prominent and distressing feature. The attack resembles closely that described by Baybutt (1959) in an infant who had received a first injection of gamma-globulin, but in that instance both parents had suffered from severe allergic disease.

Though the patient survived, the response to treatment was disappointing. Adrenaline, which was used perhaps in too small doses, had a very temporary effect on the asthma, and even large doses of antihistamine and steroids did not control the urticaria and vomiting for 48 hours.

My impression was that large doses of sodium phenobarbitone were more valuable than all the other measures, and, given the same situation again, I would use sedatives earlier.

Again in retrospect, the trial dose of tetanus antitoxin was too large, though it may be noted that the patient did not give a personal or family history of allergic disease. Parish, Laurent, and Moynihan (1957) suggest 0.2 ml. of a 1 in 10 dilution for subjects with a history of allergy, but a 1 in 100 dilution (with tenfold increments at intervals of half an hour) would be safer, though somewhat more tedious. The invalidism caused by serum sickness, the difficult decisions on whether to give tetanus antitoxin or not which face the casualty surgeon, and the occasional frightening reaction such as the present one, should give a stimulus to a bigger campaign of active immunization.

The considerable hazards of injecting tetanus antitoxin and the even greater risks of tetanus can both be eradicated by an all-out drive to increase active immunization. Personal records of all preventive inoculations—and of allergy, etc.—are very important.

Summary

A woman casualty officer developed urticarial swelling of the eyelids after giving tetanus antitoxin. Despite the absence of an allergic history, a test dose of 0.2 ml. of a 1 in 10 dilution of tetanus antitoxin precipitated a severe and prolonged allergic reaction. The asthma, urticaria, vomiting, and collapse lasted 48 hours, but subsided after adrenaline, antihistamines, and 1,900 mg. of hydrocortisone.

It is presumed that the patient was sensitized by tetanus antitoxin entering the conjunctival sacs. The intense reaction to a test dose of tetanus antitoxin confirmed the high degree of sensitivity which had developed. Such cases can be avoided only if a more vigorous active immunization campaign succeeds in making passive immunization unnecessary.

I wish to acknowledge the help given by Dr. Ivor Dunsford, of the Regional Blood Transfusion Centre, Sheffield, and the helpful comments and criticisms of Dr. H. J. Parish.

REFERENCES

- Baybutt, J. A. (1959). *J. Amer. med. Ass.*, **171**, 415.
Crawford, H., Cutbush, M., Falconer, H., and Mollison, P. L. (1952). *Lancet*, **2**, 219.
Laurent, L. J. M., and Parish, H. J. (1952). *Brit. med. J.*, **1**, 1294.
Moynihan, N. H. (1955). *Lancet*, **2**, 264.
Parish, H. J. (1958). *Antisera, Toxoids, Vaccines and Tuberculin in Prophylaxis and Treatment*, 4th ed. Livingstone, Edinburgh and London.
— Laurent, L. J. M., and Moynihan, N. H. (1957). *Brit. med. J.*, **1**, 639.

Plans are being made to build a new leprosarium in the Karonga district of Nyasaland's Northern Province, where 33 people out of every 1,000 living on the lake shore are lepers.

EFFECT OF OXYGEN THERAPY ON OEDEMA IN PATIENTS WITH COR PULMONALE

BY

P. EFFERSÖE, M.D.
Resident Medical Officer

H. SUND KRISTENSEN, M.D.
Research Assistant

AND

H. C. A. LASSEN, M.D.

Professor of Epidemiology in the University of Copenhagen
Blegdam Hospital, Copenhagen

Peripheral oedema attending cardiac decompensation in patients with pulmonary insufficiency is often more resistant to ordinary treatment with digitalis, low-salt diet, and diuretics than oedema in primary heart disease.

The cases reported below are examples of how oxygen therapy, in some instances combined with artificial ventilation, may eliminate oedema in such patients under circumstances where other causes of the elimination can be left out of account.

Case 1

A man aged 40 submitted to thoracoplasty years ago for pulmonary tuberculosis. He was admitted to hospital on August 29, 1956, with diffuse pulmonary fibrosis, pronounced pulmonary insufficiency, and cor pulmonale, but with no signs of bronchitis or active tuberculosis. Before admission he had had increasing dyspnoea and moderate oedema, which had been treated with aminophylline, digitalis, oxygen, and mercaptomerin, with no effect.

On admission the patient was cyanotic and severely dyspnoeic. The liver was palpable one handbreadth below the curvature, and there was moderate oedema. The temperature was 37–37.6° C., B.P. 125/80, pulse rate 100–120/min.; weight 89.2 kg. Administration of digitalis was continued, and 1–2 litres of oxygen per minute were given through a nasopharyngeal catheter most of the time. On September 3 the patient was confused, and analysis of the arterial blood showed: oxygen saturation, 92%; $p\text{CO}_2$, about 120 mm. Hg; pH, 7.21. The patient was therefore placed in a tank respirator with an intratank pressure of $-20/+7$ cm. of water at a rate of 20 per minute, and 1 litre of oxygen per minute was admitted through the catheter. During the oxygen-and-tank treatment the arterial blood showed: oxygen saturation, 93%; $p\text{CO}_2$, 90–80 mm. Hg; pH, 7.28. The treatment was discontinued on September 6 owing to melaena. The urine volume trebled (Fig. 1) during the first 24 hours of oxygen-plus-tank treatment (September

FIG. 1.—Case 1. Effect of oxygen therapy and tank ventilation on diuresis and body weight.

3). After four days the patient had lost 8 kg. and become free from oedema. During the period of treatment, as also during the weeks preceding this, he was given an ordinary mixed diet and a constant dose of digitalis, but no other therapy, more particularly no diuretics.

During repeated stays in hospital he several times obtained freedom from oedema in response to oxygen treatment in the tank respirator. A period of particularly thorough investigation is reported below.

The patient was readmitted on June 17, 1957, with extensive oedema but no signs of bronchitis. At home he had been given oxygen intermittently through nasal catheter, as well as mercaptopurine, digitalis, prednisone, and methylthiouracil, with no effect. In hospital, digitalis, prednisone, and methylthiouracil were administered in the previous dosages; and, in addition, the patient was submitted to moderate oxygen-and-respirator treatment. During the days before July 23 he received 2 l. of oxygen per minute through nasal catheter for an average of 14½ hours a day, during four hours of which he was in a tank respirator. Despite this his weight increased, being 84 kg. on July 23. From this date the oxygen-plus-tank treatment was therefore intensified. The patient now received oxygen for an average of 15½ hours a day, of which 8–10 hours were spent in a tank respirator with 5 l. of oxygen per minute, and the rest of the time 2 l. per minute. The arterial oxygen saturation was 66% during spontaneous respiration without oxygen and 89–92% with oxygen, while in the tank respirator with 5 l. of oxygen per minute it was 94–97%. After intensification of the oxygen-plus-tank treatment the sodium excretion in the urine increased twofold or threefold, and the patient lost 6 kg., his weight being 78.3 kg. on August 8 (Fig. 2). During the first few days of oxygen-plus-tank treatment the pCO_2 fell to 72–74 mm. Hg.

The patient died a few months later of pneumonia. Necropsy revealed pronounced cor pulmonale, congestion of the liver, emphysema, oedema, and pulmonary infarcts.

Comment.—In an oedematous patient with chronic pulmonary insufficiency due to sequels of previous

tuberculosis and thoracoplasty intense treatment with oxygen and tank respirator was three times immediately followed by elimination of the oedema. This could be attributed to no other therapeutic factors.

Case 2

A woman aged 38, with pronounced kyphoscoliosis since childhood, was admitted to hospital on June 2, 1958, owing to increasing dyspnoea, with appreciable pulmonary insufficiency (Table I), pronounced jugular stasis, but

TABLE I.—Arterial Blood Examinations in Case 2

Date	Oxygen Therapy (l./min.)	Arterial Oxygen Saturation (%)	Arterial pCO_2 (mm.Hg)	Arterial pH
June 6 ..	0	63	42	7.44
.. 14 ..	0	67	62	7.36
.. 16 ..	2	72	46	7.43
.. 16 ..	4	92	62	7.34
.. 17 ..	4	94	74	7.32
.. 24 ..	4	86	84	7.30
.. 25 ..	0	60	56	7.46

without oedema, bronchitis, or pneumonia. B.P. normal; pulse rate about 100; temperature just over 38° C., but returning to normal during the first week. She was given oxygen intermittently the first four days, using a nasal catheter.

On account of increasing oedema she again received oxygen from June 12 to June 16, in doses of 2 l. per minute, this time 16½–18 hours a day. As her weight increased in spite of this, being 53 kg. on June 16 (Fig. 3), the oxygen treatment was intensified to 4 l. per minute. Three days later the patient excreted increased amounts of sodium and carbon dioxide with the urine (Fig. 3). The urine volume increased, and the weight dropped to 50 kg. Reduction of the oxygen treatment to 10–12 hours a day resulted in prompt redevelopment of oedema and a corresponding increase in weight. During the entire period she received a diet containing almost constant amounts of salt and fluid.

The patient died later, and necropsy revealed leathery pulmonary atelectasis in the lower lobes of both lungs. No pneumonia or infarcts were detectable.

Comment.—In a patient with chronic pulmonary insufficiency and increasing oedema the latter subsided after intense oxygen therapy, even though the pCO_2 increased and the pH fell during this treatment.

Case 3

A woman aged 52, with severe pulmonary insufficiency (see Table II) due to emphysema and pulmonary fibrosis, but no acute pulmonary disease, was transferred on December 10, 1958, from another hospital. The previous day she had received 300,000 units of penicillin twice and 500 mg. of chlorothiazide because of moderate oedema. The first two days her pulse rate was 100–120 with a few extrasystoles, and her temperature was slightly raised; but the temperature then returned to normal and the pulse rate fell to 80–90 without extrasystoles.

We continued with a low-salt diet and confinement to bed, but gave no other treatment—more particularly, no digitalis, oxygen, or diuretics. On December 16 the condition was thought to have become stationary, and oxygen treatment through a nasopharyngeal catheter was therefore started, at first with 1 l. per minute. The dose was increased gradually to 2.5 l. per minute.

Spontaneous Resp.	oxygen saturation	66	82
	pCO_2	82	68
	pH	7.33	7.30
Tank	oxygen saturation	89 92	98
	pCO_2	82 81	80
	pH	7.32 7.33	7.32
Tank	oxygen saturation	94	96
	pCO_2	74	72
	pH	7.38	7.42
Serum Sodium mEq./l.		142 138	140
			134

FIG. 2.—Case 1. Effect of oxygen therapy and tank ventilation on arterial blood values, diuresis, sodium excretion, and body weight.

On December 18 transitory auricular fibrillation occurred with 4:1 block, and on December 21 there were again transitory extrasystoles. The pulse rate remained unchanged.

The urine volume increased somewhat during the first few days of oxygen treatment, but a pronounced increase of the electrolyte excretion was first noticed after five to six days of treatment (Fig. 4). The oedema disappeared completely, and the patient lost 5 kg. (Fig. 4). She was later discharged in an improved state.

TABLE II.—Blood Examinations in Case 3

Date	Oxygen Therapy (l./min.)	Arterial Oxygen Saturation (%)	Arterial pCO ₂ (mm.Hg)	Arterial pH	Serum Na (mEq/L)
Dec. 16 ..	0	65	41	7.42	125
" 17 ..	1	77	44	7.42	
" 18 ..	1½	82	47	7.48	134
" 19 ..	2	83	58	7.38	
" 24 ..	2½	92	43	7.34	137
Jan. 7 ..	0	83	46	7.41	

Comments.—A patient with chronic pulmonary insufficiency and increasing oedema, which disappeared under intense oxygen therapy, even though the pCO₂ of the arterial blood increased and the pH fell.

In this patient, who had a low serum sodium concentration, the urine volume increased in the course

of the first three days of treatment, whereas a rise of the electrolyte excretion was first noticed on the sixth day.

Discussion

Elimination of oedema during oxygen treatment of patients with cardiac oedema has been described (Barach and Richards, 1931; Richards and Barach, 1934). 12 out of 19 such patients developed increased diuresis during treatment in an oxygen chamber with 40–50% oxygen. Among these 19 patients, one with cor pulmonale responded twice by elimination of oedema. The diuresis usually started after two to six days of treatment. The oxygen treatment was found to give not only an increased oxygen saturation of the arterial blood but also an increased carbon-dioxide content in the blood. The conditions presented by Cases 2 and 3 are in close accordance with these observations.

Possible Explanations of the Effect of Oxygen on Oedema

Oxygen treatment of patients with decompensated cor pulmonale tends to normalize the abnormally low oxygen tensions in (a) alveoli, (b) arterial blood, (c) tissue, and (d) venous blood. The response of the oedema to

FIG. 3.—Case 2. Effect of oxygen therapy on body weight, diuresis, and urinary excretion of sodium, chloride, total CO₂, and urinary pH.

FIG. 4.—Case 3. Effect of oxygen therapy on body weight, diuresis, and urinary excretion of sodium, chloride, total CO₂, and urinary pH.

oxygen therapy must depend somehow or other on this tendency.

Oxygen Tension in Alveoli and Arterial Blood.—Patients with cardiac decompensation due to heart diseases other than cor pulmonale usually have normal or only slightly reduced alveolar and arterial oxygen tensions (Moltke and Worning, 1958). Accordingly, formation of oedema in these patients is not caused by a reduced oxygen tension in the alveoli and the arteries. If we take the mechanism of oedema formation to be the same in cor pulmonale as in other heart diseases, reduced alveolar and arterial oxygen tensions cannot be factors of decisive importance in the formation of oedema. Oxygen therapy is therefore rather unlikely to act via the oxygen tension in the alveoli and the arterial blood.

Oxygen Tension in the Tissues.—A reduced oxygen tension in the tissues is a feature that is common to all patients with cardiac oedema (Altschule, 1949). Tissue hypoxia may therefore be conceived to condition oedema formation in patients with cor pulmonale as well as in patients with other heart diseases. Oxygen may then be supposed to act by removing this condition. The question now arises how and from which tissues such an effect of oxygen therapy on the oedema is released.

1. The mechanism regulating respiration is greatly influenced by the oxygen tension. As we have seen elimination of oedema in association with both a rise (spontaneous respiration) and a fall (tank ventilation) of the carbon-dioxide tension and the hydrogen-ion concentration, the elimination is unlikely to be due to changes in $p\text{CO}_2$ and $p\text{H}$.

2. The blood circulation is likewise influenced by the oxygen tension. Case *et al.* (1955), in experiments on anaemic dogs, showed that a rise of the haemoglobin level in the coronary arteries causes the heart to perform the same work at a lower atrial pressure. If in our patients the myocardium was not optimally supplied with oxygen before the oxygen treatment, the latter might be accompanied by a fall of the pressure in the right atrium, even if the work of the myocardium remained unchanged. However, the work of the myocardium decreases when hypoxic patients with pulmonary insufficiency receive oxygen therapy, because this will reduce the raised pressure in the pulmonary artery, as well as the increased cardiac output, and the increased heart rate (Wilson *et al.*, 1955). If the capillary pressure varies parallel with the pressure in the right atrium, this might account for the elimination of oedema.

3. A better oxygen supply to the liver may normalize a decreased elimination of electrolyte- and fluid-retaining hormones (Chart *et al.*, 1956).

4. There is no evidence to suggest that a tendency towards normalization of the oxygen tension in the kidneys may cause elimination of oedema. On the contrary, Berger *et al.* (1949) found that hypoxia in normals was attended by an increased excretion of fluid and electrolytes; Fishman *et al.* (1951) observed—in short-period trials, it is true—that oxygen therapy to patients with hypoxia gave a reduced excretion of sodium.

5. Further, there is a possibility that receptors exist—for example, in the brain or the suprarenals—which are influenced by the oxygen tension, and which regulate the volume of the organism through the excretion of electrolytes and fluid by the kidneys—for example, on a hormonal basis.

Oxygen Tension in Venous Blood.—Oxygen tension receptors possibly exist in the central veins or in the pulmonary artery to regulate the fluid and electrolyte balance, as stated above, though such have never been demonstrated.

Does Treatment in Tank Respirator Effect Elimination of Oedema?

In Case 1 the oxygen saturation during the second period of oxygen-and-tank respirator treatment was only slightly higher than during spontaneous respiration with administration of oxygen. The question must therefore be considered whether the respirator treatment may alone have caused elimination of the oedema.

As stated above, the elimination of oedema is unlikely to be due to changes in carbon-dioxide tension and the hydrogen-ion concentration.

A probable explanation is that the respirator performs the rather straining work of respiration otherwise to be managed by the patient himself, thus improving the oxygen supply to the tissues.

The pressure variations to which our patient is exposed during artificial tank ventilation cause a higher mean pressure in the thorax compared with the rest of the body, a fact which has certain effects on the circulation: less filling of the thoracic portions of the vascular bed and a diminished cardiac output (Werkö, 1947; Motley *et al.*, 1948; Whittenberger and Sarnoff, 1950). This cannot explain the elimination of oedema, since Drury *et al.* (1947) have shown that an increase of the mean thoracic pressure is followed by a decrease of diuresis.

The number of respirations per minute was very nearly the same during treatment in the tank as while the patient was breathing spontaneously. Pressure variations in the thorax during the respiratory cycle were not measured. These would probably have been found to be greater in the tank than outside it. This might—via pressure-sensitive receptors in the thorax (Love *et al.*, 1957)—account for an increase of diuresis while the patient was in the tank respirator.

Conclusion and Summary

Oxygen therapy resulted in elimination of oedema in two patients with decompensated cor pulmonale.

In another patient with the same disease oxygen therapy and tank-respirator treatment was three times followed by elimination of oedema.

In all three patients the oedema was eliminated under conditions where other causes could probably be left out of account.

The possible explanation of these observations is discussed.

It is supposed that tissue hypoxia conditions the formation of cardiac oedema, and the oxygen therapy acts by removing this. We do not know how and from which tissues the oxygen tension exerts its influence on the fluid and electrolyte balance.

Respirator treatment alone may cause elimination of oedema. If so, this might be due to the respirator performing the work of respiration otherwise to be managed by the patient himself, thus reducing the oxygen consumption of the organism and consequently raising the oxygen tension of the tissues. Another possibility which must be taken into account is that increased pressure variations in the thorax during tank respiration might possibly influence the urinary output through the medium of pressure-sensitive receptors in the thorax.

REFERENCES

- Altschule, M. D. (1949). *Physiology in Diseases of the Heart and Lungs*. Harvard Univ. Press, Cambridge, Mass.
- Barach, A. L., and Richards, D. W., jun. (1931). *Arch. intern. Med.*, **48**, 325.
- Berger, E. Y., Galdston, M., and Horwitz, S. A. (1949). *J. clin. Invest.*, **28**, 648.
- Case, R. B., Berglund, E., and Sarnoff, S. J. (1955). *Amer. J. Med.*, **18**, 397.
- Chart, J. J., Gordon, E. S., Helmer, P., and Le Sher, M. (1956). *J. clin. Invest.*, **35**, 254.
- Drury, D. R., Henry, J. P., and Goodman, J. (1947). *Ibid.*, **26**, 945.
- Fishman, A. P., Maxwell, M. H., Crowder, C. H., and Morales, P. (1951). *Circulation*, **3**, 703.
- Love, A. H. G., Roddie, R. A., Rosensweig, J., and Shanks, R. G. (1957). *Clin. Sci.*, **16**, 281.
- Moltke, E., and Worning, H. (1958). *Acta med. scand.*, **160**, 397.
- Motley, H. L., Cournand, A., Werkö, L., Dresdale, D. T., Himmelstein, A., and Richards, D. W., jun. (1948). *J. Amer. med. Ass.*, **137**, 370.
- Richards, D. W., jun., and Barach, A. L. (1934). *Quart. J. Med.*, **27**, 437.
- Werkö, L. (1947). *Acta med. scand.*, suppl. 193.
- Whittenberger, J. L., and Sarnoff, S. J. (1950). *Med. Clin. N. Amer.*, **34**, 1335.
- Wilson, R. H., Hoseth, W., and Dempsey, M. E. (1955). *Ann. intern. Med.*, **42**, 629.

POLYMYOSITIS

REPORT ON THREE CASES FROM WEST AFRICA

BY

B. G. BARNARD, M.R.C.P.

A. M. RANKIN, M.R.C.P., M.R.A.C.P., D.T.M.&H.

Senior Registrars, Department of Medicine, University
College Hospital, Ibadan

AND

J. H. ROBERTSON, M.D.

Registrar, Department of Pathology, University
College Hospital, Ibadan

The term "polymyositis" was first introduced by Wagner (1863) when he reported a case of acute generalized muscular affection with skin involvement which ended fatally within six days. Potain (1875) described a similar case in which the illness was less acute but which terminated fatally as a result of bronchopneumonia four to five months after the onset of the disease. Hepp (1887) gave a detailed account of the clinical features of a similar disorder, which he called pseudotrichinosis, and, while there were no skin lesions, the picture was that of a subacute polymyositis. Unverricht (1877) stressed the almost invariable occurrence of skin lesions in these cases, and therefore applied the name dermatomyositis to the condition. Subsequently he described the pattern of muscular involvement and pointed out that not all cases were fatal (Unverricht, 1891).

The first reported cases of this disease from Great Britain came from Gowers (1899) and Batten (1899), and though changes occurred in both skin and muscle in their patients they still used the term polymyositis to describe the condition. Oppenheim (1899, 1903) drew attention to the occasional involvement of mucous membrane and both ocular and cardiac muscle. He pointed out that the skin lesions could be sclero-dermatous in character. Petges and Cléjat (1906) also stressed the extreme degree of atrophy and sclerosis of the skin (poikiloderma) that could occur, and described a chronic form of the disease.

It would appear from the above that much uncertainty has existed in the past about the relationship between dermatomyositis and other diseases of muscle without skin lesions, and only recently has it become established that dermatomyositis can occur without recognizable skin lesions. It is the purpose of this paper to describe three such cases, which represented clinically the acute, the subacute, and the chronic stages of the disease. All three cases occurred in Africans and are thought to be unique, as a review of the literature has shown that, apart from a single case in a Eurasian from South Africa (Sament and Klugman, 1957), the condition has so far not been reported in an African from this continent.

Case 1

A girl aged 16 was admitted to hospital with a five-days history of swelling and slight weakness of her arms and legs associated with pain on movement. The day after the onset of these symptoms she experienced some difficulty in swallowing, and this was followed the next day by the development of a nasal intonation to her voice.

At the time of examination her temperature was 100° F. (37.8° C.), and a striking clinical feature was swelling which involved particularly the arms and to a less extent the legs. The swelling in the upper limbs was confined to the forearms, while, in the lower limbs, the calves were mainly affected and the thighs only slightly so. The soft palate moved poorly but was otherwise normal, the gag reflex was elicited with difficulty, and water dripped from the patient's nose when drinking. A thorough and systematic examination of the central nervous system did not reveal the presence of any abnormalities, and the other systems were also normal.

In view of the findings on admission a tentative diagnosis of polymyositis was made, and this was later confirmed histologically.

Routine investigations were all normal, except Hb, 8.6 g./100 ml.

A biopsy specimen taken from the extensor muscles of the left forearm showed groups of muscle cells to be swollen, with intensely eosinophilic cytoplasm and a loss of their transverse striations and sarcolemma nuclei. The degeneration was patchy and was associated with a slight inflammatory infiltration composed mainly of lymphocytes and plasma cells.

As the patient was not acutely ill on admission, no specific therapy was given, pending the muscle-biopsy report. A week after admission, however, her temperature began to rise, the swelling of the arms increased, and the difficulty experienced in swallowing was greater. Assuming that the diagnosis was correct, prednisolone, 20 mg. eight-hourly, along with tetracycline, 250 mg. six-hourly, was given, the latter drug for controlling the bronchopneumonia which had developed. In addition, a Ryle tube was passed and intragastric feeding begun. In spite of these measures she steadily deteriorated, and finally died from extensive bronchopneumonia 16 days after admission.

Post-mortem Findings

The body was that of a well-nourished young female. The subcutaneous tissues of the arms and legs were the seat of a gelatinous oedema which was especially marked in the forearms. The underlying muscle was pale. Recent adhesions were present in both pleural cavities, and on the left side there was about half a pint (280 ml.) of straw-coloured effusion. Examination of the viscera showed extensive bronchopneumonic consolidation of the lower lobes of both lungs. The liver was the seat of a moderate degree of fatty infiltration and the spleen was enlarged, weighing 215 g. No other abnormal findings were observed macroscopically, and urine taken from the bladder showed no evidence of myoglobin on spectroscopic examination.