Nevertheless, the eosinophil level seemed to be of only slight prognostic significance, since it was low in all acutely ill patients even when it was apparent from the nature of their illness that they were not critically ill. The rise in eosinophils usually lagged behind the appearance of clinical improvement, similar to the delayed fall seen in stress.

However, a rising level of eosinophils in a patient who continues to appear moribund is a good prognostic sign. This was recognized by clinicians years ago (Sodeman, 1950).

In rare instances a very low level may be an indication of impending death in a patient in whom this is not apparent clinically. This occurred in two of our patients in whom an eosinopenia was discovered before the approach of death was apparent.

This study is limited, but is presented in order to stimulate further exploration into the changes which take place in the organism before death. A larger group of terminal patients should be investigated in an attempt to correlate the histological appearance of the adrenals with the level of corticoid secretion and the eosinophil level as well as any other adrenal functional studies which may be available. This should yield valuable information about the hormonal changes occurring at the end of the exhaustion stage of the general adaptation syndrome.

Summary

A carefully controlled series of 50 moribund patients suffering from a variety of diseases was followed by serial eosinophil counts until death. In 47 (94%) the eosinophil count fell to zero or close to zero and remained so until death. Suddenness of death seemed to be an important factor in the three patients who failed to develop an eosinopenia. The eosinophil count rose from low levels to normal in 12 other patients who recovered from the moribund state.

This study indicates that the adrenal cortex apparently does not fail during prolonged stress, but continues to show hyperactivity up to the very moment of death; consequently supportive therapy with cortical substances is not indicated in terminal states.

The eosinophil count seems to be of only limited prognostic significance in such cases, since changes usually accompany or lag behind the clinical findings rather than precede them.

I am grateful to Dr. Milton Ackerman, pathologist at the Atlantic City Hospital, for his consistent co-operation and help during the course of this work. I am indebted to Miss Evelyn Kress, who did most of the eosinophil counts, and to Miss Clara Louise Kuehn, who prepared the manuscript. I also wish to express my sincere thanks to Dr. Hans Selye, Director of the Institute of Experimental Medicine, University of Montreal, Canada, for reading this paper and offering many helpful suggestions.

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THE CONDUCT OF PREGNANCY COMPLICATED BY DIABETES MELLITUS

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Most authorities advise and the majority of maternity centres practise early termination of pregnancy at about the 36th week in diabetic women. It is well recognized that intrauterine death may occur in the later weeks of pregnancy, and the aim of early termination is to remove the foetus from the harmful influence of the diabetic expectant mother. Recent work (Fouracre Barnes *et al.*, 1950) suggests that this harmful influence may be due to overactivity of the maternal anterior pituitary gland. If this is so, the foetus will have been subjected to it throughout pregnancy, and intrauterine death may represent a late effect. However, early termination of pregnancy, whilst removing the foetus from the influence of the lethal factor, produces an immature infant who has already been subjected to its harmful effects and who is less able to withstand extrauterine life than an immature infant of a normal mother.

Early Termination

Peel and Oakley (1950) recommended early termination of pregnancy. In their series of 123 diabetic pregnancies there were 12 in which intrauterine death occurred (presumably before induction of labour or caesarean section was due to be carried out). In the remaining 111 treated by premature termination of pregnancy four babies were fresh stillborn and 20 died in the neonatal period. Similar results with early termination of pregnancy were reported by White (1949) in a series of 361 diabetic pregnancies. Neonatal death is thus a large factor in the production of the total foetal death rate in diabetic pregnancies treated by early termination. Since in most clinics early termination is advised, it is not surprising that there are few recorded individual series of diabetic pregnancies which have been allowed to proceed to spontaneous termination.

In a previous article (Fouracre Barnes, 1950) an attempt was made to evaluate the results of termination against those when the pregnancy was allowed to proceed to spontaneous termination. The foetal salvage rate in 22 diabetic pregnancies terminated at 36 weeks was 41%, whereas in 23 diabetic pregnancies treated over the same period and allowed to terminate spontaneously the salvage rate was 43.5%. Thus the foetal salvage rate for the two methods of delivery was approximately the same. Although intrauterine death occurred more often when the pregnancy was allowed to proceed (43.5% as compared with 27.3%), neo-

Case No.	Age (Years)	Duration of Diabetes at Time of Pregnancy (Years)	Previous Obstetric History					Present Pregnancy					Remarks
			Date	Delivery	Duration (Wks)	Result	Wt. of Baby	Duration (Weeks)	Delivery	Wt. of Infant	Result	Feeding	
1	27	1		Nil			lb. oz.	37 1/7	Forceps	lb. oz. 7 11 1/2	A	Breast + suppl. → art. feed	
2	37	15		"				37 1/7	"	7 7	A	Breast + suppl. → art. feed	Benign hypertension
3	26	18		"				38 3/7	C.S.	6 0	A	Breast + suppl. → art. feed	C.S. for uterine inertia. Puerp. pyrexia—urinary infection
4	25	9		"				35 3/7	Spont.	8 1	A	Breast + suppl. → art. feed	Puerp. pyrexia—pleurisy, hypertension
5	27	8		"				38 4/7	"	7 11 1/2	A	Breast	Mild hypertension
6	30	10		"				41	C.S.	9 8	A	Breast + suppl. → art. feed	Hydramnios + C.S. for large baby and post-maturity
7	42	12	{ *1925 *1927 *1930 *1931 *1934 *1935 *1942	Spont.	40	A	9 8	38 3/7	Forceps	8 13	A	Breast + suppl. → art. feed	Hypertension
8	34	6	{ *1932 *1945	Spont.	40	A	11 8						
9	28	2	{ *1945	Spont.	40	A	7 0	38 3/7	"	9 6	ND	—	Toxaemia Venous thrombosis at 37 weeks—treated with anticoagulants. Baby died after 1/2 hr. & punctate haem. of brain
10	22	7		Nil									
11	28	2		See Case 1				38 4/7	"	9 14	A	Breast → art. feed	
12	29	7		Nil				37 1/7	S.I.	3 8 1/2	M	—	Intrauterine death at 33 6/7 week
13	36	4	{ *1932 *1934 *1936 *1940 *1937 *1938 *1941 *1942 *1944	Spont.	40	A	8 12	38 5/7	Spont.	10 11	A	Breast + suppl. → art. feed	Hypertension
14	40	18	{ *1932 *1934 *1936 *1940 *1937 *1938 *1941 *1942 *1944	Spont.	40	A	8 6						
15	29	7		See Case 12				38 1/7	"	6 6 1/2	M	—	Intrauterine death at 37 4/7 week
16	26	1		Nil				40	"	8 13 1/2	A	Breast → art. feed	Hypertension
17	30	4		See Case 9				40 1/7	C.S.	9 15 1/2	A	Breast	C.S. for severe toxaemia
18	36	10		Nil				37 6/7	Spont.	7 4 1/2	A	Breast → art. feed	Hypertension
19	22	1		Nil				35 5/7	Forceps	8 13 1/2	M	—	Intrauterine death at 35 3/7 weeks—Hydramnios + C.S. for severe toxaemia
20	37	17	{ 1941 1942 1944 1946	C.S.	36	ND	7 7 1/2	40 1/7	"	11 6	A	Breast + suppl. → breast	Hydramnios +
21	28	11	{ 1941 1942 1944 1946	C.S.	36	ND	7 11						
22	27	2		Nil				39 3/7	Forceps	8 8	A	Breast + suppl. → art. feed	Hydramnios +
23	25	10		See Case 10				38 3/7	Spont.	9 13 1/2	A	Breast + suppl. → art. feed	
24	27	6	1949	S.I.	36	A	7 8	37	"	7 15	A	Breast + suppl. → art. feed	Toxaemia
								37 6/7	"	8 11	A	Breast + suppl. → breast	Hydramnios

C.S.=Caesarean section. M=Macerated. ND=Neonatal death. S.I.=Surgical induction of labour. A=Alive. SB=Stillborn.
* = Prediabetic pregnancy.

natal death was less frequently seen (16.6% as compared with 43.8%). Although these numbers are small, they suggest that early termination does not alter the outcome of pregnancy, but results in neonatal death of the infant rather than in a stillborn foetus.

As a result of these findings it was decided to allow pregnant diabetic women to proceed to spontaneous termination or delivery at term, except where some complication arose necessitating termination for the sake of the mother. Twenty-four diabetic pregnancies treated in this manner at University College Hospital since 1947 are recorded (see Table).

Present Series

We have admitted our patients at the 35th week of pregnancy in order that their obstetric and diabetic states may be carefully observed. In practice it has been found that the diabetes is easily controllable up to term, and in fact the insulin requirement often falls markedly a day or two before delivery (Fouracre Barns and Morgans, 1949). No difficulties have arisen with the diabetes when caesarean section has been necessary. However, during some long and difficult labours associated with the large baby diabetic control has been difficult to maintain, and very careful observation of these patients has been necessary. The majority of the patients received hormone therapy in the form of stilboestrol. This was given in tablet form by mouth from the time of the patient's first attendance, and the daily dose was gradually increased so that she received 160 mg. a day at the 36th week of pregnancy.

In only one patient was it necessary to terminate the pregnancy prematurely. This was done at the 36th week by caesarean section on account of severe toxaemia (see Case 19). There have been one neonatal death and three intrauterine deaths, the details of which are given in the table. Two of the mothers of these four unsuccessful pregnancies each had a subsequent pregnancy with the birth of a live infant (Cases 15 and 17). It will be noted that two of the three intrauterine deaths occurred before the 36th week of pregnancy, the usual time for inducing labour in diabetic pregnancies.

Two other patients were of special interest. One patient (Case 20) had three caesarean sections at the 36th to 37th week of pregnancy prior to 1947. On each occasion the baby lived a few hours only. Recently she was allowed to proceed to term, and caesarean section was carried out one day after the expected date of delivery on account of the large baby and the previous caesarean sections. She was delivered of a live baby weighing 11 lb. 6 oz. (5.1 kg.), which survived. In 1946 the other mother (Case 21) had a stillborn infant following a pregnancy terminated at the 36th week. Death was due to cerebral haemorrhage. Recently she was allowed to proceed to spontaneous termination, which occurred at the 39th week of pregnancy, and she was delivered by forceps of a live baby.

It will be seen from the table that a large proportion of our mothers went into spontaneous premature labour at the 37th to 39th week. It seems possible, therefore, that the diabetic mother herself cuts short the influence of the lethal

factor in such cases and yet allows the infant the longest possible time *in utero* compatible with intrauterine survival.

Cases 15, 17, 20, and 21 had had a previous diabetic pregnancy which resulted in a dead infant. The cause of death on two occasions was cerebral haemorrhage (Cases 17 and 21), but in Cases 15 and 20 the diabetic lethal factor was responsible for the foetal deaths. It follows, therefore, that a diabetic pregnancy which results in the death of the foetus need not be followed by subsequent unsuccessful diabetic pregnancies.

It is well recognized that the diabetic mother has difficulty in breast-feeding her infant. The cause of this is obscure. There is, however, one factor which tends to hinder her. It is that the immature baby does not suck as well as the full-time baby, and hence the earlier the termination of pregnancy the more likely is it that breast-feeding will not be established. One of our patients (Case 24) illustrates this point. In 1949, at another hospital, she was delivered prematurely at the 36th week, by induction of labour, of a baby weighing 7 lb. 8 oz. (3.4 kg.). The baby was difficult to rear in the early weeks and she was unable to breast-feed it after three weeks' energetic trial. Recently she was delivered spontaneously at the end of the 37th week of a baby weighing 8 lb. 11 oz. (3.9 kg.). This baby was at the breast within 48 hours, and breast-feeding was well established during the second week of the puerperium.

The danger of neonatal death in immature infants of diabetic mothers is real. Premature induction of labour increases this danger and produces an infant which is difficult to rear. On the other hand, by allowing the pregnancy to proceed the possibility of difficult labour and disproportion becomes greater as term is approached. In the present series forceps were needed for delivery on seven occasions and caesarean section was performed twice on account of a large infant. The obstetrician's task, therefore, of producing the less immature live infant is increased while that of the paediatrician is decreased.

Conclusion

The foetal salvage rate in this small series (20 out of 24) would appear to justify the course taken of not prematurely terminating the pregnancy. Our improved results are possibly due to the hormone therapy which these mothers have received. It is, however, more likely to be due to the close co-operation between physician, paediatrician, and obstetrician in the care of the diabetic mothers and their offspring.

We should like to record our gratitude to Professor W. C. W. Nixon, director of the obstetric unit, for permission to report these cases, and to the members of the paediatric unit under the direction of Dr. B. E. Schlesinger for their invaluable help in the care of the infants.

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In accordance with an international agreement the Government of the United Kingdom can insist on the international recognition of yellow fever inoculations performed in this country only if: (a) they are done at a centre or by a medical practitioner specifically authorized by them for that purpose; (b) the certificate is given on one of the international forms specially supplied to such centre or practitioner; (c) a vaccine approved by W.H.O. is used for the inoculation. Certificates issued other than in accordance with these conditions will probably not be accepted by foreign health authorities. A list of places where yellow fever inoculation is given free of charge will be found on the back of the notice to travellers issued with all renewals of passports or can be obtained from travel agencies or the Ministry of Health.

TWO CASES OF DIABETES MELLITUS IN INFANTS UNDER 1 YEAR

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Although the onset of diabetes mellitus occurs in 5 to 6% of cases in the first ten years of life, it is rare for the disease to develop in infancy. John (1946) listed 85 cases of diabetes in infants under 1 year. Schwartzman, Crusius, and Beirne (1947), in a more detailed review of the world literature, summarized 57 cases under 1 year and gave details of most of them. The first to survive in order of time was the 27th they describe, and was reported in 1925. Since then only 11 have survived out of the 24 of which adequate details are given. It is not easy to judge how many of these cases had passed into diabetic coma.

In the following two cases which survived, the symptoms began when the patients were under 1 year old.

Case 1

A baby boy aged 13½ months was admitted to hospital on June 18, 1950, with severe glycosuria and ketosis. His brother, aged 10, regularly attended the diabetic clinic, and their parents showed great intelligence and skill in keeping his diabetes stable. Neither of them was diabetic, and there was no known diabetes in either of their families.

The baby weighed 7½ lb. (3.3 kg.) at birth on May 3, 1949. He did well, weighed 22 lb. (10 kg.) in December, 1949, and was weaned by February, 1950. A few hours after receiving a second dose of antidiphtheria vaccine on March 19 he lost his appetite. He began to vomit solid food and became very constipated. This continued, and by the time of admission he had lost 8 lb. (3.6 kg.). By the middle of May he had become very thirsty, and developed polyuria, and by early June he had become so feeble that he fell over if sat upright. Just before admission his parents tested his urine, and found a full reduction of Benedict's solution.

On admission he had a good colour, but was drowsy and very fretful. The eye tension was lowered, the tongue dry, and the skin dry and inelastic. He was teething, but there was no evidence of infection. His temperature was 96° F. (35.6° C.), pulse 108, and respirations 24. The urine gave full reduction of Benedict's solution and strongly positive Rothera and Gerhardt reactions. The blood sugar was 440 mg. per 100 ml.

He was given either 10 or 15 units of soluble insulin subcutaneously at six-hourly intervals, and at 10.30 a.m. next day the blood sugar was 90 mg. and the ketosis was receding. The next insulin was given 11 hours later, when the blood sugar had risen to 540 mg. per 100 ml. After a short time on six-hourly insulin again it was found that eight-hourly doses (8 a.m., 4 p.m., and 12 midnight) controlled him adequately. The night dose was only two units, but this made all the difference between a blue and orange early-morning urine test. He was not weighed on admission, but was 22½ lb. (10.3 kg.) 10 days later. He was given 130 g. carbohydrate diet, which he took well. A variety of combinations of insulin were tried in order to eliminate three