FIG. 5.—Case 9. Comparison between a single dose of P.Z.I. and the same dose of lente insulin given on two occasions. Note the regularity of action of lente insulin.

blood-sugar determinations were made before breakfast, at noon, at 6 p.m., and at 9 p.m.; the patient was then changed over to a single dose of lente insulin, given before breakfast, and equal in amount to the total quantity of insulin required to stabilize the diabetes. When the patient had been on lente insulin for not less than two days the blood-sugar estimations were repeated at the same times and the results plotted in the form of graphs (Figs. 1 to 5). In addition to blood-sugar determinations, seven daily urine sugar tests were made at informative times. In two cases the blood-sugar estimations on lente insulin were repeated in order to see whether consistent results could be obtained with this insulin.

Results

In six cases comparison was made with mixed doses of S.I. and P.Z.I., the total dose varying from 36 to 60 units. In two cases the patients were previously stabilized on 68 and 76 units of S.I. respectively, given in divided doses, before breakfast and the evening meal. Two cases received single injections of 52 units of P.Z.I. and one of 28 units of globin. It will be seen that in all 11 cases lente insulin produced fasting blood sugars of the same order as those obtained with the other insulin preparations, the figures varying between 70 and 200, being 150 or less in eight. At noon lente produced a degree of control as good as, or better than, that obtained with the other insulins in all but two cases. At 6 p.m. the blood sugar on lente was comparable with but tended to be slightly higher than that produced by the other insulins, but at 9 p.m. the reverse was seen to be the case in most instances (see Table).

Comparison of Blood Sugars in the Six Cases Not Shown in Figs. 1 to 5

Case No.	Insulin	Blood Sugar in mg/100 ml.			
		8 a.m.	Noon	6 p.m.	9 p.m.
3	44 S.I.+16 P.Z.I.	165	260	140	118
	60 Lente ..	200	375	260	255
4	20 S.I.+16 P.Z.I.	168	238	95	190
	36 Lente ..	105	100	155	155
5	24 S.I.+20 P.Z.I.	110	155	130	195
	44 Lente ..	130	105	110	95
6	24 S.I.+16 P.Z.I.	155	210	170	—
	40 Lente ..	140	180	135	—
10	52 P.Z.I. ..	190	178	195	250
	52 Lente ..	95	140	175	180
11	28 Globin ..	155	245	165	—
	28 Lente ..	165	205	170	250

It would appear, therefore, from this small series of experiments that lente insulin possesses the prolonged action claimed by the manufacturers, and also that it exerts a shorter hypoglycaemic action, comparable with and equal to that of soluble insulin alone or mixed with P.Z.I. Throughout the course of these and other experiments with

lente insulin, hypoglycaemia occurred only two or three times and was never severe. There were no local reactions or undesirable side-effects. In the few cases in which tests were repeated with lente insulin the results obtained were remarkably constant.

We hope to carry out further trials on lente insulin in order to determine: (1) the length of action and time of maximum action of lente insulin in varying dosage; (2) whether there is significant variation between different batches of the same preparation; (3) whether lente insulin produces satisfactory control in ambulatory cases; (4) the arrangement of diet best suited to the action of these insulins; the diet of the cases reported was kept constant, and the carbohydrate content was arranged to suit the insulin or insulins with which comparison was made; (5) the suitability of the new insulins for initial stabilization of severe diabetics.

Summary

A preliminary trial of the new Danish lente insulin supports the claim that it exerts a prolonged hypoglycaemic action, lasting at least 24 hours, which is strong enough to control the blood sugar of moderately severe diabetics throughout the day without causing hypoglycaemia during the night. It has not in our experience produced either local or general reactions and appears to be no more likely to produce hypoglycaemic reactions than the insulin preparations at present in use.

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ACUTE BENIGN PERICARDITIS

A REPORT OF FOUR CASES IN CHILDHOOD

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Acute benign pericarditis has been recognized more often in America than in Europe, and its existence in Britain has even been denied (Andrews *et al.*, 1948). Having recently seen two typical cases, we decided to examine the notes of all children with pericarditis treated at the Birmingham Children's Hospital between 1942 and 1951, and thus discovered two other probable examples of the condition.

Case 1

Both parents of an 8-year-old boy had a feverish illness, one a week before and the other a week after their son was taken ill with shivering and left-sided chest pain. Penicillin and sulphonamides in adequate dosage had no effect on his high temperature or irritating cough. A week later he developed severe abdominal pain and was transferred to hospital. He was then only moderately ill; temperature 103° F. (39.4° C.), pulse 124, and respirations 28. Fine crepitations and distant bronchial breathing were heard at the left base; clinically the heart was normal. Chloramphenicol—40 mg. per lb. (88 mg. per kg.) per day—reduced the temperature, but pain increased and the child developed both a loud pericardial friction rub and an apical systolic murmur. Yet he was not critically ill. The E.C.G. strongly

suggested pericarditis, with raised RS-T segments in Leads I and II and P-R interval 0.18 second. An x-ray film showed a wide heart shadow with a trace of fluid at the left base (Fig. 1).

After five days aureomycin was substituted for chloramphenicol, and in the following week there was a fall in temperature and the pericardial friction disappeared. On the day after stopping aureomycin the boy complained of right shoulder pain. Apical gallop rhythm together with venous congestion and bronchial breathing at the left base suggested, and x-ray examination confirmed, the presence of a pericardial effusion, areas of consolidation in the lower lobes, and a small right pleural effusion. All these signs disappeared without treatment, and after a week the heart size was almost normal (Fig. 2).

A month after admission there was another relapse, with pain in the left shoulder, chest, and abdomen, a raised temperature, and signs of pericardial effusion. A second course of aureomycin, lasting two weeks, led to improvement, and after three weeks' freedom from symptoms he was discharged from hospital on the 59th day. There was a further relapse two and a half weeks later, but recovery was spontaneous.

The Mantoux test, cold agglutinins, streptococcus MG antibodies, Q fever complement fixation, and examination

for antibodies to four strains of Coxsackie viruses were negative repeatedly throughout the illness. A typical blood count showed white blood cells, 12,500, 83% polymorphs.

Case 2

A boy aged 9 walked into the out-patient department after two weeks' illness with fever, anorexia, and chest pain. He was pale but not ill; temperature 102° F. (38.9° C.), pulse 100, respiration 20, blood pressure 105/65. The heart was large, and there was pericardial friction but no evidence of valvular disease, nodules, or joint involvement. Blood-stained, sterile serous fluid was obtained by paracentesis of the pericardium. The Mantoux test was repeatedly negative; white blood cells 14,500, with 90% polymorphs.

Penicillin and sulphadiazine were given in adequate doses, but the friction rub persisted for a week. There was no evidence of endocarditis or persistent cardiac enlargement when discharged two months afterwards, nor when he was examined again clinically, electrocardiographically, and radiologically four years later.

Case 3

A boy aged 3½ years had central abdominal pain and anorexia, and vomited once, and three days later developed a painful cough. On the seventh day of his illness he looked moderately ill, and was orthopnoeic; temperature 98° F.

FIG. 1.—Case 1. Radiograph showing wide heart shadow with trace of fluid at left base.

FIG. 2.—Case 1. Radiograph showing return of the heart to normal size.

FIG. 3.—Case 3. Radiograph showing pericardial effusion.

FIG. 4.—Case 3. Radiograph taken five years after Fig. 3.

(36.7° C.), pulse 140, respirations 44. There were no nodules or joint changes. Venous congestion, hepatic enlargement, increased cardiac dullness, and muffled heart sounds suggested a pericardial effusion, which was confirmed by x-ray examination (Fig. 3), and 210 ml. of fluid was aspirated. The fluid was blood-stained, contained a few polymorphs, and was sterile. Relief was great, but, although receiving penicillin, the child relapsed within a week and further aspiration was required. Guinea-pig inoculation was negative.

The temperature was raised for three weeks, and, although the pericardial effusion was resolving by the end of the second week, fluid appeared at the right base. He was discharged after three months and his heart has remained normal in size, with no E.C.G. or radiological evidence of disease, for five years (Fig. 4). The Mantoux reaction was then, and is still, negative.

Case 4

An 11-year-old boy developed a temperature of 102° F. (38.9° C.) with pain in the front of the chest and abdomen aggravated by breathing. His symptoms subsided, but soon returned with such severity that he had to be propped up in bed. A week after the onset his temperature was 100° F. (37.8° C.), pulse 100, and respirations 20. There was no venous congestion or liver enlargement; the blood pressure was 120/78. His heart was enlarged, with normal sounds but loud pericardial friction, and a pleural rub at the left and later at the right base posteriorly. There were no nodules.

A week later x-ray examination showed considerable cardiac enlargement and the E.C.G. revealed a raised S-T segment with upright T in Lead II, suggestive of pericarditis. Within a week the x-ray picture was normal and the E.C.G. showed an iso-electric S-T segment with inverted T₂, which a week later had returned to normal. The white cell count was 7,600 per c.mm., with 77% polymorphs, and the E.S.R. was raised to 70 mm. in one hour (Westergren) at the height of the illness. The Mantoux test was repeatedly negative. He was discharged from hospital after five weeks, free from all symptoms and clinically normal.

Diagnosis

In America acute benign pericarditis seems to be as common in young adults as rheumatic pericarditis, though less frequent than coronary artery disease (Logue and Wendkos, 1948); in this country it may be commoner than is generally realized. Among 40 cases of pericarditis seen in the past ten years at the Birmingham Children's Hospital, 27 were rheumatic, 8 were pyogenic, 1 was tuberculous, and 1 was uraemic. The remaining three (Cases 1, 2, and 3 above) were thought to be due to acute benign pericarditis. Other examples may have been missed, for pericardial friction and/or effusion are by no means invariable in acute benign pericarditis, and in patients with atypical pneumonia pericarditis may be recognized only if serial E.C.G.s are taken (Levy and Patterson, 1950). Other cases might well be sought among children with acute unexplained abdominal pain, especially when accompanied by fever and a painful cough.

We based the diagnosis on exclusion of other recognized causes of pericarditis with effusion. Rheumatic fever was regarded as unlikely because there was no joint involvement, there were no nodules, there was no permanent damage to the heart or its valves, and the patients were not as ill as children with rheumatic pericarditis are. A tuberculous origin was rejected because Mantoux tests, carried out repeatedly for at least four months, were constantly negative, guinea-pig inoculation was negative in one case, there was no evidence of a tuberculous focus in any other part of the body, and the recovery was relatively rapid. Pyogenic pericarditis was thought to be improbable in view of the relatively low white-cell count (the highest being 14,500 per c.mm., with 90% polymorphs), the relative mildness of the illness, a failure to culture organisms from the pericardial

fluid in Cases 2 and 3, the ineffectiveness of penicillin, sulphadiazine, and chloramphenicol, the spontaneous recovery of Case 4 without specific therapy, and the absence of a primary septic focus such as osteomyelitis. There were no reasons to believe that any of the patients had renal disease, cardiac infarction, disseminated lupus erythematosus, Still's disease, myxoedema, or traumatic pericarditis.

Each of the four patients had illnesses which corresponded with that recorded for acute benign pericarditis.

1. The illness was relatively mild, and one child actually walked into the out-patient department, although he had a pericardial rub at the time. Three of our children had an obvious friction rub, but only one was critically ill, and in this case aspiration of a large pericardial effusion immediately transformed his general condition. Large effusions are uncommon, although they may occur (Levy and Patterson, 1950).

2. The pericardial fluid may be straw-coloured or haemorrhagic; it is conceivable that trauma may have been responsible for the blood-staining in our two cases.

3. Pain, a striking feature in adults, affected all four children, and in two was severe enough to simulate appendicitis.

4. Each child had associated pleurisy, and in Cases 1 and 4 it was bilateral.

5. A relapsing course such as that observed in Case 1 sometimes occurs (Taubenhaus and Brams, 1950), but the ultimate prognosis is good. All our patients have remained well, and none has any residual abnormality, but the longest follow-up period is only five and a half years.

Aetiology

Although the cause of acute benign pericarditis is unknown it has been recognized in patients with primary atypical pneumonia (Finkelstein and Klainer, 1944), a condition usually due to a virus infection. The disease has many features in common with acute benign dry pleurisy (Scadding, 1946) or Bornholm disease, and the latter is often associated with, if not always caused by, the Coxsackie group of viruses (Findlay and Howard, 1950). Friedman *et al.* (1952) examined sera of five cases of acute benign pericarditis, but found no evidence that there had been recent infection with two strains of Group A or one strain of Group B Coxsackie virus. In one case we also failed to demonstrate infection by any of four different strains of the virus. However, there are many strains of Coxsackie virus, and it remains tempting to link acute benign pericarditis with Bornholm disease even though there are minor differences in the seasonal incidence. Both diseases run a benign, sometimes relapsing, course with severe abdominal, thoracic, and even shoulder pain, which may lead to suspicion of appendicitis or coronary occlusion. Pleural friction may be present in both. Pericarditis may complicate Bornholm disease; one case of this kind reported by Heckscher (1933) and six described by Bing (1933) seem to have been very like cases of acute benign pericarditis. Our fourth patient was taken ill during an outbreak of epidemic myalgia, and during this same outbreak Dr. S. R. F. Whittaker had under his care two adults with acute benign pericarditis. Another of our patients (Case 1) developed his illness within a week of a vague febrile illness in both parents.

Treatment

It is difficult to assess response to treatment in a disease with a uniformly good prognosis and a natural tendency to relapse. Sulphonamides, penicillin, and streptomycin (Levy and Patterson, 1950) are almost certainly valueless. In one of our patients a pericardial rub developed during treatment with chloramphenicol, but this child later responded twice, though only temporarily, to aureomycin. Taubenhaus and Brams (1950) have reported favourably on the effects of aureomycin, but Friedman *et al.* (1952) state that neither aureomycin nor any other antibiotic has any effect on the illness. These last authors report that either A.C.T.H. or cortisone will lead to prompt and dramatic improvement. It seems, however, scarcely justifiable at the moment to use these agents for a disease with no apparent sequelae.

Summary

Four cases of acute benign pericarditis in childhood are recorded.

It is suggested that this disease may sometimes be a complication or manifestation of Bornholm disease.

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AN INVESTIGATION INTO STERILITY AFTER LUMBAR GANGLIONECTOMY

BY

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"We are obtaining increasing evidence that males may not be sterile or have any alteration of sexual function after bilateral excision of the first lumbar ganglion or even the upper three ganglia." This observation of White and Smithwick (1942) crystallizes a belief contrary to the usual teaching and supports a view held in this clinic for some time. Professor A. M. Boyd instigated this work because of a clinical impression arising out of and sustained by a follow-up of several hundred cases of bilateral lumbar ganglionectomy in which there was every reason to believe that the first lumbar ganglion had been removed on both sides.

Before proceeding with a discussion on sterility following this operation it is important that a clear distinction should be made between sterility and impotence. Many patients arrive at this clinic under the impression that the two terms are synonymous, and alarm and despondency are created on these grounds. No one has ever suggested that an impairment of gross sexual function follows this operation, and this should be emphasized to the patient at the outset. Furthermore, the substitution of the term "seminal anorrhoea" for sterility conveys to the practitioner a full understanding of the symptom under consideration.

For many years there has existed a widespread belief that the bilateral removal of the first lumbar ganglion results in sterility. This belief has been based on experimental evidence which has implied a loss of ejaculatory function and clinical evidence which has perhaps been given undue prominence by the fact that only the patients in whom this symptom has occurred return to complain of sterility.

During the course of this investigation it has become increasingly clear that sterility, far from being a common post-operative complication, is only rarely encountered, and even then, as is shown later, is usually the

result of a much more extensive sympathetic denervation. The present communication is in the nature of a progress report, and the work is by no means complete. The conclusions drawn from the data at present available may be modified by further evidence.

Method of Investigation

The problem has been approached by posing the following questions: (1) Is there a failure of seminal emission after bilateral removal of the upper three lumbar ganglia? (2) If so, what is the mechanism of this failure? (a) Does the semen fail to reach the posterior urethra? Or (b) is it due to reflux of the semen into the bladder through a lax internal sphincter?

The subjects of this research have been divided into three groups: patients who have been subjected to bilateral lumbar sympathectomy; patients who have had a much wider sympathetic interruption for hypertension; and patients who have had an operation of similar or greater degree of severity to act as a control of sexual resilience.

In the sympathetomized patients the level of denervation has been ascertained by the use of the electrodermometer, an electronic apparatus devised by Hall Ratcliffe and Jepson (1950) for measuring the alteration in surface resistance consequent on drying of the skin. The constancy of the post-ganglionectomy skin-resistance patterns has been described by the same authors, and when a pattern showing an upper-thigh distribution is obtained (Fig. 1) it is safe to assume that the first lumbar ganglion has been included in the section of chain removed. It is certain that when the lumbar chain is followed under the internal arcuate ligament with division of the diaphragmatic crus if necessary, and the ganglion thus exposed is removed, this pattern is obtained. The high lumbar ganglionectomy is performed as a routine at this centre, for it is only by this means that an adequate sympathetic denervation of the lower limb can be achieved (Boyd *et al.*, 1949).

The purpose of the investigation has been carefully explained to the patients, and there has been no lack of co-operation. They were instructed to obtain a specimen of semen at a convenient time, a few hours before the proposed examination, and immediately afterwards two specimens of urine. The first specimen was to wash out the urethra, and the second specimen contained the rest of the bladder contents—making a two-glass test. The volume of semen was noted, a sperm count was carried out, and centrifuged specimens of the urinary samples were examined for the presence of spermatozoa. In addition the urinary specimens were tested for fructose by the Selivanoff test.

A questionnaire was also submitted with regard to the pre-operative and post-operative sexual function, with particular reference to any alterations noticed.

This simple routine has given the answer to Question 1 without difficulty—that is, does sterility occur in these cases? There is no doubt that in the majority of them the bilateral removal of the upper three lumbar ganglia does not cause sterility. If, however, a more extensive

FIG. 1.—Pattern shows area of sympathetic denervation achieved by bilateral removal of L1, 2, and 3.