with AIDS or AIDS related complex showed abnormal losses of the antibody. There were, however, two well patients and one with persistent generalised lymphadenopathy who also showed loss of antibody to core protein. It is certainly possible that these patients may subsequently develop symptoms, but none had any clinical evidence of immunosuppression at the time of writing. The importance of the reappearance of antibody to core protein observed in two patients is not clear; one had AIDS related complex, so it does not seem to reflect recovery from infection.

This small cohort of haemophiliac patients allowed us to study the antigen and antibody responses to HIV infection acquired at a known time from a single source. Although the infectious dose administered to each patient was different, much of the variability in the course of infection was clearly the result of differences in susceptibility of the patients to infection. Human leucocyte antigen and other population markers have been investigated as possible related factors (unpublished observations).

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Early growth delay in diabetic pregnancy: relation to psychomotor development at age 4

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Abstract

Ninety nine consecutive insulin dependent and 101 non-diabetic pregnant women were examined by ultrasonograph to assess early fetal growth. In 42 of the diabetic mothers and three of the non-diabetic mothers the scan showed early intrauterine growth delay. At 4-5 years of age all children available for study were evaluated by the Denver developmental screening test. Only 23 of the 34 children of diabetic mothers with early intrauterine growth delay had normal test scores compared with 46 of the 50 children of diabetic mothers with normal intrauterine growth. The children failed in personal-social development, gross motor development, and particularly in language and speech development. Children of diabetic mothers with normal early fetal growth had scores very similar to those of the children of non-diabetic mothers, of whom 76 of the 86 tested had normal scores.

This study suggests that children with a history of growth delay in early diabetic pregnancy should be screened for possible developmental impairment.

Introduction

We have shown that growth of the embryo in very early diabetic pregnancy may be impaired, so that ultrasound scanning at eight to 14 weeks shows a smaller fetus than expected from the menstrual history.¹ Such growth retarded fetuses have an increased risk of malformations.² There is clinical evidence that impaired metabolic compensation at conception and in early pregnancy may be related to early intrauterine growth delay^{1,3} as well as to malformations.⁴ This paper reports the results of the Denver developmental screening test^{5,6} in children aged 4 years with a history of fetal growth delay in early diabetic pregnancy. The study tested the hypothesis that these children would show developmental delay.

Patients and methods

During October 1976 to February 1980 ultrasound scanning (JFP) with measurement of fetal crown-rump length was performed in 99 insulin dependent diabetic mothers (about half of all diabetic pregnancies) and 101 non-diabetic mothers (2.4% of non-diabetic pregnancies). Details of these studies have been reported.^{2,7} Three fetuses of the non-diabetic mothers and 42 of the diabetic mothers were smaller than normal in early pregnancy—that is, retrospectively defined as a female fetus being seven or more days and a male fetus five or more days smaller than expected from the menstrual history.⁸ In the diabetic women delivery was induced 18 to 20 days before term. All infants of the diabetic mothers and some infants of the non-diabetic mothers were admitted to the neonatal intensive care unit.

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When the surviving children were about 4 years old an invitation to attend for examination was mailed to the families. The children, listed according to birth date, were seen by two of us (MBP and SAP). The examiners had no access to the hospital records until after the clinical study and were especially kept unaware of a history or otherwise of early intrauterine growth delay; in some instances during the interviews, however, they came to know whether the mother had diabetes or not. The Denver developmental screening test was performed in all cases. The examiners' observations were supplemented by a semistructured interview covering the parents' impression of the child's development, language and speech, attention span, clumsiness, behaviour, and problems with eating and sleeping. Whenever possible, data on children lost to follow up were obtained from the general practitioner. Further details of characteristics of the mothers and children in the study group will be reported separately.

To compare the incidence of failure in the Denver developmental screening test and its subtests the one sided Fisher exact test was used. Analysis tested the hypothesis that children of diabetic mothers with early intrauterine growth delay would show developmental delay.

Results

Eighty four children of the diabetic mothers (91% of survivors) and 86 children of the non-diabetic mothers (85%) were seen (table I). Mean ages at

TABLE I—Reasons for lack of follow up in 99 children of insulin dependent diabetic mothers and 101 children of non-diabetic mothers; relation to early intrauterine growth

	Children of diabetic mothers			Children of non-diabetic mothers
	Total	Growth delay	Normal growth	
No of fetuses	99	42	57	101
Children seen	84	34	50	86
Lost to follow up:				
Deaths	7	5	2	0
Unwilling	6	2	4	8
Living abroad	2	1	1	4
Not traced	0	0	0	3

follow up were 51.6 months (range 43-78) and 52.6 months (range 42-70) respectively. Table II shows the mothers' educational level. There was no significant difference in educational level between the diabetic mothers with early intrauterine growth delay and the diabetic mothers with normal intrauterine growth. Table III gives the results of the Denver developmental screening test. As a whole the children in the diabetic group performed only slightly worse than those in the non-diabetic group. Among the 34 children of diabetic mothers with early intrauterine growth delay, however, only 23 (67.6%) had normal test scores; by contrast, scores in the group with normal growth in early fetal life were very similar to those of the children of non-diabetic mothers. Table IV gives the parents' impressions of their children.

In evaluating the results we looked at the possible influence of neonatal factors. The mean gestational ages in the two groups of children of diabetic mothers did not differ significantly. Table V lists the children with severe neonatal problems (asphyxia, prematurity, neurological symptoms) in

TABLE II—Educational level of mothers in relation to early intrauterine growth of children

	Diabetic mothers			Non-diabetic mothers
	Total	Growth delay	Normal growth	
No of mothers	84	34	50	86
Mean age in years (range)	25.5 (17-37)			27.0 (19-35)
Education (No (%) of mothers):				
8-10 Years of school	34 (40.5)	14 (41.2)	20 (40.0)	8 (9.3)
10 Years of school and vocational training	48 (57.1)	19 (55.9)	29 (58.0)	62 (72.1)
12-13 Years of school and higher education	2 (2.4)	1 (2.9)	1 (2.0)	16 (18.6)

TABLE III—Results of Denver developmental screening test at 4 years of age in 84 children of diabetic mothers and 86 children of non-diabetic mothers; relation to early intrauterine growth. Results expressed as numbers (percentages) of children

	Children of diabetic mothers			Children of non-diabetic mothers
	Total	Growth delay	Normal growth	
No of children	84	34	50	86
Normal test scores	69 (82.1)	23 (67.6)*	46 (92.0)	76 (88.4)
Failed in personal social development	2 (2.4)	2 (5.9)	0	0
Failed in fine motor adaptive development	3 (3.6)	1 (2.9)	2 (4.0)	3 (3.5)
Failed in gross motor development	9 (10.7)	6 (17.6)	3 (6.0)	5 (5.8)
Failed in language and speech development	10 (11.9)	8 (23.5)†	2 (4.0)	5 (5.8)

*p=0.0053.
†p=0.0091.

TABLE IV—Parents' impression of their child; relation to early intrauterine growth. Results expressed as numbers (percentages) of children

	Children of diabetic mothers			Children of non-diabetic mothers
	Total	Growth delay	Normal growth	
No of children	84	34	50	86
Behaviour problems	3 (3.6)	3 (8.8)	0	3 (3.5)
Language and speech problems	23 (27.4)	8 (23.5)	15 (30.0)	4 (4.7)
Developmental problems	6 (7.1)	3 (8.8)	3 (6.0)	1 (1.2)
Other problems	9 (10.7)	5 (14.7)	4 (8.0)	1 (1.2)

TABLE V—Development in relation to neonatal complications and early intrauterine growth. Figures are numbers of children

Neonatal complications	Normal development		Retarded development*	
	Normal growth	Growth delay	Normal growth	Growth delay
Severe asphyxia	1	0	0	1
Prematurity:				
31 Weeks	1	0	1†	0
32-33 Weeks	2	0	0	0
34 Weeks	1	0	0	1
Seizures	0	2‡	0	1
Neuromuscular excitability	0	3	0	0

*Children failed in language and speech and gross motor development.
†Child also had seizures.
‡One child also had intraventricular haemorrhage.

relation to early intrauterine growth and later development. The three children of non-diabetic mothers who were smaller than normal in early pregnancy developed normally.

We have the following information on children lost to follow up. One of the three children of diabetic mothers with early intrauterine growth delay was regularly seen by a speech therapist. Two of the five children of diabetic mothers with normal intrauterine growth had developmental problems (one was seen by a speech therapist; the other had severe psychomotor retardation). One of 12 children of non-diabetic mothers had Waardenburg's syndrome.

Discussion

From other studies it appears that nearly all children who have abnormal scores in the Denver developmental screening test have developmental difficulties and are likely to have problems at school.^{9 10} On the other hand, children who are having difficulty in the classroom are generally not identified by the test. The test standardisation sample was American and the test has not been standardised for Danish children. We therefore used it as a tool for comparing groups rather than for evaluating the individual in

relation to test norms and future ability. The results of the Denver developmental screening test were not associated with the mothers' level of education or vocational training.

The difference between the parents' and our evaluation of language and speech development may be explained by the way the parents were questioned. Their answers included either problems resolved at time of follow up or problems considered by the examiner to be unimportant.

That the children of the diabetic mothers scored slightly (but not significantly) worse than the control children is in keeping with most other studies, which found a higher incidence of minor and severe cerebral dysfunction and handicap and intellectual delay in children of diabetic mothers.¹¹⁻¹⁶ Only Persson and Gentz reported normal neuropsychological development and normal IQ scores.¹⁷ Interestingly, however, in this series poor performance in the Denver developmental screening test was apparently confined to children who had been small in early fetal life. Compared with those with normal intrauterine growth these children seemed to have more problems in personal-social development, gross motor development, and language and speech development; the difference, however, was significant only for language and speech ($p=0.0091$). Allowing for neonatal problems did not change these results.

Other studies have shown poor eye and hand coordination¹⁸ and poor perceptual performance¹⁹ in 4-5 year olds who were small for dates at birth and whose intrauterine growth, monitored by serial cephalometry, had slowed before 26 weeks' gestation. Though this growth disturbance almost certainly differs from that in early diabetic pregnancy, which is not followed by impaired growth in the second or third trimester,² the findings suggest that early growth impairment compromises brain development.

Our observations underline the importance of good metabolic compensation at conception, nidation, and in early pregnancy so as to prevent early growth delay and therefore avoid disturbances in development. Children who were smaller than normal in early diabetic pregnancy should be considered at risk of possible developmental delay and be followed up so that any lack in psychomotor development may be detected and cared for.

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ONE HUNDRED YEARS AGO

We all know, and are glad to know, that an effort is being made in India to extend medical aid to native women in India who are cut off by the iron barriers of caste and custom from receiving it at the hands of male practitioners, native or foreign. An attempt is now being made to educate a class of native "women doctors" to meet this want. We have before us a copy of the scheme as promulgated in the Government *Gazette* of Calcutta, published in the *Overland Englishman* of November 29th, 1887. The details of the scheme submitted by the Director of Public Instruction are simply astounding. It is difficult to believe that anyone in the present day can have such an inadequate conception of modern medicine as to lay down such rules as are here authoritatively published by a gentleman holding the responsible position of Director of Public Instruction. According to this enlightened instructor of the public on medical education, all the preliminary knowledge required before entering on the study of medicine is the following:—"Reading and explaining a Bengali book of the standard of difficulty of Raj Krisna Mookirja's History of Bengal; writing from dictation an easy Bengali book, and arithmetic to easy fractions and simple rule of three." With this amount of mental furniture, Bengali girls, aged 16, are deemed, in the opinion of this public instructor, to be capable of entering on the study of modern medicine, and after three years of study to be turned loose, so far as we can see from the scheme before us, without examination to exercise their skill on their unfortunate fellow-creatures. Here is Sir Alfred Croft's opinion

on this extraordinary scheme:—"I am fully aware that it is by no means certain to succeed, owing to the want of education among women in Bengal and to the obstacles which social conditions impose. Material benefits would follow if, happily, it should be successful. If it fails, little or no cost is incurred and no harm done." No harm done! The scheme is cheap, "little or no cost is incurred!" That in the opinion of this educational authority is enough. The Lieutenant Governor of Bengal, not without some misgivings, has given his sanction to this dangerous experiment, not being perhaps better "instructed" than its author. But what are we to say of the medical officers, Dr. Mackenzie, Surgeon-Major Chundru, and Surgeon-Major Coates, "who are in favour of trying the system." The least we can say is that in giving even a qualified assent to this scheme, they are as much misled as its author and the high official who has sanctioned it. They may plead Dr. Johnson's frank excuse when he fell into error on some literary matter, "Ignorance, Sir, sheer ignorance," but if they are ashamed to offer such a poor plea, as well they may be, then any other excuse they can offer for their weakness in giving assent to such a scheme must be inadequate. We are glad to see that other members of the profession, although their names are not given, had sense and courage enough to withhold their consent from the vain attempt to graft on the education of a school board monitor of a child's class even the simplest elements of the healing art.

(*British Medical Journal* 1888;ii:33)