneal cavity was quite insignificant in comparison with the amount of effusion into the abdominal walls and lumbar region. Now these parts are drained by the intercostal and lumbar veins, which empty themselves into the azygos veins, and it would seem a reasonable deduction that the trouble in the chest in addition to pressing on the great veins pressed also on the vena azygos major. The subsequent post-mortem examination showed this to be the case. It struck me that this great disproportion between the œdema into the peritoneal cavity and that into the subcutaneous tissue of the abdominal walls and loins might be a useful diagnostic point in distinguishing between anasarca due to cardiac or renal disease on one hand, and that due to mechanical obstruction in the chest on the other. And I have since then several times found this point of much help in diagnosis. This œdema is usually bilateral, but in one case of malignant mediastinal growth that I met with it was unilateral and limited almost entirely to the right half of the abdominal wall and the right loin. This was due to the fact that the tumour obstructed the right lower azygos vein before it was joined by the vein from the left side. It was thus possible to localise the tumour more exactly, as being below the level of the eighth dorsal vertebra. In another case to which I shall refer the œdema was limited to the left side.

One character of such œdema sometimes met with, when the inferior vena cava is obstructed as well as the azygos vein, is brawny hardness of the skin of the legs and abdomen, with almost complete absence of pitting. Not long since I was asked to see a patient with such a condition of the lower half of the body, and the appearance at once suggested the diagnosis of posterior mediastinal tumour occluding the azygos major in addition to other veins. This was not an early case, and upon examination other physical signs were found demonstrating a growth occluding the lower division of the right bronchus, thus supporting the above suggestion, which was subsequently verified.

A case of brawny œdema of this distribution was reported to this Institution a few years back by Dr. W. Carter, which recovered completely on the administration of mercury. This may have been specific in origin. At any rate, I have learned that tumours occluding this vein are not rarely gummatous in nature, and are therefore capable of being benefited by treatment. The following case is an interesting example.

A large-looking man was admitted into the Royal Southern Hospital with anasarca of all parts except the face, neck, and arms, with fluid in the pleural and peritoneal cavities, and considerable enlargement of the liver. These symptoms had all come on in the course of three weeks without any previous illness to account for them, the heart and kidneys being found healthy. On examination the œdema was found to be far more marked in the subcutaneous tissue of the loins and abdominal wall than elsewhere. These facts at once pointed to mediastinal obstruction, and other physical signs were found showing evidence of pressure on the left lower bronchus. Owing to the rapidity of development a diagnosis was made of gummata of the posterior mediastinum, and the patient was treated with mercury and iodide of potassium. Improvement was immediate. Almost in a day the œdema began to diminish, and a week later the note reads: "The œdema is entirely absent, the back and thighs being clear." The signs of pleural and peritoneal effusion had also disappeared. I kept the patient under observation in the ward for three weeks longer, but there was no return of symptoms, and he went out feeling quite well. There was, however, distinctly less air-entry into his left lower lobe than into the right, so that although the supposed gummata had diminished sufficiently to relieve the venous obstruction, there remained its effects causing some obstruction to the bronchial tract.

This patient kept well for seven months, and then was readmitted with a recurrence of all his symptoms. The

¹ A paper read before the Liverpool Medical Institution.

same treatment was adopted with the same benefit. This was two years ago, and as he has not appeared again I am hoping that he has kept well. On this second occasion the lumbar pad of œdema was slight on the right side, but much greater on the left, showing that the tumour was more limited, and pressing especially on the left lower azygos vein.

One other case of a different kind causing similar venous obstruction deserves mention.

In March, 1910, a young man, aged 18, was sent to me with a somewhat unusual history. His illness, which was only of three weeks' duration, had commenced with a dull aching pain behind the sternum, which lasted four or five days. He soon afterwards noticed that his abdomen was swelling. On admission into hospital he had marked anasarca over his legs and abdomen and loins, and to a lesser extent over his thorax, arms, and face, with effusion into the serous cavities. But the chief feature of the swelling was, as in the previously mentioned cases, excessive subcutaneous effusion over the lower abdominal wall and lumbar region, as compared with other parts. This appearance again at once suggested thoracic obstruction, and I was not surprised to find his heart and kidneys healthy. On examining the chest I found an area of dulness over the middle part of the sternum, extending for $1\frac{1}{2}$ inches to the right of the bone, and there were physical signs pointing to obstruction of the lower division of the right bronchus. On X-ray screen examination an unusually broad median shadow was seen, extending to the right side. The space behind the great vessels, between them and the spine, as seen in the oblique diameter, was clear. It, therefore, appeared that this was a case of some obstruction in the anterior mediastinum, extending backwards to press on the right lower bronchus and the azygos major. The history suggested the probability of its being an inflammatory exudation—i.e., an anterior mediastinitis—and some facts suggested that it may have started in the thymus gland. This patient was also treated with iodide and mercury. He made good progress, and in about four weeks he appeared to be completely cured. The œdema and the serous effusions had all disappeared, and the air entry into the right base was practically equal to that into the left. The patient was a school-teacher and resumed his work. He kept well for many months, but I am informed that subsequently he had a return of apparently similar symptoms, and died rather suddenly.

2. Respiratory obstruction.—My next point refers to pressure upon the respiratory tract. This may occur alone in early cases, but generally when the patients come under observation it is found in association with venous obstruction, and I have already had to refer to it in association with the latter. The obstruction in early cases is defined and limited, and thus helps to demonstrate the locality of origin of the tumour. The physical signs of bronchial obstruction are, as a rule, so clear and so easily detected that I have been surprised to find how frequently the condition is overlooked—entirely because the examiner has not before his mind the possibility of its existence, being more concerned with the quality than the quantity of air entry. The association of three physical signs—normal resonance, diminished or absent tactile fremitus, and diminished or absent breath sounds—is almost distinctive of the condition. The importance of the alteration in fremitus was insisted upon by Professor T. R. Glynn before this Institution some years ago, and I can fully endorse his remarks on the importance of this sign in diagnosis, the apparent exceptions admitting of explanation on other grounds.

The following two cases are illustrations of the fallacies that may be fallen into owing to insufficient attention to these three signs—in one, obstruction of the upper lobe being mistaken for phthisis; in the other, obstruction of the lower lobe for pleuritic effusion.

A man, aged about 40 years, was sent to the hospital as a case of phthisis of the left apex. There was marked diminution of air entry into the left upper lobe, and there was some impairment of resonance. But upon consideration it was felt that there was no proper correspondence between the amount of loss of resonance and the amount of loss of air entry. Further, it was found that tactile fremitus was diminished rather than increased, thus bringing the case into the group of those with physical signs pointing to bronchial obstruction. Further examination of the patient showed groups of enlarged lymphatic glands in other parts of the body, and the diagnosis was made of Hodgkin's disease with special enlargement of the intrathoracic glands. Post-mortem examination subsequently showed that enlarged glands completely occluded the left upper bronchus. The fallacy here was that the enlarged glands themselves led to loss of resonance, and suggested thickening of the pleura, or consolidation of the lung.

As an illustration of possible fallacy in connexion with the lower lobe the following case is interesting.

A man who did not seem very ill was sent into the Royal Southern Hospital as a case of bronchitis, with fluid at the left base. This diagnosis was made on the strength of the fact that there were loud inspiratory sounds with rhonchi heard all over both lungs, with the exception of the left base, where no sounds could be heard. On examination I found that there was absence of breath sounds over the left lower lobe, and also of tactile fremitus. But the resonance was only slightly impaired, much less than would have been the case if there had been pleural effusion. Thus the group of signs pointed to bronchial obstruction. Over the same area there was also audible a loud systolic murmur which suggested the possibility of an aneurysm, the existence

of which was proved by an X-ray examination. It was afterwards found that a large aneurysm of the descending arch had almost completely occluded the left lower bronchus.

In association with obstruction of a bronchus, or one of its main divisions, a very usual symptom is more or less dyspnoea, particularly on exertion, but in several of my cases the dyspnoea was extreme, out of all proportion to the amount of obstruction. And, curiously enough, these proved to be the most favourable cases. Certainly in some of them, and probably in all, the tumour was gummatous in nature, and improvement was obtained by antisyphilitic treatment. I would remind you of a similar observation made by Professor R. J. M. Buchanan in his cases of gummata of the lung—viz., that the amount of dyspnoea was extreme and out of proportion to the extent of involvement of the lung.

3. Pressure upon nerves.—In many instances, especially in the case of slowly growing tumours, pressure upon nerves causes the first indication of trouble. The nerves most apt to be involved are the phrenic, the intercostals, the vagus or its recurrent branch, and the sympathetic. Occasionally there is evidence of affection of one only of these nerves for many weeks before any other symptom develops. Thus, irritation of the sympathetic may lead to inequality of the pupils, which should always be examined in any case presenting symptoms of mediastinal pressure. In other cases laryngeal paralysis due to pressure on the recurrent nerve may be an early and only symptom. I should add, however, that both these results occur far more frequently in the case of aneurysms than of mediastinal tumours. Pressure upon the vagus may cause a variety of symptoms. A rapid or irregular pulse is not infrequent, and Skoda mentions dysphagia, vomiting, and hiccough as effects of irritation of this nerve. Curiously enough, I have within the last few months met with instances of each of these three effects.

1. A man, with evidence of mediastinal pressure due to a malignant growth originating in the œsophagus, was seized with violent hiccough which persisted continuously for about six days, causing great exhaustion. That this was a reflex effect was, I think, demonstrated by the fact that it appeared to yield at once to treatment of a kind that could have had no effect, had it been due to damage to the nerve. The treatment, which I had adopted with success in a previous case of hiccough lasting for about 50 hours after an anæsthetic, consisted merely of a rectal injection of diluted port wine. In this case vagal irritation also produced persistent tachycardia.

2. A few months ago I was asked to see a lady who for several days had had persistent vomiting without any apparent cause after the ingestion of any kind of food. Examination of the stomach revealed no abnormality, but on examining the base of the left lung I found definite physical signs of a tumour obstructing the left lower bronchus, and there was a small hard enlarged gland above the left clavicle. I admit that in this case it would be quite reasonable to suggest that the thoracic tumour was secondary to a primary growth of the stomach which was the actual cause of the vomiting, and which was not within reach of palpation. The history, however, did not support that view, but rather suggested reflex vomiting.

3. About two months ago a man was admitted into hospital suffering from marked dysphagia. X-ray examination revealed an enlargement of the aorta. The patient died, and a fusiform dilatation of the ascending part of the arch was the only abnormality found. This could not have pressed on the œsophagus, and the dysphagia could only be explained by reflex vagus irritation.

Pain, however, is the most frequent evidence of pressure on the intrathoracic nerves, and owing to the intercommunications between the phrenic and sympathetic and the intercostal and cervical nerves the areas to which the pain may be referred are numerous and extensive. A common seat of pain is across the sternum, and another is from the nape of the neck down to the top of the shoulder. Other patients refer the pain to the arm on the affected side, and others, again, round the side of the thorax or the epigastrium. The pain persists day after day, though it varies in intensity from time to time. In one case the pain was referred to the middle intercostal spaces at the back and side. It had persisted for some weeks and was supposed to be pleuritic. Examination disclosed diminished air entry into the left upper lobe, but there was also patchy dulness and increased vocal fremitus. Thus the signs indicated not only bronchial obstruction, but also condensation of the lobe, and the diagnosis of cancer of the root of the lung obstructing the bronchus and extending into the lung itself was subsequently found to be correct. In this case there was also left recurrent laryngeal paralysis, which is comparatively rare in mediastinal cancer.

In two cases the patients had complained of pain over the tip of the shoulder for many weeks before there was any other evidence of ill-health, and in both cases the pain had been considered to be rheumatic. In these cases the pain could be explained by the communication between the phrenic and superior acromial nerves. In one of them pain

had lasted for three months before any other symptom appeared, and then paraplegia, due to secondary deposit, suddenly supervened. Examination of the chest at this time revealed obstruction of the left upper bronchus.

4. Lastly, I would like to mention one other occasional early symptom of malignant growths of the lower mediastinum, and that is pericarditis. A pericardial rub in old people is almost as diagnostic of malignant growth as it is of rheumatism in the young, or of Bright's disease in middle age. I consider idiopathic pericarditis in elderly people as of grave import. As an example I would mention the following case.

The patient was a lady, over 60 years of age, whom I was called to see about two years ago. She had been in her usual health until about a week previously, when she began to feel out of sorts, lost her appetite, and on two successive mornings had fainting attacks without apparent cause. When I saw her the only abnormality I could find was a pericardial friction sound, and on the strength of this, as the result of my experience in previous cases, I ventured to diagnose a malignant mediastinal growth, in spite of the fact that the lady stated that she had suffered from rheumatic fever in her young days. I saw her again ten days later, and there was then evidence of diminished air entry into the right lower lobe. After another interval of ten days I found her much reduced in strength, with effusion in her right pleural cavity. Not long afterwards she died with all the symptoms of a rapidly developing malignant growth. In this case the growth occluded the right lower azygos vein, and led to oedema of the right half of the abdominal wall and loin.

The *diagnosis* of mediastinal tumours must be made from the subjective symptoms and evidence of pressure on neighbouring structures. The cases most commonly overlooked are those where pain is the only symptom, and where this is referred to the back of the neck or arm, or more particularly the shoulder. In the case of obstruction of air entry into a lobe of the lung, in addition to the signs already mentioned, sucking-in of the intercostal spaces corresponding to that lobe is occasionally observed during inspiration. Considerable help may be obtained by X ray examination, but only in cases where the tumour is not permeable to the rays. The tumours vary much in this respect, but fortunately in a good proportion of cases the tumour does cause a shadow. As far as aneurysms are concerned, it is usually possible by radiography to prove or negative their existence. Calcareous lymphatic glands will also give evidence of their presence. Some cases of lympho-sarcoma will disclose themselves, and carcinomata in the posterior mediastinum generally cast a more or less distinct shadow. The importance of examining for enlarged supraclavicular glands as evidence of secondary deposits must not be overlooked.

Treatment.—If there be any possibility that the tumour is specific in character, and particularly if the Wassermann reaction be positive, antisyphilitic remedies should be vigorously tried. Even without a positive Wassermann reaction, and especially if the evidence is in favour of the trouble being mediastinitis, the same treatment should be adopted. Iodide of potassium and mercury should be given internally, and mercurial inunction used over the area involved. In cases of anterior mediastinitis the possibility of surgical interference, by means of trephining the sternum, should be borne in mind. In cases diagnosed as tubercular, general hygienic measures should be adopted, and the use of tuberculin in appropriate cases should be considered. In the great bulk of cases, however, their malignant nature does not hold out any hope of beneficial treatment.

In conclusion, may I recapitulate the points that I wish to emphasise: (1) the importance of obstruction of the azygos veins in explaining symptoms and localising obstructions; (2) the importance of paying full attention to the *quantity*, as well as the *quality*, of the air entry; (3) the importance of estimating properly the significance of referred pains, especially of shoulder pain, which, though rheumatic in type, persist in spite of treatment; and (4) the seriousness of idiopathic pericardial friction in elderly people.

Liverpool.

THE VACCINE TREATMENT OF HAY FEVER.

By A. G. HAYNES LOVELL, M.D., F.R.C.S.

IN view of the papers of Mr. L. Noon and Dr. J. Freeman in THE LANCET of June 10th and Sept. 16th, 1911, respectively upon the treatment and prophylaxis of hay fever by means of a standardised vaccine made of pollen toxin, the following cases, which I have had under my care this season, seem to be of interest.

Six patients came to me for treatment. One, who said she had suffered from hay fever for the last two years, on being tested by the "ophtharmo-reaction" method showed herself not to be susceptible to 5000 U.P. She was not a case of true hay fever, and so was not treated. The other five cases were all positive on testing with 150 U.P., and all report themselves very distinctly benefited by the inoculation treatment, though none of them were cured. Complete cure, however, was not expected, as in none of these cases were the inoculations started early enough in the "off season." I hope to treat some or all of them during the "off" season this year in the hope of complete prophylaxis next year.

The appended summary of the cases shows very marked benefit from treatment in Cases 1, 3, and 4, and some appreciable relief in Cases 2 and 5.

CASE 1.—Ophtharmo-reaction: At start, slight, 50 U.P.; very definite 150 U.P.; (tested by Dr. Freeman). At end, very slight, 50 U.P. History: Hay fever for about 35 years; asthma at same time for 26 years. Asthma only occurs in association with hay fever. Family history of asthma. Nasal condition: Deviated septum to right, right inferior turbinal fused to septum as result of cautery 15 years ago; left inferior turbinal enlarged. I divided adhesion and reduced the turbinates. Doses given: 11 doses, 15 U.P. each, except on three occasions when there were slight symptoms; then 7 U.P. were given. Dates of doses: April 18th to July 10th at about 10-day intervals. Apparent immediate effects of doses: No negative phases. Patient's report: "The amount of asthma was next to nothing, but I felt it a little on exertion. I have had no bronchial asthma as I usually have. The hay fever has not affected the nose at all. The eyes have been a little sore, but less than other years. So on the whole it is a considerable alleviation."

CASE 2.—Ophtharmo-reaction: At start, slight, 50 U.P.; definite 150 U.P. At end, *nil* to 50 U.P.; very slight, 150 U.P. History: Hay fever for about 12 years; attacks like hay fever after dances. Nasal condition: Cauterised with but little effect in previous years. No apparent abnormality. Doses given: 8 doses—50, 20, 20, 10, 10, 10, 5, and 7 U.P. respectively. Dates of doses: April 24th to July 15th; intervals varying from 7 to 14 days. Apparent immediate effects: Several doses, especially first and last two, seemed to produce a definite negative phase followed by periods of relief. Patient's report: Thinks she has suffered to a less degree than in previous years, the constitutional symptoms being less, but she has led a quieter life, owing to an injury from a fall.

CASE 3.—Ophtharmo-reaction: At start, slight, 150 U.P. History: Hay fever since childhood; asthma only once, and that followed the use of pollantin snuff. In family several cousins suffer from hay fever. Nasal condition: No apparent nasal trouble. Has been cauterised previously without effect. Doses given: 7 doses, 50, 40, 20, 15, 15, 15, and 10 U.P. The hay fever had not started when first two doses were given. Dates of doses: May 2nd to June 25th, at 7 to 10-day intervals. Apparent immediate effects: First dose produced a streaming cold, starting 4 hours later and lasting 36 hours. The second dose produced one in 2 hours, lasting half an hour. The others produced no negative phases. Patient's report: The frequency of attacks, their duration and severity have been very much less than ever before.

CASE 4.—Ophtharmo-reaction: At start, slight, 150 U.P.; very definite, 500 U.P. History: Hay fever since childhood every year and sharp attacks of stinging pain in eyes and difficulty with breathing. Doses given: 7 doses, 30, 30, 10, 10, 5, 5, and 5 U.P. Dates of doses: May 10th to July 7th, at about 9-day intervals. Apparent immediate effects: No negative phases. Patient's report: Much better, scarcely suffering at all; no breathing trouble, no acute attacks of sneezing, and only on three occasions slight itching in the eyes, never lasting more than 15 minutes, and really not worth mentioning. Attacks shorter and less frequent. No asthma.

CASE 5.—Ophtharmo-reaction: At start, slight, 150 U.P. History: Suffered for 12 years during May and June; gets asthma at end of the season. Nasal condition: Inferior turbinal enlarged and blocking meatus on right side. Doses given: 3 doses, 10, 10, and 10 U.P. Dates of doses: June 13th to 27th, at 7-day intervals. Apparent immediate effects: No negative phases. Inoculation given during bad attacks relieved them at once.

I publish these results in hope that other practitioners may do likewise, to enable us to form a more accurate estimate of the value of the vaccine treatment of this troublesome complaint.

Hans-crescent, S.W.

LITERARY INTELLIGENCE.—Messrs. W. B. Saunders Company have in the press for immediate publication a work on *Psychoanalysis*, by Dr. A. A. Brill, Clinical Assistant in Psychiatry and Neurology, Columbia University Medical School.—A book is announced by Messrs. J. and A. Churchill from the pen of Dr. Fred J. Smith, of the London Hospital, entitled "*Law for Medical Men.*" It contains extracts from Acts of Parliament especially applying to medical practice, and will be on sale immediately. The same firm will issue "*Practice and Problem in Abdominal Surgery,*" by Mr. Alfred E. Maylard, Surgeon to the Victoria Infirmary, Glasgow.