The patient's mental condition improved only slightly, but she became more cooperative. However, delirium with delusions sometimes recurred. Hypokalæmia was corrected after only $2^1/_2$ months. Gradual recovery from adrenocortical hyperfunction was evidenced by: (1) a drop of morning plasma-hydrocortisone level (but without the typical diurnal rhythm); (2) later a normal response to the 2 mg. dexamethasone test; and (3) normal values of plasma-hydrocortisone with a return to a normal diurnal rhythm 3 months after admission. The patient was then transferred to a psychiatric institution where her condition did not improve significantly. After 1 year, plasma-hydrocortisone values were: 9 A.M. 16·6, 4 P.M. 10·3, μg. per 100 ml. Glucose-tolerance curve was nearly normal, and serum-potassium was 4·7 meq. per litre.

This study suggests that chronic alcoholic encephalopathy may be accompanied by adrenocortical hyperfunction and be eventually confused with Cushing's syndrome. Our patient differs from those described by Dr. Butler and Dr. Besser in two main features: (1) normalisation of adrenocortical function without improved mental condition; (2) the finding of hypokalæmia, which was most probably secondary to corticosteroid excess.

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COITAL FREQUENCY AND DOWN'S SYNDROME

SIR,—Since German [1] put forward his speculation about coital frequency and Down's syndrome, several ideas have emerged about the feasibility of testing this notion. One of the suggestions is that illegitimacy would perhaps be conducive to more cases of Down's syndrome. Lack of rhythmicity and possibly a crude use of the safe-period method will be associated with a greater chance of an aged ovum getting fertilised.

Of 31 cases of Down's syndrome I have seen in the past year and a half for genetic counselling, 9 were illegitimate children born to mothers below the age of twenty. Among these 9 young mothers, illegitimacy with the associated coital irregularity stands out as a likely determinant. It is noteworthy that the illegitimacy-rate among these 31 mothers is 29% in contrast to the estimated rate of 3% for a socioeconomically comparable population of unaffected children.

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SERUM-INSULIN IN REMISSION OF JUVENILE DIABETES

SIR,—Dr. Hernandez and co-workers (July 27, p. 223) describe a juvenile diabetic in whom they measured immunoreactive plasma-insulin levels during a period of remission. The insulin response to oral glucose was compared to that in "ordinary" juvenile diabetics. They found that it was much higher, and noted a resemblance to the response seen in maturity-onset diabetics. Their patient had been treated with insulin for 6 months before remission. He must therefore inevitably have developed plasma-antibodies against insulin.

The results obtained on plasma which contains insulin antibodies will be either spuriously high or low, depending on the technique used to separate free and bound labelled insulin. In double immunoassays, as for instance the one used by Dr. Hernandez and co-workers, the values will be too high, and it is not possible to demonstrate whether the plasma contains anti-insulin or not by these techniques. Insulin antibody can be detected by using chromatographic techniques. Unfortunately Dr. Hernandez and co-workers do not mention this problem and how they circumvented it. Accordingly their results are difficult to interpret.

We have studied three juvenile diabetics during and after remission. One of our patients had a low titre of insulin antibodies in plasma, and this was detected by our chromatographic technique.[1] The interference of the patients' anti-insulin could be diluted[2] by a dilution of 1/10. We found increased insulin production during remission. It is furthermore our impression that the degree of remission is related to the degree of improvement in insulin-secretory capacity.[3]

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A NEW POLYDACTYLY/IMPERFORATE-ANUS/VERTEBRAL-ANOMALIES SYNDROME?

SIR,—Dr. Say and Dr. Gerald (Sept, 21, p. 688) report a triad of polydactyly, imperforate anus, and vertebral anomalies in man. Professor Fuhrmann (Oct. 26, p. 918) observed a familial case of polydactyly and imperforate anus.[4] According to Dr. Say and Dr. Gerald the triad is comparable to "dominant hemimelia" in mice, which is characterised by polydactyly or oligodactyly of the hind-limbs, hypoplasia or aplasia of the tibia, and various anomalies of the vertebræ and ribs.[5 6] Besides minor abnormalities in the gastrointestinal and urogenital systems, heterozygous mice have no spleen and 44% of homozygous mice show imperforate anus.

Among 103 patients with anal atresia born in the administrative area of Münster between 1950 and 1961 (0·22 per 1000 of all births) there was 1 with bilateral duplication of thumb and "blindness" who died at the age of 14 days. No X-rays were taken of the vertebral column. The father was 34, and the mother 35 years old when the patient was born. There had been 2 miscarriages, and 4 normal children were alive.

In view of the findings in mice, Dr. Say and Dr. Gerald wonder whether the proposed syndrome in man may include limb deformities other than polydactyly. My observations here may help to elucidate this problem.

In the series of 103 patients with anal atresia, 3 had unilateral hypoplasia or aplasia of the thumb, and a further 1 an "abnormality of the thumb".[7] The main findings in these patients, and in 2 others with similar anomalies, are briefly recorded.

Case 1.—This boy, born in 1955, was the second of male twins. He had an imperforate anus, with fistula from rectum to urethra, absence of right thumb, 1st metacarpal, and thenar eminence, spina bifida occulta C5–T4, flattening of the left side of L4, and deformed sacral vertebræ. The other twin is normal. Serological analysis revealed dizygosity. Parents and 4 sibs are normal (1 miscarriage). The father was 50, and the mother 37 years old at the birth of the twins.

Case 2.—This girl, a first-born child, was born in 1957, when the father was 27 and the mother 33 years old. She had anal atresia with rectovaginal fistula, absence of left thumb, bifid and fused vertebræ in various parts of the spinal column, abnormalities of ribs, and (?) aplasia of left lung. She died at the age of 10 months.

Case 3.—This girl was born in 1956 with anal atresia complicated by rectovaginal fistula. "Right thumb without osseous connection to the hand." She died in the 2nd month of life. No X-rays were taken of the spine. The father was 37, and the mother 43 years old when patient was born.

Case 4.—This girl was born in 1950, when the mother was 24 years old. "Anal atresia, abnormality of the thumb."

Case 5.—This girl, a second child, was born in 1965, when the father was 29, and the mother 21 years old. She had atresia of anus and œsophagus with fistula to the trachea, "abnormality" of the left thumb, rudimentary right thumb, septal defect, and aplasia of the spleen. She died 1 day after birth.

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