SUMMARY

The medical records of British Army patients admitted to hospital with anaemia between 1949 and 1958 were studied. The causes of the anaemia are set out and classified. Anaemia in young men is uncommon but not so uncommon as previously published figures have suggested. Poor diet may be a cause of anaemia in young men in this country.

I should like to thank Mr. S. Rosenbaum, M.A., Principal Scientific Officer, Army Medical Statistics Department, The War Office, for making available the medical records and for providing the statistical work.

REFERENCES


MACLEOD'S SYNDROME
A REPORT OF THREE NEW CASES AND A REVIEW OF THE LITERATURE

BY

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This paper presents three new cases of a syndrome first described in detail by Macleod as “Abnormal Transradiancy of One Lung” (Macleod, 1954). Additional cases have been described by Dornhorst, Heaf & Semple (1957), Belcher et al. (1959), Bates (1959), Margolin et al. (1959), Darke, Crispin & Snowden (1960) and Fouché, Spears & Ogilvie (1960). The condition may be asymptomatic but most patients present with one of the common complaints of chest disease, notably cough, recurrent chest infections or shortness of breath. On examination the breath sounds are reduced in intensity on the side affected and there may be a localised or a generalised wheeze. The problem of diagnosis is first raised by the chest radiograph for there is striking transradiancy of one lung or lobe due at least in part to a small pulmonary arterial tree.
Macleod’s Syndrome

CASE REPORTS

Case 1

A 30-year-old platoon sergeant had bilateral pneumonia as an infant, and had been told that he was asthmatic until he was seven years old. He remained well until he was 27 years old when he became a heavy smoker, increasing from ten to fifty cigarettes a day. From this time he noticed increasing shortness of breath on training exercises. When seen at the age of 30 years he had become short of breath marching at a normal pace although he could continue indefinitely and he did not become cyanosed.

Breath sounds were faint on the right side. On both sides of the chest the expiratory phase was prolonged and there were expiratory and inspiratory rhonchi.

The PA chest radiograph showed increased transradiancy and small vessels on the right, the right diaphragmatic leaf being low and failing to move upwards on expiration. There was no mediastinal swing on respiration.

Tomograms showed very small arterial trunks on the right, but on the left the arteries were large and obviously wider than normal well out into the lung field. The right bronchogram showed poor peripheral filling most marked in the middle and lower lobes, but was otherwise normal.

Bronchospirometry was carried out at the London Chest Hospital by Dr. Smart and Dr. Capel. Both the vital capacity and the oxygen uptake were reduced, the reduction in the oxygen uptake on the side affected being proportionately more than the reduction in vital capacity. This is characteristic of the condition.

Obstructive airway disease was also present. The Forced Expiratory Volume (FEV$_{0.1}$) was less than 1,000 ml when the patient was first seen, but it increased to 1,900 ml after treatment with choline theophyllinate (“Choledyl”) and an isoprenaline spray. In short, this sergeant had mild asthma and a virtually functionless right lung.

Case 2

A 25-year-old corporal was admitted in 1956 complaining of cough, left-sided pleural pain and shortness of breath. A similar illness had occurred in 1954 but there was no history of chest trouble before this. He had smoked ten cigarettes a day since 1951.

Breath sounds were faint on the right but examination was otherwise normal. On bronchoscopy an increase in bronchial secretions was seen.

The chest radiograph showed increased transradiancy on the right, the vessels being small. The movement of the right diaphragm was slightly restricted. On expiration the right leaf of the diaphragm remained at a lower level than the left and the heart moved to the left.

Tomograms confirmed that the vessels to the right lung were small, but there was great enlargement of the main, lobar and segmental arteries on the left. There was a calcified gland at the left hilum. The left bronchogram was normal,
Fig. 1.—Right bronchogram of Case 2. There is poor peripheral filling, and bronchiolar pools are present in the lower lobe.

Fig. 2.—Forced expiration radiograph of Case 3, showing "trapping" on the left. Increased transradiancy is present on this side.

Fig. 3.—9 cm. tomogram of Case 3, showing normal right pulmonary arteries and small left pulmonary arteries.

Fig. 4.—Left bronchogram of Case 3 showing dilatation and occlusions of the lingular bronchi (left oblique view).

MACLEOD'S SYNDROME
but on the affected side there was poor peripheral filling and some small bronchial dilatations in the right lower lobe (Fig. 1).

The patient was discharged from the Army and has been followed up at the Sheffield Chest Clinic under the care of Dr. H. Midgley Turner. He has had repeated chest infections and a chronic cough producing purulent sputum. He is becoming increasingly short of breath and has to walk slowly even on the flat. In December, 1958, he developed a chest infection with "bronchospasm" necessitating treatment with corticosteroids. Respiratory function tests in January, 1959, showed reduction in vital capacity, $FEV_{0.1}$, and maximum breathing capacity. Since leaving the Army he has been unable to hold down a steady job and he is at present doing office work.

Case 3

A National Service man working as a storeman at the Connaught Hospital had a routine radiograph which showed increased transradiancy of his left lung (Fig. 2). At the age of nine months he had "bronchitis and pneumonia" but since then he has remained well. He is now 20 years of age and he plays football for the hospital although he finishes last on cross-country runs. For the last two years he has smoked five cigarettes a day.

He has a high-arched palate and he is colour-blind (Ishihara). The left side of the chest is smaller than the right, moves poorly, and the breath sounds are reduced on this side. "Trapping", the failure of normal emptying during forced expiration, occurs on the left, the left diaphragm failing to move up and the heart moving to the right. The PA chest radiograph shows the main and lobar arteries on the left to be small, and this is confirmed by AP tomography (Fig. 3). The right bronchogram is normal but on the left side bronchial dilatation and occlusions are seen in the lingula with poor peripheral filling in the basal segments (Fig. 4).

Alterations in the lung density were measured as the transradiancy changed during respiration by an image intensifier and photo-cell, and it was found that the change in transradiancy in all regions was smaller on the left than on the right. This probably represents reduction in ventilation on the abnormal side. Radio-isotope studies showed that ventilation and gas exchange were moderately reduced in the left lower zone (Laws & Steiner, 1960; Hugh-Jones, 1960).

A summary of the clinical and radiological findings in the three cases appears in Table 1.

DISCUSSION

The cause of this interesting condition remains uncertain as few pathological reports are available. A series of specimens are to be reported by Dr. Lynne Reid who kindly discussed her material with me before publication. The main changes affect the terminal bronchioles. There is an increase in the wall musculature and in the fibrous tissue surrounding them. Occasionally complete blockage can be demonstrated, alveoli distal to such blockages being adequately ventilated by collateral routes. Considerable disruption of the walls of respiratory bronchioles...
Macleod's Syndrome

Table 1. Summary of three new cases of Macleod's Syndrome reported in this article.

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset of symptoms</td>
<td>27 years</td>
<td>25 years</td>
</tr>
<tr>
<td>Side affected</td>
<td>Right</td>
<td>Right</td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td>Increasing shortness of breath and wheezing</td>
<td>Cough, left-sided pleural pain and shortness of breath</td>
</tr>
<tr>
<td>Radiological findings</td>
<td>Increased trans-radiancy on the right. Normal bronchogram.</td>
<td>Increased trans-radiancy on the right. Bronchiolar pools in the right lower lobe.</td>
</tr>
<tr>
<td>Tomograms show the right pulmonary artery to be small and the left to be large.</td>
<td>Tomograms show the right pulmonary artery to be small and the left large.</td>
<td>Tomograms show small left pulmonary artery.</td>
</tr>
<tr>
<td>Respiratory function tests</td>
<td>FEV 1,450 ml.</td>
<td>2,250 ml.</td>
</tr>
<tr>
<td>FVC 2,400 ml.</td>
<td>3,060 ml.</td>
<td>3,750 ml.</td>
</tr>
<tr>
<td>FER 60%</td>
<td>69%</td>
<td>Oxygen—15</td>
</tr>
<tr>
<td>Regional function</td>
<td>Bronchospirometry Right</td>
<td>21%</td>
</tr>
<tr>
<td>VC 1,200 ml.</td>
<td>1,700 ml.</td>
<td>(41%) (59%)</td>
</tr>
<tr>
<td>Childbirth illness</td>
<td>Bilateral pneumonia at 6 months and asthma till 7 years.</td>
<td>——</td>
</tr>
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</table>

Definitions.

Forced Expiratory Volume: The volume in millilitres expelled during the first second of a forced expiration, following a deep inspiration.

Forced Vital Capacity: The total volume expelled during such an expiration.

Forced Expiratory Ratio: The ratio of the above, the FEV being expressed as a percentage of the FVC. It is normally above 70–75 per cent.

and alveoli occurs. The characteristic air-trapping is probably due to the increased resistance of collateral channels of ventilation.

Inflammatory changes may be present but appear to be of long standing. Many patients have had severe respiratory illness in childhood (Belcher et al., 1959), and the material available is consistent with the view that such infections produce damage at the bronchiolar level, the bronchi themselves remaining in many cases virtually normal. The poor peripheral filling seen bronchographically probably indicates bronchiolar obstruction which may be responsible for the reduced lung ventilation; increased flow resistance at the level of the smaller air passages is suggested by recent studies of air flow and pressure relationships (Darke et al., 1960).

Arterial flow is known to diminish with a reduction in regional ventilation. This is probably the explanation of the small arterial size in this condition.

While congenital hypoplasia of the pulmonary artery is difficult to exclude as a cause of Macleod’s Syndrome, such a lesion does not explain the presence of airway obstruction and bronchial deformity; especially as a normal bronchogram may be obtained in congenital absence of a pulmonary artery (Bates, 1959; Macleod, 1960). Normal pulmonary vascular markings and the absence
of emphysema have been noted in one case during infancy, although the patient's right lung now presents a characteristic appearance (Lees, 1960).

The natural history of the syndrome is better documented. The presenting symptoms of patients in whom an entire lung was involved are summarised from the literature in Table 2. Cases in which the abnormality was restricted to a single lobe have been excluded although this is not uncommon (Belcher et al., 1959). The ages given are those at which symptoms first appeared, when this can be determined from the histories.

Of the 29 cases, 6 were asymptomatic and were discovered on routine radiography. The average age of these 6 cases was 29 years. Twenty-three had symptoms, 17 having a cough or repeated chest infections, 14 shortness of breath, and at least 5 wheezing. Their average age was 27 years.

The time of presentation appears to be determined by the appearance of a

Table 2. Presenting symptoms of 29 cases of Macleod’s Syndrome in which an entire lung was affected. The ages given, calculated from the histories, are those at which symptoms first appeared.

<table>
<thead>
<tr>
<th>Series</th>
<th>Age at onset</th>
<th>Nil</th>
<th>Cough and Infections</th>
<th>Wheeze</th>
<th>Dyspnoea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swyer &amp; James (1953)</td>
<td>...</td>
<td>...</td>
<td>Infancy</td>
<td>+</td>
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<tr>
<td>Macleod (1954)</td>
<td>38</td>
<td>+</td>
<td>+</td>
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<td></td>
<td>22</td>
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<td></td>
<td>Below 32</td>
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<td>24</td>
<td>+</td>
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<td>20</td>
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<td>30</td>
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<td>32</td>
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<td>18</td>
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<td></td>
<td>18</td>
<td></td>
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<tr>
<td>Dornhorst et al. (1957)</td>
<td>11</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td></td>
<td>35</td>
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<tr>
<td>Belcher et al. (1959)</td>
<td>Below 49</td>
<td>+</td>
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<td></td>
<td>Below 55</td>
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<td></td>
<td>41</td>
<td>+</td>
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<td></td>
<td>52</td>
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<tr>
<td>Elder et al. (1958)</td>
<td>26 years</td>
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<tr>
<td>Margolin et al. (1959)</td>
<td>19</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>32</td>
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<td>Bates (1959)</td>
<td>26</td>
<td>+</td>
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<td>Dyson et al. (1960)</td>
<td>37</td>
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<td>+</td>
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<tr>
<td>Darke et al. (1960)</td>
<td>34</td>
<td>+</td>
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<td></td>
<td>17</td>
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<td>18</td>
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<tr>
<td>Present series</td>
<td>27</td>
<td>+</td>
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<td>25</td>
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<td></td>
<td>20</td>
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<tr>
<td>Total number of cases affected</td>
<td>29</td>
<td>6</td>
<td>17</td>
<td>5</td>
<td>14</td>
</tr>
</tbody>
</table>
complication rather than by the condition itself. Commonly presentation is precipitated by a respiratory infection, or the reduction of an already low respiratory reserve by a new factor such as excessive smoking.

The youth of the patients is surprising especially as most were reported by physicians seeing a wider age group than does the Army Chest Centre. Only a few cases have been followed. Case 2 has deteriorated, but no change was found in any of five of Macleod's original nine patients who were followed up for a minimum of four years (Dornhorst et al., 1957; Macleod, 1960).

**Radiological and laboratory findings**

In most cases the diagnosis is established radiographically. The plain film suggests unilateral reduction in vessel size and this can be confirmed by tomography or angiography. A reduction in pulmonary artery size occurs in several types of gross lung disease especially when lung ventilation is reduced. In Macleod’s Syndrome the reduction is particularly striking and a reciprocal enlargement may be present on the opposite side (Belcher et al., 1959). This was seen in cases 1 and 2.

Bronchograms are usually abnormal on the affected side. Because of the obstruction of the terminal bronchioles and the reduced ventilation the peripheral branches do not fill. Case 2 shows bronchiolitis, small pools the size of pin-heads being seen in the periphery of the right lower lobe. Case 3 has bronchiectasis of the lingula. Previous reports describe such appearances.

The failure of normal emptying during forced expiration has already been mentioned, and the reduced change in transradiancy on the affected side was recorded by an image intensifier and photo-cell in case 3 (Laws & Steiner, 1960).

Assessment of respiratory function is handicapped by the difficulty of separating the contributions of a healthy and a diseased lung. Measurement of the overall efficiency of ventilation shows reduction of the maximum breathing capacity and FEV<sub>0.1</sub>. In the cases described the FEV varied between 60 and 69 per cent, the reduction being due to trapping. Studies on anaesthetised patients show that there is marked resistance to both air entry and outflow (Darke et al., 1960). It is therefore likely that the trapping is not due to valve mechanisms but to obstruction of the smaller air passages. This is in accord with the bronchographic and histological evidence.

Several methods of assessing regional lung function are available. Bronchospirometry shows great reduction in oxygen uptake and a smaller reduction of tidal volume and vital capacity on the affected side (Belcher et al., 1959). This investigation was carried out under local anaesthesia in Case 1, the vital capacity being 41 per cent and the oxygen uptake 21 per cent of the total.

An isotopic method of studying ventilation has recently been introduced (Dyson et al., 1960). The patient takes a breath of air containing radio-active oxygen or carbon dioxide, simultaneous measurements of radio-activity being made over both lungs. The quantity of isotope entering the lungs, the rate of absorption during breath holding, and the speed of elimination when breathing starts again are measured. Several cases of Macleod’s Syndrome have been
studied by this method. In Case 3 reduced ventilation and absorption of radio-oxygen and carbon dioxide were found in the lower zone, but in the upper zone there appeared to be a compensatory increase in ventilation (Hugh-Jones, 1960).

Gas analysis and flow measurements have also been carried out at bronchoscopy using a continuously recording mass-spectrometer, and this method confirms the findings of other techniques.

Cardiac catheterisation has been carried out on only one case. A normal resting pulmonary arterial pressure was found, but on exercise or after occlusion of small branches passing to the normal side there was a marked rise in pulmonary arterial pressure (Elder et al., 1958). It is therefore likely that the pulmonary vascular resistance of the affected lung is increased. The delayed filling seen on angiograms is consistent with this view.

**Diagnosis and management**

Unilateral increase in transradiancy is not in itself a diagnosis and may be seen in a number of conditions. The differential diagnosis includes faults in centring the film and asymmetry of the chest wall and musculature. “Congenital lobar emphysema of infants” and the obstructive emphysema of partial bronchial obstruction produce similar radiographic appearances although the affected lung is usually increased and not reduced in size. A collapsed bronchiectatic segment may produce increased transradiancy in the surrounding lung, and finally congenital absence of a pulmonary artery may occur although this is rare (Madoff et al., 1952).

While a definite diagnosis should be made, the patient’s comfort must be considered. The following diagnostic criteria are therefore suggested:

1. Increased transradiancy in a region shown by tomography to be supplied by a small pulmonary artery.
2. Evidence of trapping on a forced expiration radiograph.
3. A bronchogram showing patency of the main bronchi without there being a collapsed segment or lobe.

Studies of regional lung function though invaluable in doubtful cases are not required routinely.

No curative treatment for this condition exists. Nevertheless the patients should be advised to stop smoking for there is a strong clinical impression that smoking aggravates the shortness of breath of many forms of chest disease. The nature of the condition should be explained to the patient, and the general practitioner should be told of the functional disability, as apparently trivial chest infections may become serious in patients with only one functioning lung. Patients are advised to report any new symptom immediately, and to select light rather than heavy work.

**SUMMARY**

Three new cases of Macleod’s Syndrome are described. The whole of the right lung was affected in two cases and the whole of the left lung in one.
Choriocarcinoma of the Uterus

The cause, natural history and investigation of the syndrome are discussed, and simple diagnostic criteria are suggested.

It is proposed that all patients should be told in simple terms of the nature of their disease.

My thanks are due to Lieut.-Colonel J. Mackay-Dick, O.B.E., for his encouragement) Dr. Lynne Reid for her information on the pathology of the condition, Dr. George Simon for the radiographic reports, Dr. P. Hugh-Jones, Dr. J. Smart and Dr. L. Capel for their help in the investigation and discussion of these patients, and to Dr. H. Midgley Turner for the follow-up of Case 2.

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Swyer, P. R., & James, C. W. (1953). Thorax, 8, 133.

CHORIOCARCINOMA OF THE UTERUS

BY


Royal Army Medical Corps
British Army of the Rhine

Choriocarcinoma is a rare condition, the incidence of which has been variously estimated as between one per cent (Novak, 1948) to sixteen per cent (Essen-Moller, 1912, quoted by Munro Kerr & Chassar Moir, 1949) of various series of hydatidiform mole follow-up investigations. But it must not be forgotten that the condition also occurs after abortion or normal pregnancy, indeed probably more commonly.

Way (1951) quoting Brews (1939) mentioned that of 24 cases at the London Hospital from 1885 to 1937 only 8 followed vesicular mole whilst 11 followed