

returned to normal as judged by cine-radiographic recording of a barium swallow. The cuffed tube was then removed from her trachea and replaced by a silver tube for a few days. This was then removed. The tracheostomy did not close spontaneously, and a plastic closure was carried out on Jan. 27. At the time of her return home, the patient felt well, but still had myopathic facial weakness and considerable weakness of her pelvic girdle muscles.

Biopsy

In the early stages of the illness no diagnosis was made, but, as it evolved, the development of widespread muscular wasting and weakness with firm tender muscles raised the possibility of polymyositis. This diagnosis was clinched by biopsy of the left deltoid on Aug. 23, 1960. The report of the histological appearance was as follows: "There is connective tissue increase in the interstitial spaces, the vessels of which are surrounded by an inflammatory exudate. The latter is mainly composed of large mononuclear cells, with indented nuclei. Near the exudate, the muscle-fibres show advanced necrosis with phagocytosis. These changes can be found also in scattered muscle-fibres some of which show features suggestive of regeneration."

Discussion

When, by the end of July, 1960, the clinical picture had developed fully, this patient's condition conformed very closely to the classical descriptions of polymyositis. There was a story of subcutaneous oedema with transient arthralgia, and the subacute development of widespread weakness involving the facial, pharyngeal, and limb muscles. Muscle wasting was more pronounced around the limb-girdles than in the distal segments of the limbs. This distribution is highly characteristic, and has led in the past to confusion of this condition with muscular dystrophy, although the rate of progression of the muscular disorder in most cases of polymyositis suggested to some workers that they were dealing with a different disease. Its recognition as a nosological entity was delayed by the rigid views held about dermatomyositis. An acute or subacute muscular disorder without a coexistent rash was considered to be in a different category. The association of dermatomyositis with malignant disease was held to be very common, and the diagnosis was made reluctantly in the absence of evidence of neoplasia. Muscle biopsy and electromyography have led to the recognition of polymyositis in patients without neoplasms, skin lesions, or even muscle pain and tenderness: some patients have no constitutional symptoms either. These cases may be difficult to distinguish from muscular dystrophy (Walton and Adams 1958).

Siekert and Fleisher (1956) and Pearson (1957) reported raised levels of serum-glutamic-oxaloacetic-transaminase in patients with polymyositis. The level in our patient was not estimated until Oct. 4, 1960, when it was within normal limits (18 units per ml.). At this stage there was no clinical evidence of progression of the disease, and the estimation may have been made too late in its natural history. The level is likely to be high only while muscle necrosis is continuing.

Death in patients with polymyositis is not invariably due to this disease. In the group associated with neoplasms, death may be caused by the progression of the malignant disease. In the group of 40 patients reported by Walton and Adams (1958), there were 13 deaths during the period of observation: 7 of these were due to polymyositis and, of these, 5 were due to respiratory complications. These are a common cause of death (accounting for up to 50% of deaths in patients with severe dermatomyositis) and often they are associated

with pharyngeal paralysis which leads to aspiration of oropharyngeal secretions into the lungs. Although polymyositis—particularly the acute and subacute varieties—is a disease of relapses and remissions (Garcin 1955), most patients who are alive a year after the onset are out of danger (Sheard 1951). Consequently, it is vital to attempt to tide the patient over relapses. The most dangerous single complication is pharyngeal paralysis, which may be followed by fatal aspiration pneumonia.

The patient who cannot swallow should not be nursed either sitting or supine: he must be semiprone or prone. If the dysphagia seems likely to persist for some time the airway should be protected by tracheostomy and insertion of a cuffed tracheostomy tube. It is then possible to assist respiration by intermittent positive pressure if spontaneous respiration fails.

We have been unable to find a report of the successful use of tracheostomy and I.P.P.R. in a patient with pharyngeal paralysis and respiratory failure due to polymyositis. This technique was obviously life-saving in our patient. The patient's disease is now in remission, but we do not know how long this will last. Remissions of nine (Weinberger 1933) and nineteen (Wedgwood et al. 1953) years have been reported. The disease can be regarded as controlled but not as cured.

Summary

Successful tracheostomy with intermittent positive-pressure artificial respiration in a patient with pharyngeal palsy and respiratory failure due to polymyositis is reported.

Respiratory failure was due to a combination of aspiration pneumonia and weakness of abdominal and intercostal muscles.

Protection of the airway by a cuffed tracheostomy tube, and adequate ventilation by a Radcliffe respirator, maintained life while antibiotics and physiotherapy combated the pneumonia and until the polymyositis remitted.

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REFERENCES

- Garcin, R. (1955) *Rev. neurol.* **92**, 465.
 Pearson, C. (1957) *New Engl. J. Med.* **256**, 1069.
 Potain (1875) *Bull. Soc. méd. Hôp. Paris*, **12**, 314.
 Sheard, C. (1951) *Arch. intern.* **88**, 640.
 Siekert, R. G., Fleisher, G. A. (1956) *Proc. Mayo Clin.* **31**, 459.
 Walton, J. N., Adams, R. D. (1958) Polymyositis. Edinburgh.
 Wedgwood, R. J. P., Cook, C. D., Cohen, J. (1953) *Pediatrics*, **12**, 447.
 Weinberger, M. (1933) *Wien. med. Wschr.* **83**, 100.

THE ACTION OF CHORIONIC GONADOTROPHIN IN THE OBESE

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IN 1954 Simeons described the fat-mobilising powers of chorionic gonadotrophin derived from human pregnancy urine (C.G.). With daily injections of 125 units, patients were able to tolerate a 500-calorie diet for six weeks, during which time they lost an average of 20–30 lb. Simeons thought that C.G. led to the dispersal of fat away from the more favoured sites and that "fat in transit" might be more readily available for metabolic purposes than fat in "fixed deposit". He later elaborated this thesis (Simeons 1960); and Lebon (1961), using a similar technique, obtained equally successful results in obese patients.

RESULTS OF THE TWO TRIALS

| Trial | Treatment | No. of patients | | | | Average for patients completing trial | | | | | | | | |
|-------|--------------------------|-----------------|---|------------------|---|---------------------------------------|-----------------------|-------------------------------|-----|-----|-----|-----|-----|--|
| | | Starting trial | | Completing trial | | Age | Starting weight (lb.) | Weight loss (lb.) in week no. | | | | | | Total weight loss (lb.) |
| | | M | F | M | F | | | 1 | 2 | 3 | 4 | 5 | 6 | |
| I | Diet + c.g. injections | 4 | 9 | 4 | 8 | 39 | 182 | 5.5 | 3.6 | 3.6 | 3.3 | 2.4 | 2.6 | 21.0 (14-31 ³ / ₄)* |
| | Diet + saline injections | 4 | 8 | 4 | 6 | 40 | 185 | 5.2 | 3.3 | 2.9 | 2.6 | 2.8 | 2.2 | 19.0 (9-27 ¹ / ₄)* |
| II | Diet + saline injections | 2 | 9 | 1 | 7 | 34 | 183† | 7.2 | 4.0 | 3.6 | 1.8 | 3.1 | 2.7 | 22.4 (14-27)* |
| | Diet alone | 2 | 8 | 1 | 6 | 39 | 156† | 5.6 | 2.6 | 3.3 | 1.0 | 2.4 | 2.4 | 17.7 (13 ¹ / ₂ -20 ¹ / ₂)* |

* Range of weight loss.

† Average starting weights were 178 lb. and 173 lb. for these groups respectively. Patients failing to complete the course were lighter than average in the first group and heavier than average in the group on diet alone, and this led to the larger difference in average starting weight for patients completing the trial. Analysis of the individual results showed that there was no relationship between starting weight and total weight loss.

In 1959 I began to use this treatment in my practice and obtained results comparable to Simeons'. Over 150 patients have since begun the course, in addition to the 46 referred to in this paper. Some, as always in these cases, defaulted from treatment, while others, though attending daily for their injection, did not keep to the rigid diet I had prescribed (based on Simeons' diet) and did not lose as much weight as those who did. Several patients returned for second, third, and even fourth courses of six weeks' treatment. Some came back because they did not lose enough the first time, others because they had too much fat to lose at one go and their loss, though adequate during each six-week course was not enough to bring them to a reasonable weight. Many have lost (in two or three courses) 4 and even 5 stones; 3 stones in two courses was not uncommon. Few of these patients have returned to their obese state. Others have returned for second and third courses because they had—over six months or a year—replaced all or most of the lost weight, and had found that the injections enabled them to lose weight where other methods had failed.

The Trials

From what my patients told me it was clear that rigid maintenance of the 500-calorie diet was essential if they were to lose anything like 20 lb. in six weeks. On the other hand, I wanted to know just what part the injections of chorionic gonadotrophin played in this treatment. Two trials were carried out.

In the first, two groups of patients were given either c.g. as described by Simeons or saline control. Both substances were presented to me in identical vials as a powder to be reconstituted (in the identical way Parke Davis present their chorionic gonadotrophin 'Antuitrin S'). The vials were numbered in random order. I did not know which contained c.g. and which NaCl until the trial was over. One vial of powder made up with 10 ml. solvent (the same solvent for drug and control) lasted one patient one full course of six weeks: they had 0.25 ml. daily for six days each week. In no case was a vial prepared for one patient and used for another.

In the second trial patients were selected from a random code either to undergo the diet plus the daily injections of saline or the diet alone. As each new patient presented, one of a series of numbered and sealed envelopes was opened. A card inside indicated to which group the case has been allotted.

I was thus able to compare the effects of c.g. on weight reduction with those of an inert control substance; and secondly, I assessed the value of a daily injection of the inert substance.

The results of both trials have been condensed into the table. In each week of the first trial, except the fifth, the average weight loss was slightly more in the group having the c.g.

than in the group injected with saline. These differences were not significant at the 5% level.

In each week of the second trial the average weight loss was more in the group having injections of saline, but these differences were not significant at the 5% level. However the difference in average total weight loss in this trial was significant ($0.01 < P < 0.02$).

Discussion

The main point which emerges is that the stimulus of a daily injection helps the patient to lose weight. Why is this so? We must look at the facts a little more closely. In the second trial there was a further difference between the two groups. Those for injection not only had to come to my surgery six days every week, but they were also weighed by me on my scales every day. Failure to lose weight from one day to the next or even worse, the slightest gain in weight, led to a careful review by me of their previous day's diet. As one patient (a school-mistress) said to me: "You know, Doctor, every time I look at a piece of food I think of what is going to happen when I get on your scales tomorrow morning." On the other hand, those on the diet alone had only to report to me twice a week to be weighed. We might presume that when they were tempted by food they may have said to themselves: "Never mind if I do eat it, I can always make up for it in the next couple of days."

It would be a boon to those who are overweight to have some drug that would enable them to lose weight safely without having to fight their appetite urges. c.g. is not an answer, nor does it seem appreciably to increase their weight loss if they do adhere to a very rigid 500-calorie diet. On the other hand, those on the diet alone constantly complained of feeling tired or weak. The patients on either c.g. or the inert placebo were keen to tell me how much benefit they got from the injections and how previously they had failed to keep to any diet they had tried (for obesity is usually a chronic disease and we rarely see a patient who has not tried other methods of shedding their excess weight).

One advantage of assessing such a therapy in general practice is that most of our patients come back to us, both successes and failures. We do not need to send for them for follow-up for sooner or later they return, even if it is only to have their passport signed before going on holiday or to accompany their children when they have their polio booster vaccination. This method, a 500-calorie diet supported by a daily injection, not only causes the patient to lose quite a bit of surplus fat rapidly (a psychological asset in any treatment is rapid success) but it also appears to help them re-educate their eating habits for

they rarely regain all their lost weight. Some continue to lose a little and then stabilise themselves; the majority, after losing 20 lb. or so, put back about 5 lb. and stay there for up to a year.

Over the two years I have used this method I have also noticed that the weight loss was most satisfactory in those who managed to attend my "group session". Sitting in the waiting-room at 8.30 each morning they would compare notes. As each patient returned to the waiting-room from my surgery after being weighed and injected the others would eagerly ask for a progress report (or so my receptionist told me). New arrivals to the group would be encouraged by those already faring well. Fortunately those who fell by the way did not come back to heckle!

The treatment therefore seems to have some value and I now use injections of saline with good results. The weight loss from a 500-calorie diet maintained for six weeks is sufficiently high to act as its own testimonial for this treatment. Alas, it is difficult to persuade a patient to adhere to the diet without some stimulus. It would not be safe to restrict the diet for much longer than six weeks at a time because essential food items can easily be overlooked.

Summary

(1) Kept on a 500-calorie diet for six weeks, patients lose approximately 20 lb. in weight.

(2) In a double-blind trial, patients given daily injections of chorionic gonadotrophin lost slightly more weight than patients given a daily injection of saline. This difference was not significant at the 5% level.

(3) In a second trial patients weighed daily and given daily injections of saline lost significantly more weight than those weighed only twice a week and given no injections.

(4) Patients weighed daily under supervision seemed to find it easier to adhere to a strict diet.

I wish to thank Mr. G. T. Nelson, of Parke, Davis & Co., for supplies of 'Antuitrin S' and control material.

REFERENCES

- Lebon, P. (1961) *Lancet*, ii, 268.
Simeons, A. T. W. (1954) *ibid.* ii, 946.
— (1960) *Man's Presumptuous Brain*. London.

STAPHYLOCOCCAL SEPTICÆMIA

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IN the early stages of acute fulminating staphylococcal septicæmia, toxæmia may kill the patient before antibiotics become effective. Urgent measures are necessary and the administration of staphylococcal antitoxin may be lifesaving; the time gained gives antibiotics a chance to eliminate the infection. When, despite antibiotics, the response is inadequate, the administration of human γ -globulins may prove beneficial. The following case illustrates the value of combining these three therapeutic agents.

Case-report

A 16-year-old boy was admitted to the Western Infirmary, Glasgow, on Sept. 28, 1959. He had previously been fit, but two weeks before admission had received a mild injury to the left hip during a game of rugby.

On admission he was grossly dehydrated, breathless, and restless. There were tender erythematous patches on his forearms. He had widespread muscle stiffness, abdominal tenderness, and gross meteorism. His temperature was 102.4°F, pulse-rate 120 per minute, and respiratory rate 45 per minute.

Septicæmia was diagnosed, and a blood-culture was taken. Electrolyte and fluid disturbances were corrected. Pending the

result of blood-culture, intramuscular penicillin 500,000 units 6-hourly was given. Despite this, the patient remained critically ill and was not expected to survive. He was restless and completely disorientated, with a continuous tachypnœa of 40–50 per minute. X-rays of the injured hip showed no abnormality. For a short time during the day after admission his blood-pressure became unrecordable and his pulse barely perceptible. Both forearms, the abdominal wall, and the left leg were œdematous. The limb muscles were very tender. Serum-enzyme estimations indicated severe tissue damage (aldolase 33.2 Bruns units, glutamic oxalacetic transaminase 150 Frankel units, and glutamic pyruvic transaminase 90 Frankel units). On the second day after admission the total-serum-globulin level was 1.05 g. per 100 ml. and electrophoresis revealed a distinct decrease in the concentration of the β and γ fractions.

On the morning after admission, the blood-culture showed a coagulase positive *Staphylococcus aureus*. Penicillin was continued for a further 24 hours. It was then reported that the organism was resistant to 0.5 units in the test medium and was a penicillinase producer. (Subsequently the organism proved untypable by the standard phages.) Penicillin was then replaced by chloramphenicol and erythromycin, to which the organism was sensitive in vitro. This, however, produced no clinical response, and three blood-cultures taken while the patient was on these antibiotics were positive.

On the 3rd and again on the 4th day 20,000 units of staphylococcal antitoxin was given. This produced a dramatic improvement but the improvement lasted only one day.

In view of the lack of response to chloramphenicol and erythromycin it was decided, on the 4th day, to recommence penicillin but at a much higher dosage of 36,000,000 units a day, in the hope that this might swamp the penicillinase production of the organism. (For the 1st week the penicillin was given by continuous intravenous drip, thereafter 6,000,000 units was injected 4-hourly intramuscularly.) Also on the 4th day, 1.5 g. of human γ -globulins was given intravenously followed by a further 1.0 g. on the 6th day.

Within 24 hours of starting the high dosage of penicillin and giving the first dose of γ -globulins a remarkable change took place. The patient's pulse, respiratory rate, and temperature fell to 110, 38, and 99.6°F respectively. He lost his mental confusion and for the first time looked as though he could survive.

The improvement continued; and, after 26 days, penicillin was withdrawn; the serum- γ -globulins became normal. In the 6th week after admission X-rays of the pelvis and hips showed clear evidence of septic necrosis of the left sacroiliac joint. Whether this arthritis was primary or secondary will remain in doubt; in either event the process must have been slow, possibly because of treatment. The patient was discharged from hospital after nine weeks when he was clinically well, although healing of the sacroiliac arthritis was not observed for a further 9 weeks.

Discussion

It is difficult to assess the contribution of each of the three therapeutic agents—i.e., staphylococcal antitoxin, γ -globulins, and antibiotics—used in the present case. The therapy was solely dictated by the patient's critical condition and the need for rapid improvement.

There can be no doubt that staphylococcal antitoxin had a beneficial effect in the early stage when the patient appeared to be moribund, and that this allowed time to be gained for subsequent measures. The effect, though short-lived, sufficed to tide the patient over. The results are in keeping with those of Blair (1958) and of Parish and Cannon (1960).

There is ample evidence of the value of giving globulins or combining them with antibiotics (Harris and Schick 1954, Knouf 1957, Fisher and Manning 1957a, Waisbren 1957), especially in a patient with low γ -globulins. Whether γ -globulins act by supplying natural antibodies or in a non-specific way is uncertain; but Fisher and