times the ovarian and testicular tissues may merge, making removal of the unwanted part more difficult.

There are several indications for hormone therapy. Androgens may be necessary for their virilizing effects; oestrogen may be of great psychological value in producing artificial menstrual periods and in promoting breast development; in the adrenal type of female pseudohermaphroditism corticosteroid administration suppresses excessive androgen production by the adrenal glands, and when started soon after birth it enables these girls to develop into normal women, to menstruate, and to give birth to children. Swyer and Bonham (1961) reported a successful pregnancy in a patient of this type in whom cortisone therapy was not started until the age of 24 years.

In most cases of hermaphroditism reconstructive surgery is necessary, and in no part of plastic surgery is the need for adequate function more compelling than in that of the sex organs. As in any multiple-stage reconstruction, the whole procedure must be carefully planned in advance, because each stage lays the foundation for the next. As illustrated by Case 3, this is particularly true in the choice of method for correcting the ventral curvature of the penis (chordee), and it must be ensured that the method chosen will be adaptable to the subsequent type of urethroplasty.

Summary

Four cases of intersex—a true hermaphrodite, a female pseudohermaphrodite, and two male pseudohermaphrodites of different types—are reported and the main features of these conditions described. True hermaphrodites are rare, and only about 80 cases have been reported in the literature. The great majority of cases of female pseudohermaphroditism are of the adrenogenital type. The non-adrenal female pseudohermaphrodite is the rarest type of intersex. Case 2, an example of this group, is of particular interest on account of a chromatin-negative nuclear sex pattern—a finding which is usually taken to exclude female pseudohermaphroditism. Male pseudohermaphrodites may be broadly divided into those having a predominantly female appearance (including the syndrome of "oestrogen-producing testes") and those having a predominantly male appearance.

The investigation of a case of intersex entails the appraisal of all the factors concerned in the patient's sexual structure, including the somatic sex, the genetic sex, and especially the patient's own sex orientation. Hormone studies are positively diagnostic of female pseudohermaphroditism of the adrenogenital type, and, except in this group, laparotomy and gonadal biopsy should be performed. Such investigations should be carried out as early in life as possible so that a definite decision on the sex of rearing may be made. In older patients the two most important considerations are the patient's own sex orientation and the sex of upbringing. As these are nearly always in accordance, a change of sex after the first two years of life should rarely be considered. In exceptional cases, however, the patient's sex orientation may change, and it may then be that the psychological upheaval of sex reversal is to be preferred to the unhappy state of continued rebellion against the sex of rearing.

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INFANTILISM TO FATHERHOOD IN THE MALABSORPTION SYNDROME

BY

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The literature on the malabsorption syndrome is voluminous, and has naturally been concerned with the aetiology, the pathology, and the treatment with gluten-free diet, which indeed was a major discovery in the treatment of what at one time was a condition with a bleak prognosis. The introduction of the gluten-free diet (Dicke, Weijers, and van de Kamer, 1953) not only corrected the steatorrhoea in cases of coeliac disease but has ensured that children with this disease grow at an optimal rate (Anderson, Frazer, French, Gerrard, Sammons, and Smellie, 1952; Sheldon and Lawson, 1952). Gerrard, Ross, Astley, French, and Smellie (1955) found in a series of 32 children and adolescents who had not been treated with a gluten-free diet that steatorrhoea, stunted growth, and anaemia were the commonest residual clinical findings.

Little has been written, however, on the long-term follow-up of these cases. One study of value is that of Gerrard, Ross, and Smellie (1955), who reported an account of the late treatment of older children and adolescents in response to a diet free from wheat gluten. In particular they described the effect of this treatment on the growth and development of 18 children and adolescents who had been diagnosed as having coeliac disease 3 to 14 years previously. However, their follow-up of the benefits of this diet on growth covered a period of only 4 to 25 months; the results were striking. Sheldon (1955) found that there was an initial spurt of growth during the first six months on a gluten-free diet, and that some children with coeliac disease continued to grow satisfactorily when gluten was reintroduced in the diet. His follow-up unfortunately ceased at 12 years. Lindsay, Nordin, and Norman (1956) reassessed 25 young adults who had coeliac disease in childhood, 15 years after their initial assessment by Hardwick (1939). They found that these

patients were small, thin, delicate-featured, and pale, with immature secondary sexual characteristics. In women the menarche had tended to occur late. Statistically they were significantly underweight, but the departure from normal height was just not significant.

During the past eight years there has been the opportunity to study the effects of treatment on a youth with coeliac disease, who presented with infantilism at 18½ years, and who eight years later fathered a normal child.

Case Report

A painter aged 18 years 5 months was first seen in September, 1952, suffering from infantilism. At birth in April, 1934, he weighed 9¾ lb. (4.4 kg.), he was breast-fed, and his infancy was normal. In childhood he had had varicella, measles, mumps, and pertussis. It had, however, been noted that his motions had always tended to be loose, bulky, frequent, offensive, and putty-coloured. At 8 years, owing to loss of weight, anorexia, and these abnormal motions, he was admitted to the Children's Hospital under the late Dr. Norman Price, where on the clinical history and fat-balance studies he was diagnosed as a case of coeliac disease and put on a low-fat diet. He failed to attend later, as he lived in a country village outside Bristol. His mother and father were fit and well, and one brother of 15 years was tall and healthy; another brother had died at 8 months with an acute respiratory infection. Shortly before he was seen he had been categorized as grade 4 for National Service.

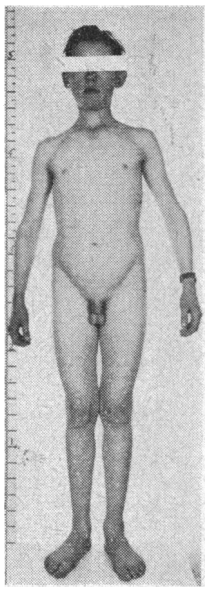

FIG. 1. — Photograph taken on September 24, 1952.

At 18½ years this youth had a good appetite and ate anything. His general health was fairly good, and he played cricket and football; but he still had frequent bulky, loose motions three or four times daily.

On examination in 1952 he looked like a tall boy of 11½–12 years (Fig. 1): height 61½ in. (156 cm.); span 61½ in. (156 cm.); weight 6 st. 13 lb. (44 kg.). His abdomen was rather protuberant, his muscles were atonic, and there was complete absence of secondary sexual characteristics. His voice was not broken; his penis was prepubertal in size, and both testes, measuring 1 in. (2.5 cm.) in the long axis, were in a non-pigmented scrotum (Fig. 2).

General examination showed no other abnormalities. *X*-ray pictures of the sella and chest were normal.

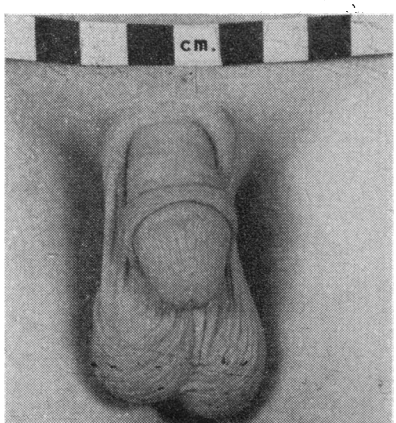

FIG. 2. — Photograph of genitalia. September 24, 1952.

His skeletal age (Greulich and Pyle, 1959) was 13, giving a predicted height of 69.9 in. (177.5 cm.). 17-Ketosteroids were 2.4 mg./24 hours. W.R. and Kahn test were negative. Cholesterol, 210 mg./100 ml. Hb 94%, with a normal film and normal W.B.C. Testicular biopsy showed well-formed seminiferous tubules containing mainly Sertoli cells with very few spermatogonia and spermatocytes, and mitoses were infrequent (Fig. 3).

From the psychological point of view virilization was of the first priority to him, and his treatment was divided into three parts: (1) androgens with normal diet (October, 1952, to November, 1953); (2) androgens with restriction of wheat flour (November, 1953, to May, 1956); and (3) androgens with gluten-free flour (May, 1956, to April, 1958).

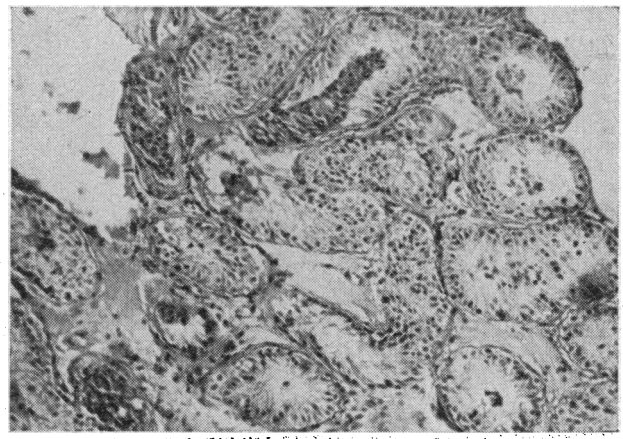

FIG. 3.—Testicular biopsy in 1952. (×110.)

From October, 1952, he was treated fairly intensively with methyltestosterone 60 mg. daily, and later, in addition, with injection of testosterone isobutyrate 50–100 mg. or testosterone phenylpropionate 50–100 mg. weekly. The injections were given from March, 1953, for 18 months, and methyltestosterone 60 mg. daily was continued for a total period of five and a half years.

His progress was followed at regular intervals, with records of height and weight, serial clinical photographs, and skiagrams of his left hand and wrist and other epiphyses. Skeletal ages (Greulich and Pyle, 1959) were assessed, and predicted heights were obtained from the tables of Bayley and Pinneau (1952). Testicular biopsies were done when he was first seen and later at the end of treatment, and several seminal analyses were arranged.

Results of Treatment

There was a gradual improvement in his muscular and sexual development, although frequent bulky motions continued until wheat flour was prohibited; however, he tended to lapse when he weakened and ate bread or cakes made with ordinary flour. His general development and progress was similar to that of any other treated hypogonadal male, and both the anabolic and androgenic effects of treatment are well shown in Figs. 4, 5, and 6. He masturbated at intervals, and in fact erection had occurred within the first months of androgen treatment. In December, 1954, two years after starting treatment, the semen volume was only 1 ml. with azoospermia after centrifuging the semen.

In May, 1955, he admitted to eating flour occasionally, and had had lapses with loose bulky motions; it was then that arrangements were made for his mother to bake specially for him with gluten-free flour.

By April, 1958, a seminal analysis showed an ejaculate of 3 ml. with a sperm count of 45 million/ml. with 90% progressive motility, and normal morphology. All androgen treatment was then stopped.

A second testicular biopsy was done in October, 1958, and on both sides the tubules were normal in size with some capsular thickening, but germinal cells were active and spermatogenesis was apparently normal (Fig. 7).

At the age of 25 he was a well-built, well-muscled man: weight 12 st. 8 lb. (80 kg.); height 67¼ in. (171 cm.). He

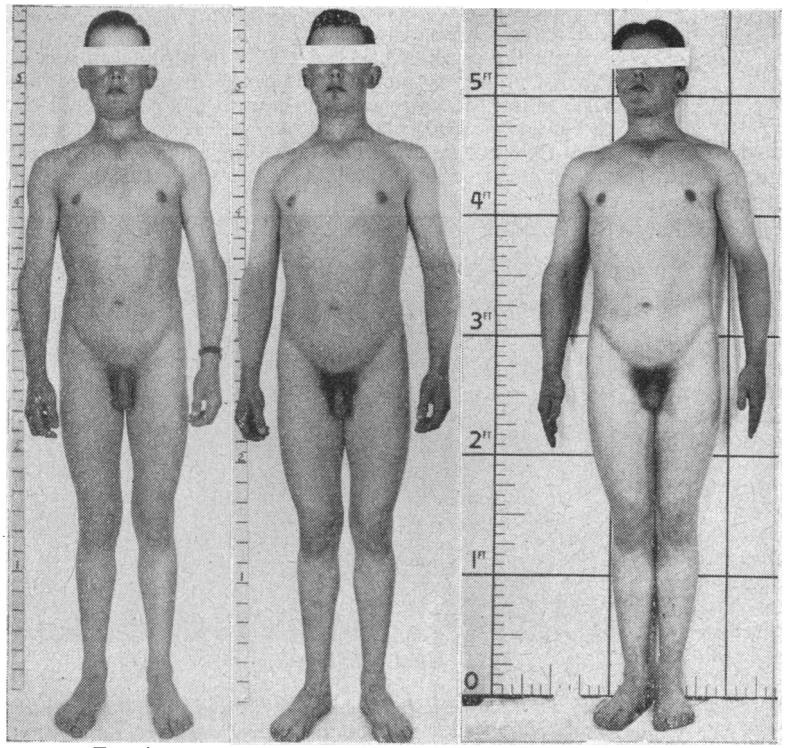

FIG. 4 FIG. 5 FIG. 6

FIG. 4.—Photograph taken on June 24, 1953. FIG. 5.—Photograph taken on May 26, 1954. FIG. 6.—Photograph taken on June 15, 1955.

was normally hirsute, and his genitalia were fully developed. He married, and in November, 1960, his wife gave birth to a normal male child.

A very rapid anabolic effect was observed in his growth after starting androgen treatment, and the growth chart (Fig. 8) showed an increase in height of 3¾ in. (9.5 cm.) in the first year, with a gradual levelling off. Height is also plotted against skeletal age. Predicted heights are also shown, and after one and three quarter years of treatment this had fallen from 70 in. (178 cm.) to 67 in. (170 cm.), revealing a marked maturation effect on the epiphyses after intensive and prolonged androgen treatment.

There was also a very steep increase in weight due to muscular development, but when he was finally persuaded to stop eating any flour there was a further acceleration in weight gain. His weight, however, fell after the third year of treatment when he admitted to eating bread again. At this stage gluten-free flour was available, and immediately his weight began to soar, and was maintained at about 12 st. 10 lb. (81 kg.).

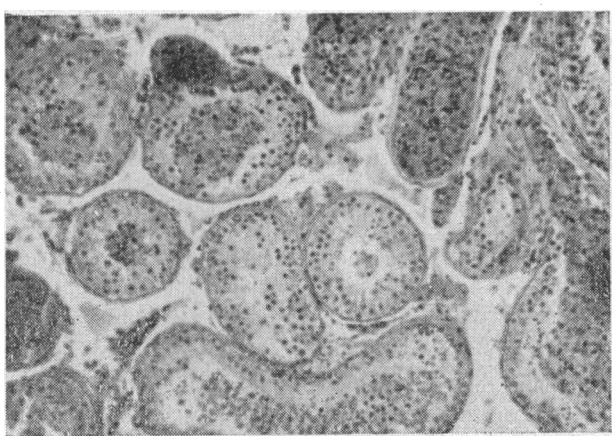

FIG. 7.—Testicular biopsy in 1958. (×110.)

Serial *x*-ray films showed that his skeletal age when first seen was 13 years, and even though he was being given intensive androgen treatment there was no marked acceleration of maturation until he stopped eating flour after one year, and the skeletal age then advanced from 14 to 16 years in the second year of treatment.

There seems little doubt in this case that, although androgens produced a considerable anabolic and growth-stimulating effect, the ultimate improvement in weight gain occurred when gluten-free flour was incorporated in the diet.

Summary

The case of a youth of 18½ years with infantilism due to the malabsorption syndrome is described, with a follow-up record of his response to continued androgen treatment during three periods —on normal diet, with restriction of wheat flour, and finally on a diet containing gluten-free flour. While on continuous androgens for five and a half years adult growth and development occurred with normal spermatogenesis. The final test of his fertility was achieved by the birth of a son to his wife, eight years after his starting treatment.

I am indebted to Professor A. C. Frazer for his comments, and to Dr. H. J. Eastes for the final follow-up information. My thanks are due to the department of medical photo-

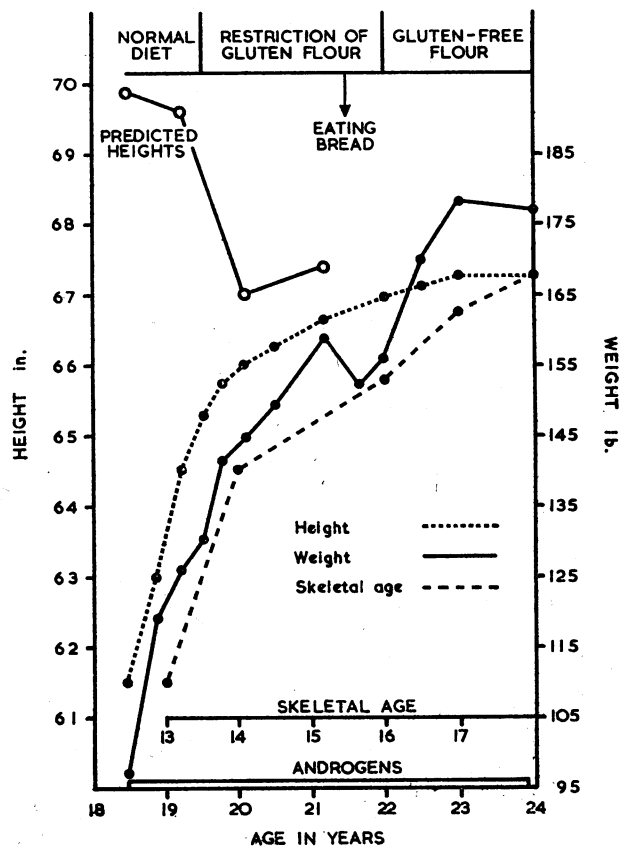

FIG. 8.—Growth chart.

graphy for the clinical pictures, to Professor T. F. Hewer for facilities for microphotography, and to Dr. A. L. Taylor for the sections. Supplies of testosterone isobutyrate were kindly made by Messrs. Ciba, and testosterone phenylpropionate by Organon Laboratories.

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CONTROLLED TRIAL OF HYPNOSIS IN THE SYMPTOMATIC TREATMENT OF ASTHMA

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Hypnotism has been used as a method of treatment for various psychoneuroses and in psychosomatic disorders for hundreds if not thousands of years. Varying reports about its efficacy in the treatment of asthma have recently appeared in the literature. Magonet (1955), Fry (1957), Ambrose and Newbold (1958), and Meares (1960) have all claimed good symptomatic relief for even the most severe cases of asthma, and Stewart (1957) reported nine complete remissions out of 12 cases of asthma, with partial remissions in two. It is clear that what has been described by these previous publications has been based on clinical impressions and there had been no properly controlled studies. Furthermore, the authors employed various degrees of psychotherapy with their hypnotic suggestions, most insisting that psychotherapy was an essential part of the treatment.

Morrison Smith and Burns (1960), in the only controlled study yet published, found that hypnotic suggestion failed to give any improvement, either immediate or delayed, in a series of 25 children. However, their treatment extended over a period of a month only.

This paper sets out to assess, in a controlled study over a longer period, the value of suggestion in the hypnotic state against suggestion produced by any new method of symptomatic treatment.

Method

Two groups of asthmatic subjects, allocated by random selection, were treated as out-patients for six months, after one month's observation; one group was treated by hypnosis, and another, to serve as a control, was given a bronchodilator new to the patients. Intake to the trial lasted for 12 months—from October, 1959, to September, 1960.

Patients Accepted.—Patients were new to the asthma clinics, and were invited to take part in the trial on arrival. Subjects of any age and either sex were eligible; all declared themselves willing to undergo hypnosis or to accept a new drug; asthma had to be present for at least one year. Patients were excluded who had repeated attacks of bronchitis or who produced regularly more than 2 oz. (60 ml.) of sputum daily; so were subjects with emphysema or pulmonary fibrosis as seen on an *x*-ray film, subjects with bronchiectasis demonstrated by bronchography, and those with a history of earlier psychotic breakdown. No patient who was on continuous treatment would be acceptable to the trial and in fact no steroids were employed during it.

Assessments at Start of Observation Month.—When a patient had been accepted notes were made on whether the asthma was triggered off by known antigens, infections, or physical or emotional factors. Degrees of severity of asthma were recorded as: mild, those whose main symptom was a non-continuous wheeze and who had experienced fewer than two severe attacks a year; medium—cases with 2 to 12 severe attacks a year; or severe—cases with uninterrupted spasm or more than 12 severe attacks a year. An attack was defined as spasm severe enough to prevent work, school attendance, or other normal activities. Notes were also made on the length of asthmatic history, and season in which attacks were worse. Patients were examined and *x*-rayed, and eosinophils were sought in blood and sputum. They were then issued with a diary and instructed in a simple coding technique similar to that employed successfully in chronic bronchitis trials (Waller *et al.*, 1957; Francis and Spicer, 1960). They were instructed to write two letters each day. One related to wheeziness: A=absence of wheeze (arbitrarily assigned a score of 0), B=occasional wheezes (score 1), C=wheezing for two hours or more (score 2), D=attack of asthma (score 3). The second letter related to drug (tablet or inhaler) employed as a relief when spasm occurred—recorded as T (tablet) or P (pump), with the number of times used each day. The patients were told to make these diary entries daily while living what for them was a normal life. Each patient was seen briefly half-way through the observation month, only to ascertain that diary recordings were being entered accurately and without difficulty.

After the observation month all continued to take emergency bronchodilators, controls now employing the newly issued ones and patients in the hypnosis group using what they had previously used; and daily diary-recording continued.