culture are given as dpm of total incorporated radioactive thymidine. In the initial phase of the disease, before prednisone therapy began, lymphocytes showed depressed responses to phytohaemagglutinin and in the mixed lymphocyte culture. Both tests were normal during the period of recovery in hospital and remained so thereafter.

Discussion

This patient developed pulmonary candidiasis in the absence of common predisposing factors. Her immune system, however, was temporarily compromised. The cellular system was functionally deficient during the initial phase of the disease, as shown *in vivo* by negative responses to skin tests with candidine and tuberculin, and *in vitro* by abnormal stimulation of lymphocytes with phytohaemagglutinin and in the mixed lymphocyte culture. All these reactions returned to normal with clinical recovery. The humoral immune system was also transitorily abnormal, as shown by the lack of rise of *C. albicans* haemagglutinating antibodies for 10 months, with a subsequent rise to titres of 1:20. Such a specific lack of antibody formation against *C. albicans* in systemic candidiasis has not been observed before (Müller, 1972).

We suggest that the preceding respiratory infection, which was probably viral in nature, was responsible for the transitory cellular immune deficiency, since depression of cellular immunity is known to occur in several viral infections (Wheelock, Toy, and Stjernholm, 1971). The humoral deficiency occurred either independently or was secondary to the cellular defect as discussed by Mitchell, Mishell, and Herzenberg (1971).

The successful treatment of this life-threatening fungal pneumonia with 5-fluorocytosine is noteworthy.

Summary

Severe pulmonary infection with *C. albicans* developed in a previously healthy girl, in the absence of any condition known to predispose to fungal infection. In a critical stage of the illness she was treated with 5-fluorocytosine (100 mg/kg per day orally), and thereafter recovered completely.

Immunological studies showed that the patient's cellular and humoral immune systems were transitorily depressed. A viral infection preceding the mycotic invasion was a possible cause of the temporary immune deficiency.

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The low birthweight African baby

About 10 years ago Gruenwald (1963) clearly differentiated two types of low birthweight babies—those whose birthweight was low because of true prematurity, and those who had suffered intra-uterine growth retardation and were consequently small for gestational age. This concept has since been elaborated upon by many workers (Battaglia and Lubchenco, 1967; Yerushalmy, 1967; Ounsted, 1968) and forms the basis for all modern studies on this subject. The incidence of the two groups is well established in advanced socioeconomic communities (Butler and Bonham, 1963; Gruenwald, 1966), but no evaluation has been carried out in an underprivileged African community.

The following is a survey of the relative incidence of the two types of low birthweight babies in an African subeconomic community and an assessment of the significance of known aetiological factors in these cases.

Materials and methods

Baragwanath Hospital serves an African population exclusively; of 18,000 newborns annually, 3500 (19.5%) weigh less than 2.5 kg. This has necessitated the

establishment of special wards to accommodate the large number of low birthweight babies, and even then the pressure on beds is such that only those below 2 kg can be hospitalized. Special techniques are involved in the management of these babies (Kahn, Wayburne, and Fouche 1954).

The material of this study comprised 250 low birthweight babies who were investigated over 8 months, between November 1971 and June 1972. Of these, 110 (44%) were males and 140 (56%) were females. The group includes all cases admitted to one of the two premature baby units at the hospital. Babies dying within the first few hours of life and therefore before admission to the premature baby unit were not included in the study. These comprised 3% of the total number of low birthweight babies.

Because of the lack of sophistication in this population, information regarding the last menstrual period is unreliable and an assessment of gestational age was therefore based on the 21 criteria described by Dubowitz, Dubowitz, and Goldberg (1970). Full physical examination was carried out in each case with a particular view to determining the presence of congenital anomalies.

An obstetric history was obtained to determine the incidence of infections and toxæmia of pregnancy. Mothers were questioned about smoking habits and a

clinical assessment was made of their nutritional status, particularly the presence of pellagra, scurvy, and nutritional oedema.

Wassermann reactions were carried out randomly in 204 of the mothers.

Results

All cases studied are shown in the Fig., reflecting the relation of birthweight to gestational age of Battaglia and Lubchenco (1967). 182 (73%) of the babies were small for gestational age, 71 (39%) males and 111 (61%) females; while 68 (27%) were appropriate for gestational age, 39 (57%) males and 29 (43%) females.

Toxaemia of pregnancy had been present in 23 mothers (9%). Of these, 20 had babies who were small for gestational age. This comprised 11% of all the mothers with babies who were small for gestational age. 3 of the mothers with toxæmia had babies who were appropriate for gestational age and this comprised 4% of all the mothers whose babies were appropriate for gestational age.

Of the 204 mothers who were serologically tested for syphilis 33 (16%) had positive reactions. 146

FIG.—250 cases plotted on chart relating birthweight to gestational age (Battaglia and Lubchenco, 1967).

had babies who were small for gestational age, 22 (15%) of these mothers being serologically positive, and 58 had babies who were appropriate for gestational age, 11 (19%) of these being serologically positive.

Sixty-six (26%) of the babies were twins. 58 occurred in the group that was small for gestational age, comprising 32% of all the babies in this group; 8 occurred in the group that was appropriate for gestational age, comprising 12% of all the babies in this group.

Four of the babies had significant congenital anomalies; 1 with Down's syndrome, 1 with microcephaly, and 2 with congenital heart anomalies. 3 were small for gestational age and 1 was appropriate for gestational age.

None of the mothers in the entire group admitted to smoking more than 5 cigarettes per day. Only 3 of the mothers had overt malnutrition; 2 had mild pellagrous changes, and 1 had slight nutritional oedema.

Discussion

This study clearly shows that the majority of the low birthweight infants born in this population group (73%) have experienced intrauterine growth retardation and are small for their gestational age. This is at striking variance with the relatively low incidence in sophisticated population groups (Battaglia and Lubchenco, 1967; Yerushalmy, 1967).

It is noteworthy that this study shows a greater proportion of girls in the small-for-gestational-age group. This is in keeping with Ounsted's findings (1968); she postulates that as female fetuses grow more slowly than male fetuses, any group of babies that is small for gestational age is likely to be biased in favour of females.

In evaluating the possible aetiological factors for this high incidence of babies who are small for gestational age, certain features are evident. Toxaemia of pregnancy is not a very significant factor here, though it is one of the commonest single known factors in the aetiology of small-for-gestational-age babies in other population groups (Gruenwald, 1963). It occurred in 9% of all our mothers and in only 11% of those mothers who had babies who were small for gestational age.

Syphilis, which is a relatively common intrauterine infection in our population group, appeared to play no part in the aetiology of babies who were small for gestational age. Positive serological tests occurred in 16% of the mothers who were tested. Only 3 of these had babies who had clinical stigmata

of congenital syphilis. The incidence of positive serological tests was virtually the same, however, in mothers whose babies were small or appropriate for gestational age.

There seems little doubt that multiple pregnancy contributed significantly to the high incidence of babies who were small for gestational age. 32% of these babies were twins as opposed to 12% who were appropriate for gestational age.

However, apart from the multiple pregnancy group, there still remains a large group of small-for-gestational-age babies where the aetiology is unexplained. It is thus apparent that the cause of the very high incidence of these babies in this population is largely unexplained.

Although there was little overt malnutrition among the mothers in our group, there is no doubt that they come from a poor socioeconomic background where malnutrition is prevalent. However, the relation between maternal malnutrition and small-for-gestational-age babies is very controversial in published reports. Ounsted (1971) stated that the effect of poor maternal nutrition in fetal growth is surprisingly slight, and Drillien (1970) commented that severe and acute food shortage in the human female seems to result in a failure to conceive and an increase in early abortions, rather than a decrease in birthweight of those fetuses which survive long enough to be viable. These views are largely supported by the work of Smith (1947), Antonov (1947), and Gruenwald *et al.* (1967). There are, however, a number of studies (Donnelly *et al.*, 1964; Moodie *et al.*, 1970; Naeye, 1972) which suggest that poor maternal nutrition can indeed slow fetal growth rate and may be a significant factor in the aetiology of intrauterine growth retardation.

In the absence of other factors it seems likely that the high incidence of intrauterine growth retardation seen in this population relates to the poor socioeconomic background and, in particular, to nutritional factors. We are carrying out further studies to explain this.

Summary

In this study, 250 low birthweight babies coming from an under-privileged African community were analysed in terms of birthweight and gestational age. It was found that the vast majority tended to be small for gestational age and, as might have been expected, there was a greater proportion of females than males.

Aetiological factors to explain this pattern remain largely speculative. Multiple pregnancy accounted

for part of the small-for-gestational-age group, and for the rest it was thought that malnutrition was significant.

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Urinary hydroxyproline in children with growth hormone deficiency

Clinical value in diagnosis and prognosis

Although a course of exogenous human growth hormone (HGH) is known to cause a rise in the total hydroxyproline excretion of growth hormone-deficient children (see Kivirikko, 1970, for review), there have been few assessments of the value of total hydroxyproline excretion in diagnosis of growth hormone deficiency (Teller *et al.*, 1973, 3 children; Van den Brande *et al.*, 1973, 4 children), and we are not aware of any studies concerning its use in the subsequent management of these children.

The potential use of the measurement has increased recently because autoanalyser methods are available, and the total hydroxyproline:creatinine ratio (THP:Cr) in single samples of urine correlates significantly with growth velocity (Wharton, Gough, and Pennock, 1973).

This investigation was planned to study the prognostic as well as the diagnostic value of urinary THP:Cr in a further 7 growth hormone-deficient children.

Methods

Two groups of children attending the endocrine clinic at Birmingham Children's Hospital were studied.

Group 1. In this group were 7 children in whom growth hormone deficiency was suspected. Urine was collected from these children during a nitrogen retention test consisting of three equal periods; (a) baseline, (b) 3 or 5 days when the patients received HGH daily (M.R.C. Raben, batches 6-9, 10 mg nominally), (c) post-HGH period (Brown, Stimmler, and Lines, 1967). The children received a constant previously self-selected daily diet of known protein content starting 2 or 3 days before the pre-HGH period and lasting throughout the test. The dietary protein and hydroxyproline remained constant throughout the test. All urine passed was saved either in 24-hour pooled collections, starting and finishing at 10.00 a.m. daily, or as individual urine specimens. The plasma growth hormone levels after insulin hypoglycaemia (Stimmler and Brown, 1967) were measured in each child. 4 children believed to be growth hormone deficient (i.e. maximum growth hormone level below 10 μ IU/ml, a fall in nitrogen excretion during HGH greater than 30%) were given Raben HGH therapeutically for 1 year (10 IU twice weekly) and their subsequent height velocity was observed.

Group 2. In this group were 3 children receiving HGH. Random urine samples were collected from 3