2. Emphasis is laid on the early recognition of this condition which usually will rapidly lead to death unless early treatment is instituted.

3. The clinical features of spontaneous perforation or large traumatic rupture are epigastric pain, shock, cyanosis, interstitial emphysema of neck and pneumothorax or hydropneumothorax.

4. Smaller perforations during gastroscopy most often occur in the upper end of the œsophagus and are heralded by the occurrence of interstitial emphysema involving the neck.

5. The etiology and pathogenesis have been discussed of both the spontaneous and instrumental perforations.

6. Early surgical intervention with repair of the perforation or at the least open drainage of the mediastinum is the recommended treatment.

We wish to thank the Department of Veterans' Affairs for permission to publish Cases 1, 3 and 5 of Instrumental Perforation which were seen at Shaughnessy Hospital.

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ELECTROENCEPHALOGRAPHIC STUDIES IN DIABETES MELLITUS

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IN RECENT YEARS there has been an increasing amount of evidence appearing to show that labile diabetes is not entirely associated with the status of diabetes *per se*. One usually associates the term of labile diabetes with diabetes in young patients where wide swings of control are known to occur with reactions after being followed by bouts of acidosis. Several cases have been reported recently where this condition exists in patients beyond the age of adolescence, and indeed this is the experience of any internist who has treated any extensive number of diabetic patients.

These labile diabetics constitute major problems in management not only from the standpoint of the control of the diabetes *per se*, but because many of them exhibit personality traits which are difficult to handle from the standpoint of the patient-doctor relationship. The reported findings of abnormal electroencephalographic records in these patients has led to new physiological considerations and to new methods of therapy. It would also appear from reviewing the literature that the findings of disturbed carbohydrate metabolism, personality changes and abnormal electroencephalographic changes are not entirely confined to diabetes mellitus.

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It is interesting to note that Addison in his first description of the disease which bears his name recognized the psychiatric disturbances which are common in this disease. Subsequent students of this disease were so impressed with this particular aspect of the disease that they considered the disorder as stemming primarily from the central nervous system. It has subsequently become well established that abnormal electroencephalographic records are not uncommon in Addison's disease, that they are not improved, nor are the psychiatric disturbances, by high carbohydrate feedings or desoxycorticosterone either alone or in combination, but that the administration of adrenal cortical extracts and more recently cortisone results in improved carbohydrate utilization, some alleviation of psychiatric symptoms and improvement of the electroencephalographic tracings. It is also interesting to note that Engel and Margolin[1] in 1942 reported five cases in which the following factors were present in common—flat sugar tolerance curves, a tendency to hypoglycæmic reactions, neuropsychiatric disturbances and abnormal electroencephalograms. The disease entities were rheumatoid arthritis, anorexia nervosa, ulcerative colitis, periarteritis nodosa, and one case of acute anxiety. All of these conditions are now known to derive at least temporary benefit from the use of cortisone and ACTH. There also are a small, but significant, group of diabetic patients who exhibit all of the above common factors with the exception of the flat sugar tolerance curve.

If one turns from diabetes mellitus to the opposite condition of spontaneous hypoglycæmia, one finds several cases in the literature where this condition is associated with psychiatric disturbances and abnormal electroencephalographic findings. Fabrykant and Pacella[2] have reported eight such cases where spontaneous hypoglycæmia has been associated with abnormal electroencephalograms. Personality changes were noted in all patients and in some hypocalcæmia was also present. These cases were also characterized by flat sugar tolerance curves and many exhibited hypoglycæmic symptoms in the presence of normal blood sugars. In this particular group the symptoms were uniformly relieved by the administration of glucose.

To return to the more immediate problem of diabetes, Greenblatt, Murray and Root[3] have carried out a series of electroencephalographic studies in 75 diabetic patients. Forty cases of simple uncomplicated diabetes served as the control series. In this group 32 cases were found to have normal E.E.G. records, 5 were borderline and 3 were definitely abnormal. This is about what one would expect in a cross section of the average non-diabetic population, since it has been observed that about 10% of the population have abnormal E.E.G. records. None of these cases had any evidence of past seizures, personality disturbances or neurological disorders. In the remaining 35 cases, all of whose diabetic careers were punctuated with frequent instances of severe reactions, eight had normal E.E.G. records, 9 had borderline tracings, and 18 had abnormal records. The clinical symptoms observed were dizziness, weak spells, disturbances of memory, aphasia or paresis, temper tantrums, petit mal attacks, convulsive attacks, and spells of unconsciousness.

In both groups there were no significant differences in age, duration of disease, duration or amount of insulin intake, or type of insulin administered.

This evidence would seem to indicate that disturbances within the central nervous system, probably not related to the diabetes *per se*, may be responsible for this labile state of control. Subsequently Fabrykant and Pacella[4] have reported a series of 7 labile diabetic patients, 3 of whom have responded favourably to anti-convulsant therapy.

In the last 100 diabetic patients admitted to the diabetic service in the University Hospital, 8 cases of extremely labile diabetes have been found. Of this group it is proposed to discuss only three at this time.

CASE 1

The first patient, J.R., a boy of nine years of age was admitted because his local physician was unable to control the excessive glycosuria and at the same time prevent frequent insulin reactions. His diabetes was of three years' duration. No family history of epilepsy could be elicited. During the first year of his diabetes, control was relatively satisfactory. In the two years prior to his admission, control became increasingly difficult with frequent reactions interspersed between periods of profuse glycosuria and acidosis. A severe convulsion precipitated his most recent admission to hospital following which he remained apparently semicomatose for a considerable period of time. He had several reactions while in the local hospital. Because it had been observed that he had recovered from a few of these reactions without the administration of glucose, the family physician advised the parents that these episodes were probably psychogenic in origin. Reactions continued to occur despite continued glycosuria and high blood sugars. He was then transferred to the University Hospital for further study.

The physical examination of this child revealed no abnormalities. The electrogram showed continuous delta activity recorded from both frontal areas. He was put on dilantin and phenobarbital and discharged from the hospital. He returned to the hospital again because of the recurrence of reactions and difficulty in control, resulting from withdrawal of anti-convulsant therapy. Because of this "control" period outside hospital he was again placed on therapy resulting in minimal glycosuria, normal fasting blood sugars and relatively easy diabetic control.

The lability of his blood sugars is shown in Fig. 1 Arrows indicate the days on which "reactions" took place.

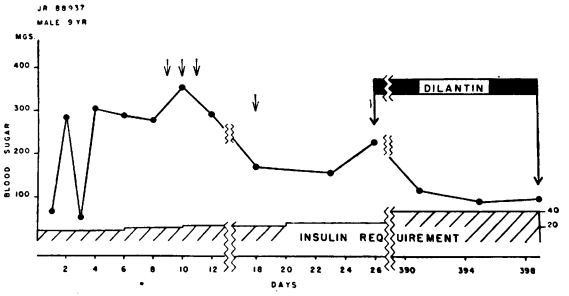

Fig. 1

CASE 2

The second patient, J.O., a young girl aged 22 years, first developed diabetes in 1941. At that time it was observed that she appeared to be a bright intelligent girl who was doing well in school. Physical examination at that time did not reveal any abnormal findings. There was no family history of epilepsy. Her diabetes was brought under control and she did not return to the University Hospital again for seven years. During the interval she had only been hospitalized once for restabilization of her diabetes. An acute iritis precipitated her return to the University Hospital. At this time she had completed grade twelve without undue difficulty. Physical examination showed marked conjunctival and ciliary injection, cloudiness of the anterior chamber, a small irregular pupil, posterior synechiæ with pigment deposits on the anterior surface of the lens. A few circumscribed hæmorrhages were noted in both fundi, but otherwise no unusual findings were noted. Her blood pressure was 118/90. There had only been an increase of eight units in her daily insulin requirement over the

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period of seven years, the dosage being forty units on admission.

Shortly after her admission to hospital it became obvious that she was going to be most difficult to control. She had several episodes of what appeared to be insulin reactions. The first few reactions were treated symptomatically, but because of the frequency of their occurrence, blood sugars were done during two succeeding reactions revealing values of 91 mgm. % and 132 mgm. %. At that time the explanation for her reactions was that she presumably had been out of control for a long period of time and that she was developing hypoglycæmic symptoms at normal blood sugar levels as a result of precipitous drops from high values. On all occasions she responded well to glucose fed by mouth.

She was discharged from hospital only to return in six months' time with a fractured femur. During this interval at home it had been noted that she had begun to show periods of mental confusion. There was no change in her physical status, other than that related to her fractured femur.

Within two days of admission to hospital she again had two severe reactions, from which she did not recover quickly following glucose administration. At this time an electrogram was done showing profound cerebral dysrhythmia, diffuse continuous delta activity with scattered sharp waves and spikes. Two repeat electrograms after starting anti-convulsant therapy failed to show any appreciable improvement, although clinically there was marked improvement in the ease with which her diabetes was controlled. A pneumogram done at a later date showed evidence of cortical atrophy most prominent in the frontal areas.

A subsequent admission five months later for removal of a Smith Peterson nail showed no improvement in her electrogram, but her diabetes was relatively easy to control and no reactions occurred.

Fig. 2 shows the wide fluctuations in her fasting blood sugars prior to instituting anti-convulsant therapy. During the control period no changes were made in her diet. No changes were made in the type of insulin used or the time spacing of individual doses. The total daily insulin requirement varied slightly from 80 to 90 units daily. After anti-convulsant therapy was instituted the marked lability of fasting blood sugars disappeared and there was a slight decline in the total daily insulin requirement.

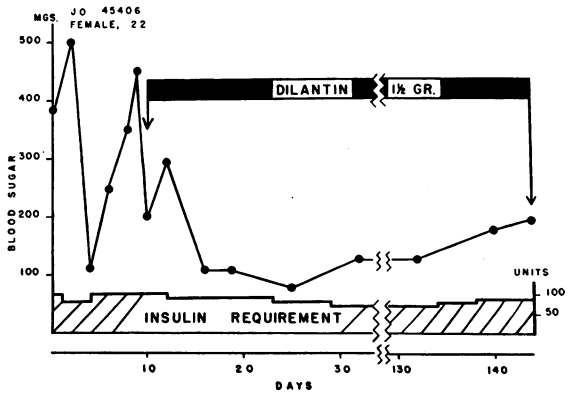

Fig. 2

The third patient, R.S., a male aged 21 years of age sought advice because of frequent insulin reactions which so interfered with his job as a typewriter mechanic that he was on the point of being discharged by his company. He had become quite depressed as a result of his condition and it was only with great difficulty that he was persuaded to enter hospital. Physical examination and the routine laboratory examinations showed no abnormal findings. An E.E.G. was done which showed poorly organized background activity. Random delta activity was observed throughout the record. The findings constituted a generalized cerebral dysrhythmia.

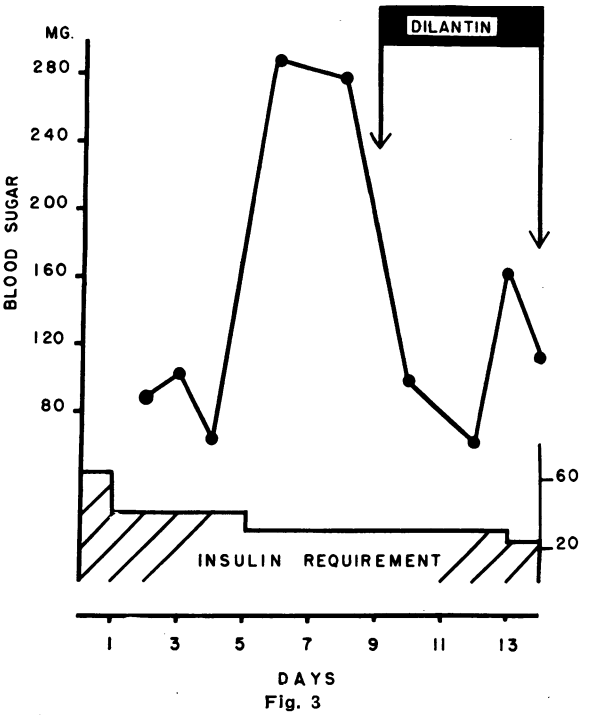

Fig. 3

Following the institution of anti-convulsant therapy, there was marked improvement in his diabetic control and a considerable decrease in the daily insulin requirement. He returned to his work and during the last two years there have only been occasional insulin reactions, but they have been minor in nature and have been controlled easily by the patient himself.

The lability of his fasting blood sugars is shown in Fig. 3.

COMMENT

It has been well established for some time that abnormally low blood sugars do not necessarily invoke the clinical entity known as an insulin reaction. Blood sugars may remain below 50 mgm. % for as long as twelve hours without the appearance of signs and symptoms commonly associated with hypoglycæmia. On the other hand the clinical picture of hypoglycæmia may become manifest in the presence of relatively normal blood sugars. This has given rise to the concept that such reactions occur as the result of precipitous drops in blood sugars from very high levels, although they may not reach the commonly accepted levels usually associated with hypoglycæmia.

In the cases presented here, it was observed that clinical reactions appeared in the face of normal blood sugars and also in the presence of sugars of definitely hypoglycæmic levels. It has also been observed that some of these reactions responded to the administration of glucose and that others did not, and also that in some instances recovery from reaction took place with-

out the administration of glucose. In the latter instance it is quite possible that these were true insulin reactions, but that sufficient glucose was mobilized by the body to remedy the situation, hence giving rise to an apparent recovery without the administration of glucose.

It therefore seems possible, as Fabrykant and Pacella suggest, that there may be two mechanisms involved in so-called insulin reactions. The first may be and probably is due to a true hypoglycæmic effect, in consequence of which the brain is deprived of sufficient glucose to carry on normally. In the second instance, a clinical picture of reaction may occur in the presence of normal blood sugars and presumably normal glucose supply to the brain, which is due to the cerebral dysrhythmia itself and not due to the diabetes *per se*.

In four of our five cases of labile diabetes where abnormal electrograms were found, appreciable relief from their symptoms was obtained on anti-convulsant therapy. In the fifth case no appreciable benefit was observed. In the three remaining cases whose diabetes was extremely labile but who had normal electrograms, no benefit resulted from anti-convulsant therapy. In one case, despite the fact that there was no appreciable improvement in the electrogram, there was marked improvement in the ease with which the diabetes could be controlled.

SUMMARY

1. The association of a disturbed carbohydrate metabolism, psychiatric disturbances, and abnormal electrograms is found in several clinical conditions.

2. Three cases of labile diabetes have been presented whose control was entirely unsatisfactory and not compatible with a normal life outside of hospital. In all instances abnormal electrograms were found.

3. Prior to the institution of anti-convulsant therapy these patients presented extremely labile diabetes, characterized by frequent reactions, uncontrollable glycosuria, and evidence of personality changes.

4. The institution of anti-convulsant therapy resulted in a marked improvement in diabetic control and has enabled these individuals to lead a relatively normal life, not necessitating a return to hospital to control the labile status of their diabetes.

The author wishes to express his appreciation to Dr. G. K. Morton who interpreted the electroencephalograms done on the patients in this series.

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NEPHROCALCINOSIS

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THE TERM NEPHROCALCINOSIS usually implies the deposition of calcium salts in the renal parenchyma bilaterally in sufficient quantity to be visible in an x-ray film without their being present in the pelvis or calyces. The condition is rare. The etiology is varied, as it is found in a number of different pathological processes. It has been found in hyperparathyroidism, in chronic pyelonephritis, glomerulonephritis, in intoxication with vitamin D, in poisoning by certain chemicals and in pyloric and high intestinal obstruction associated with hypochloræmia alkalosis, etc.

Greenspan[1] reported a case of nephrocalcinosis with chronic hyperchloræmic acidosis and the syndrome of lower nephron insufficiency in an adult. The calcification was confined to the renal medulla. He draws attention to the fact that some observers have noted in a few rare cases of idiopathic nephrocalcinosis that the calcification was confined to the renal medulla. In these a unique form of chronic renal failure with hyperchloræmia was present as in his case but has been reported only in infants. The calcification in these is apparently confined to the distal tubules, hence the lower nephron syndrome effect. The fact that Greenspan's patient received sulfathiazol for the treatment of pneumonia some time before, suggests the sulfonamides as a possible etiological factor in the condition. Whatever the etiological factors involved, the disturbed calcium and phosphorus metabolism causes deposition of calcium salts in the renal parenchyma. One must remember that wherever cell dystrophy and cell death occur, there