It is noteworthy that iritis was present in three of our four patients, whereas in our experience of 215 consecutive cases of Reiter's disease it was found only in 17%. Radiographic evidence of sacro-iliitis was seen in two of the three male patients, but there was no suggestion of spinal involvement as found in classical ankylosing spondylitis.

The nature of the cardiovascular lesions described here is unknown, and, although potentially dangerous, they have not caused serious functional disability in three of the patients. One patient received prednisone therapy, during which time the erythrocyte sedimentation rate became normal, as did the previously prolonged P-R interval.

Summary

Three cases of Reiter's disease with aortic incompetence are described. The aortic lesion is believed to have developed during the course of Reiter's disease. This complication appears to be unusual, as no similar cases have been reported in the literature.

A fourth patient, a woman with iritis, transient arthritis, cervicitis, and aortic incompetence, came to necropsy and is also recorded, though the diagnosis of Reiter's disease could not be made with certainty.

A characteristic feature of the electrocardiogram was a prolonged P-R interval present at some time in all our patients.

The nature of the cardiac lesion is unknown.

Similar cardiac lesions have been described in a number of patients with ankylosing spondylitis, and this could give rise to some diagnostic difficulties.

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The *Hospitals Year Book*, 1961, has recently been published by the Institute of Hospital Administrators. The main change in this edition is that the directory of Northern Ireland Hospital Services has been revised and expanded to bring the information given about hospital management committees and their hospitals in Northern Ireland into line with that given in the sections for Great Britain. The *Year Book* is obtainable from the Institute, at 75 Portland Place, London W.1, price 59s. 6d., postage 2s. 3d.

FATAL DIABETIC KETOSIS

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There has been a marked reduction in the number of deaths from diabetic ketosis during the past 20 years. The low mortality of between 2 and 5%, in a series reported by Harwood (1951) and Joslin *et al.* (1959), has led to a general belief that fatal ketosis is now exceptional, and that when it occurs it is due to faulty treatment. However, mortality rates of about 15% reported from Melbourne (Greenaway and Read, 1958) and Cincinnati (Skillman *et al.*, 1958) do not support this. The absence of a published series from hospitals in this country in recent years has prompted the present study, in which 19 fatal cases are described.

Material

The results of treatment of 160 episodes of severe ketosis are considered. These were consecutive admissions to the General Hospital, Birmingham, in the five years between January, 1955, and December, 1959, and were contributed by 122 patients (2 patients had ketosis five times, 2 four times, 4 three times, and 16 twice). Fourteen of the patients had ketosis more than once in the same year. We have included in the series only those patients who showed obvious and visible air hunger on admission to hospital, for at this stage it can safely be claimed that ketosis has become severe and that coma is impending. The level of plasma bicarbonate was not regarded as a sufficiently reliable guide to be used as a criterion of clinical severity (Owens and Rockwern, 1939; Collen, 1942; Black and Malins, 1949; Harwood, 1951; Hudson *et al.*, 1960).

Results

Age, Sex, and Seasonal Incidence.—There were 60 episodes in males and 100 in females; the series does not include those in children under 10. The Table shows the number of episodes in each 10-year age-group for both sexes, and Fig. 1 compares the incidence of ketosis in males and females with the prevalence of diabetes in all patients attending the hospital diabetic clinic. Thus the series is of comparable age and sex composition to those of Harwood (1951) and Cohen *et al.* (1960), but the mean age of admission is 10 years above that of the Joslin Clinic series (Joslin *et al.*, 1959). The significant excess in the incidence of ketosis in adolescent girls has been found before (Joslin *et al.*, 1937; Owens and Rockwern, 1939). Unlike the findings of most American authors (Danowski, 1957; Cohen *et al.*, 1960), Fig. 2 shows that the episodes of ketosis were seasonal, being especially common in November and December and uncommon in May and June. We consider the seasonal incidence to be associated with respiratory infection, which was a common precipitating cause of ketosis.

Overall Mortality.—In the 160 episodes of ketosis 19 patients died, a mortality rate per episode of 12% (see Table and Fig. 1). We have included every death occurring in patients after admission to hospital with ketosis, even though it might have taken place many days afterwards. This is because in every case it seemed likely that delayed death would not have taken place had the patient not been in ketosis. Similarly, we have included all cases where ketosis and another serious illness occurred together, because it always seemed probable that ketosis had played some part in the fatal outcome. Ten deaths occurred within 24 hours and could be directly attributed to the ketosis; in nine patients death was delayed, and occurred between 2 and 15 days after admission. Since age has been one of the most important factors in determining the mode of death we have arbitrarily divided the fatal cases into three age-groups: 60 years and over, 20 to 59, and under 20.

Deaths in Patients Aged 60 and Over.—In the 30 episodes in this group 10 patients died, a mortality rate per episode of 33%. In seven patients death was delayed, and in five of these it was due to the effects of arterial thrombosis, which emerges as the commonest single cause of delayed death in the whole series. The thrombosed vessels were the abdominal aorta, the right common iliac, the right subclavian, the left internal carotid, and major branches of the splenic and renal arteries respectively. In every case the occlusion seemed

to result from, rather than be the cause of, the ketosis, and the effects became apparent after the ketosis was controlled. The two other cases of delayed death were due to bronchopneumonia. Of the three elderly patients who died after admission to hospital, the history and symptoms of ketosis were atypical in two, and there was delay in diagnosis and treatment. In the third case the severity of the ketosis masked the presence of intestinal obstruction long enough to cause a fatal outcome.

Age Incidence of Ketosis for Both Sexes, with Number of Deaths

Age-group of Patients	Episodes in		Deaths	
	Males	Females	Males	Female
10-19	11	24	2	1
20-29	13	11	0	1
30-39	12	6	0	0
40-49	9	18	3	0
50-59	6	20	0	2
60-69	6	14	1	3
70-79	3	7	1	5
Total	60	100	7	12

Mean age of admission was 39.6 years.

Deaths in Patients Aged 20-59.—In the 95 episodes in this group, six patients died, a mortality rate per episode of 6.3%. Four of these were extremely ill from uncomplicated keto-acidosis and showed a number of unfavourable prognostic signs (Rabinowitch *et al.*, 1939). Thus compared with the survivors of the same age-group the mean duration of symptoms was twice as long (54 hours compared with 29 hours), the mean initial blood sugar twice as high (1,150 mg./100 ml. compared with 610 mg./100 ml.), and all presented in coma with systolic blood-pressure below 100 mm. Hg. Yet in two episodes death might have been avoided since the stomach had not been aspirated, and at necropsy there was inhaled vomit in the bronchi. Of the two other patients not in deep coma, one had acute pancreatitis and peritonitis and the other a myocardial infarction.

Deaths in Patients Aged 10-19.—In the 35 episodes in this group three patients died, a mortality rate per episode of 8.6%. All three cases were quite unexceptional in respect of the severity of the ketosis. The mode of death was so similar and so unlike the other fatal cases in the series that they merit more detailed description.

Case 1.—A 13-year-old girl not known to be diabetic had symptoms of a month's duration. She had vomited for two days and had air hunger for a few hours prior to admission, when she was drowsy but not unconscious. Her B.P. was 125/75, her blood sugar 530 mg./100 ml., and she had heavy glycosuria and ketonuria. Treatment consisted of 80 units of soluble insulin on admission and a further 40 units two hours later, together with an intravenous infusion of 1 litre of hypotonic saline lactate (Na 98 mEq/l, Cl 68 mEq/l, lactate 30 mEq/l). This was followed by 1 litre of potassium-containing solution (Na 56 mEq/l, K 24 mEq/l, Cl 44 mEq/l, lactate 24 mEq/l, HPO₄ 12 mEq/l). Six hours later her clinical condition had improved, her blood sugar was 260 mg./100 ml., but she remained drowsy. She lost consciousness 10 hours after admission and died within a few minutes. At necropsy the only abnormal finding was cerebral oedema and bilateral tentorial pressure cones; histological examination of the brain showed patchy neuronal atrophy of anoxic type.

Case 2.—A 15-year-old boy not known to be diabetic was at work the day before he was admitted to hospital. He had severe symptoms of about a month's duration. He had slight air hunger, but consciousness was unimpaired. His B.P. was 135/80, and blood sugar 540 mg./100 ml. He

FIG. 1.—Incidence of severe ketosis in men and women in 10-year age-groups, compared with the prevalence of diabetes in the same age-groups in all patients attending the diabetic clinic.

FIG. 2.—Seasonal incidence of severe ketosis.

had heavy glycosuria and ketonuria. Treatment consisted of 80 units of soluble insulin and oral fluids. He suddenly became unconscious six hours after admission, his B.P. fell, and his breathing was for a short time periodic and then ceased. At this time the blood sugar was 288 mg./100 ml., Na 130 mEq/l, K 5.3 mEq/l, and HCO_3^- 12.1 mEq/l. In spite of an infusion of noradrenaline, a tracheotomy, and artificial respiration (I.P.P.) he died 30 hours later. At necropsy the macroscopic appearance of the brain was normal, and microscopical examination showed changes similar to those in Case 1, but more severe.

Case 3.—A well-built 16-year-old male diabetic, who had been on insulin for five years, started to vomit two days before admission. This had been precipitated by an infection of the upper respiratory tract. He was drowsy but rational; he had marked dehydration and air hunger. His B.P. was 120/70, blood sugar 546 mg./100 ml., HCO_3^- 9.5 mEq/l. He had heavy glycosuria and ketonuria. Treatment consisted of 250 units of soluble insulin and 4.5 litres of the hypotonic saline lactate, followed by 1.5 litres of the potassium-containing solution. During the first seven hours he passed nearly 2 litres of urine. He remained drowsy but otherwise seemed better. Eight hours after admission he suddenly became unconscious and was found to have large unequal pupils, hypotonic limbs, and bilateral extensor plantar responses. At this time his blood sugar was 200 mg./100 ml., Na 150 mEq/l, K 3.9 mEq/l, Cl 110 mEq/l, HCO_3^- 22 mEq/l, and urea 46 mg./100 ml. Soon after, a very marked increase in the urinary output was noted. This was found to be at the rate of 16 ml./min., with a specific gravity of 1003. The intense polyuria responded to "pitressin"; 5 mμ pressor units slowed the rate of urine flow immediately, but had to be repeated hourly. He did not regain consciousness; his respiration failed and the B.P. fell. He survived a further six days in a respirator, having continuous noradrenaline infusion. At necropsy the brain showed widespread necrosis of the hypothalamus and mid-brain, and we presume that the sudden unconsciousness followed by diabetes insipidus and progressive failure of respiration had resulted from this.

Discussion

Comparison of the percentage mortality figures from different centres for diabetic ketosis is difficult. This is in part because there is no agreement on the definition of severe ketosis, and partly because, as Rabinowitch *et al.* (1939) pointed out, no single feature expresses the severity of the individual case. There is therefore no certainty that any two series are composed of cases of comparable severity. Differences in the type of hospital, in the social structure of the population served, and in the level of general medical knowledge about diabetes outside the hospital all serve to influence the composition of any series. It is also well known that the prognosis of ketosis is grave over the age of 60, so that to some extent the mortality rate of any series is dependent on its age structure (Joslin *et al.*, 1959). These many variables make it difficult to assess to what extent differences in treatment influence the mortality rate. There seems little doubt, however, that the best results are obtained where a group skilled and experienced in the management of the condition undertake the treatment of every case (Harwood, 1951; Nabarro *et al.*, 1952).

From the sources of admission there is reason to believe that the present series is representative of the incidence of ketosis in the diabetic population. No special arrangements were made for treatment of the patients who were admitted under and treated by the physician of the day. Therapy was based on the principles suggested by Nabarro *et al.* (1952), and consisted of the immediate administration of large doses

of soluble insulin together with intravenous infusion of hypotonic lactate-containing solutions. Potassium was given after about four hours and antibiotics were given from the start. We feel, therefore, that the mortality rate in this series is comparable with that of other large general hospitals in this country. Recent reports from elsewhere support this; thus Skillman *et al.* (1958) had 25 deaths in 172 episodes, and Greenaway and Read (1958) 11 deaths in 69. It is also of interest that in a series from this hospital collected in 1946–8 (Black and Malins, 1949) the mortality rate was no higher, in spite of the fact that at this time the importance of potassium depletion was not appreciated and the only fluid administered intravenously was isotonic saline.

The importance of arterial thrombosis as a cause of delayed death in elderly patients with ketosis has not been commented upon. It is hardly surprising, however, that haemoconcentration and circulatory failure should predispose to thrombosis in arteries already damaged by atheroma. The routine use of anticoagulants in cases such as this seems a justifiable prophylactic measure.

Of the 19 deaths in the series the three in adolescence followed a pattern not hitherto described. Structural cerebral damage has been found before in fatal diabetic coma (Dillon *et al.*, 1936); and Kety *et al.* (1948) have shown that a lowered cerebral oxygen uptake is a feature of fatal cases. In the cases described by these authors, however, the patients were unconscious on admission and had ketosis of the utmost severity. They are in contrast, therefore, to the above group, where loss of consciousness occurred suddenly when the response to treatment seemed adequate. Greenaway and Read (1958) report on seven cases, four of them fatal, where collapse characterized chiefly by a fall in blood-pressure occurred in similar circumstances. They thought the phenomenon to be unrelated to water or electrolyte repletion or adrenal insufficiency, but were unable to explain its cause. The clinical picture and necropsy findings in our patients suggest that sudden deterioration of this character is of central origin. In all three the sudden loss of consciousness was accompanied by signs of brain-stem disorder, while in one there was direct evidence of functional disturbance of the hypothalamus as evidenced by the unusual situation of coexisting diabetes mellitus and insipidus. The non-specific character of the pathological changes, together with the fact that the blood sugar and the blood electrolytes commonly measured were returning to normal at the time of the deterioration, suggests that other unrecognized metabolic factors were responsible.

Summary

The age and sex incidence in 160 episodes of severe diabetic ketosis is compared with the prevalence of diabetes at a hospital clinic. There is a large excess in the incidence of ketosis in adolescent girls.

The incidence of ketosis is common in November and December and rare in May and June.

Nineteen patients died—an overall mortality per episode of 12%. Ten deaths occurred within 24 hours of admission; in the remainder it was delayed and was the result of a superadded complication.

The death rate was high in patients over 60, and the commonest cause of death was thrombosis of a major artery.

Three deaths occurred in adolescence owing to progressive cerebral damage at a time the ketosis was

improving. In one there was massive destruction of the hypothalamus and mid-brain which gave rise to diabetes insipidus.

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THE RELIEF OF PAIN BY COOLING OF THE SKIN

BY

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In 1949 Dr. Janet Travell described the use of ethyl chloride spray in the treatment of acute wryneck. In 1951 Dr. W. A. Bain drew my attention to this work and suggested that this form of treatment might be of use in my department. Since that time I have used ethyl chloride in the treatment of so many painful conditions with such success that I should now be loath to run a busy casualty department without its help. In 1952 Travell described the use of the ethyl chloride spray in the treatment of painful muscle spasm giving a full bibliography, and pleaded for a wider trial of this simple therapeutic measure. In 1956 I reported locally my experiences with it (Ellis, 1956). Further advances have been made since then, and I should like to draw attention to the value of this treatment as revealed by nine years' experience of its use in this department, in the hope that others may try it.

Cooling of the skin by spraying with ethyl chloride has been used to treat all kinds of skeletal muscle pain, and also the pain of renal colic, of dysmenorrhoea, of migraine, and of causalgia; Taverner (1960) reports its use in post-herpetic neuralgia. The usual treatment of such conditions is by analgesics, from salicylates up to morphine and pethidine. Such analgesics succeed in dulling the pain to a greater or less extent, whereas the virtue of the spray treatment is that it abolishes the pain. That the pain may recur in some cases is no denigration of its efficacy, for many of these conditions

require repeated doses of analgesics over a prolonged period to afford adequate comfort to the patient.

Types of Pain Relieved

Certain types of pain in which the spray has given dramatic relief are now described in more detail.

Lumbago

This term is used to cover a wide variety of types of low back pain. The acute, severe form presents a reasonably clear-cut clinical entity. The patient is seized with acute pain on getting out of bed in the morning or while bending and lifting a heavy weight. He presents a rigid back, and attempts to move increase the pain. Examination shows complete obliteration of the curve of the normal lumbar lordosis, often with scoliosis. When the patient lies prone on the examination couch the rigid straight back persists.

Treatment of this type of case is probably the most satisfactory use of the spray, for, in addition to relief of the pain, the deformity of the back can be seen to disappear. The lumbar region is vigorously sprayed for some 20 to 30 seconds. During the next few minutes the return of the normal lumbar curve can be seen to take place under the eyes of the surgeon, together with the disappearance of the scoliosis. When the patient turns to lie on his back he will admit that the acute pain has gone, but for some time there is a residual dull ache.

The after-treatment of such cases is usually rest in bed. With the abolition of pain and rigidity the patient can rest in comfort for whatever number of days is considered necessary. Some patients, however, have so much relief that they return to work on the same or the following day. Patients running their own small businesses are particularly grateful for the relief from the crippling pain, as it now allows them to continue at their work.

The more chronic types of low back pain often do not respond so dramatically. Travell has observed this also. But a large number of these cases do obtain such a considerable measure of relief that the spray is recommended as the first line of attack.

Acute Stiff Neck

I have often seen the dramatic sudden relief produced in this type of case, as reported by Travell. The patient who complains of a sudden "crick" in the neck on getting out of bed in the morning, and presents with acutely painful wryneck, is well known. Spray applied to the painful side of the neck brings dramatic relief.

Fibrositis

In the many cases of pain in muscles, in fascia, and around joints that can be lumped under this title, I regard the use of the spray as the first line of attack. Of the hundreds of patients who have attended this department in the last nine years, some have had complete relief after a single application of the spray. Others have had recurrences of pain and have required several sprays over some days. Two cases among my surgical colleagues are noteworthy. Each was afflicted with acute shoulder pain when called in to do emergency operations in the private wing. As a last resort, and without much hope of relief, they asked for the spray treatment. The spray gave them full, painless movement, and they were able to operate without disability.