All comparisons of the foetal loss rates between the various groups and the control group discussed above have been subject to the χ^2 test and have been found to be statistically significant.

Discussion

Our observation of an abnormally high foetal loss rate for pre-diabetic periods of up to 20 years confirms the findings of Miller, Hurwitz, and Kuder (1944) and Miller (1945). Our observation of a maximum foetal loss rate among young diabetics in the years immediately before the diagnosis of diabetes still further confirms the findings of these workers.

The similarity of the foetal loss rate in the immediate pre-diabetic phase and in the post-diabetic period raises a doubt whether the immediate pre-diabetic period is in fact pre-diabetic. Herzstein and Dolger (1946) point out that the 0-5-year period is not wholly pre-diabetic, as it may include an unspecified number of undiagnosed diabetics, since it is never easy to determine the exact date of onset of diabetes. We cannot entirely accept this view, for the following reasons: first, in the majority of young diabetics the disease comes on acutely, leaving little doubt about its approximate date of onset; secondly, the features of diabetes, such as glycosuria, polyuria, loss of weight, etc., tend to be aggravated by pregnancy, and it therefore seems unlikely that had clinical diabetes been present during the 0-2-year period it would have been completely overlooked by the obstetrician in the majority of cases; lastly, and most important, Table III shows a significant increase in the foetal loss rate for at least a decade before the diagnosis of diabetes was made, and it is impossible to believe that these young patients were suffering from undiagnosed diabetes for as long as five years.

It seems, therefore, that there is a factor conducive to foetal mortality which may be active for as long as 20 years before the diagnosis of diabetes and very active for the immediately preceding five years. The precise nature of this factor still remains uncertain. It is probable that the factors responsible for the large babies, the high foetal loss rate, and the ensuing maternal diabetes have a common basis in some general metabolic disturbance in the mother, and that the features of clinical diabetes, such as polyuria, glycosuria, thirst, etc., are a very late stage of this metabolic disturbance, an early feature of which is a high foetal loss rate.

Summary

Insulin therapy has increased the fertility of diabetic women and has made pregnancy a relatively safe proceeding for the mother, but has failed to produce a very significant decrease in the foetal mortality rate in diabetic women.

The pre-diabetic obstetric histories of 165 women in whom diabetes was diagnosed between the ages of 25 and 69 have been analysed. The overall pre-diabetic foetal loss rate was twice the non-diabetic control rate.

In those patients in whom diabetes was diagnosed before the age of 45 the pre-diabetic foetal loss rate was three times the non-diabetic control rate. The maximum pre-diabetic foetal loss rate, which was six times the control rate, occurred in the two years immediately before the diagnosis of diabetes was made and was as high as that observed after the onset of clinical diabetes.

In those patients in whom diabetes was diagnosed after the age of 45 the pre-diabetic foetal loss rate, which in this group was one and a half times the non-diabetic control rate, failed to show the dramatic rise immediately before the diagnosis of diabetes observed in the younger group of women.

There appeared to be no relation between the severity of the ensuing diabetes and the pre-diabetic foetal loss rate.

The onset of clinical diabetes may be a late stage in some general metabolic disturbance an early feature of which is a high foetal loss rate.

We are greatly indebted to Mr. George Waugh, F.F.A., A.I.A., F.S.S., for his invaluable work, under the aegis of the Scottish Statistical Research Bureau, in collating and analysing the data in this paper, and to Dr. C. A. Bignold, Medical Officer of Health for Ayr County, for so kindly putting his maternity service records at our disposal.

REFERENCES

- Allen, E. (1939). *Amer. J. Obstet. Gynec.*, **38**, 982.
 Bandstrup, E., and Okkels, H. (1938). *Acta obstet. gynec. scand.*, **18**, 136.
 Barns, H. H. F. (1941). *J. Obstet. Gynaec. Brit. Emp.*, **48**, 707.
 Bennowitz, H. G. (1826). Quoted by Skipper, E. (1923).
 Dolger, H., and Herzstein, J. (1944). *J. Amer. med. Ass.*, **125**, 931.
 Duncan, J. Matthews (1882). *Trans. Obstet. Soc. Lond.*, **24**, 256.
 Eastman, N. J. (1946). *Obstet. Gynec. Survey*, **1**, 3.
 Henley, W. E. (1947). *N.Z. med. J.*, **46**, 386.
 Herrick, W. W., and Tillman, A. J. B. (1938). *Surg. Obstet. Gynec.*, **66**, 37.
 Herzstein, J., and Dolger, H. (1946). *Amer. J. Obstet. Gynec.*, **51**, 420.
 Kramer, D. W. (1935). *Ibid.*, **30**, 68.
 Lawrence, R. D., and Oakley, W. (1942). *Quart. J. med.*, n.s. **11**, 45.
 Lecorché, E. (1885). *Ann. Gynec. Obstét.*, **24**, 257.
 Mengert, W. F., and Laughlin, K. A. (1939). *Surg. Obstet. Gynec.*, **69**, 615.
 Miller, H. C. (1945). *New Engl. J. Med.*, **233**, 376.
 — (1946). *J. Amer. med. Ass.*, **131**, 700.
 — Hurwitz, D., and Kuder, K. (1944). *Ibid.*, **124**, 271.
 Offergeld, H. (1908). *Arch. Gynäk.*, **86**, 160.
 Ronsheim, J. (1933). *Amer. J. Obstet. Gynec.*, **25**, 710.
 Shir, M. M. (1939). *Ibid.*, **37**, 1032.
 Skipper, E. (1933). *Quart. J. Med.*, n.s. **2**, 353.
 Von Noorden, C. (1909). Quoted by Eastman, N. J. (1946).
 White, P. (1946). In Joslin and others' *Treatment of Diabetes Mellitus*, 8th ed., p. 777. Kimpton, London.
 Williams, J. Whitridge (1909). *Amer. J. med. Sci.*, **137**, 1.

PREGNANCY COMPLICATED BY DIABETES MELLITUS

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During the past twenty years 45 patients with definite diabetes mellitus have been observed in 58 pregnancies at University College Hospital. The incidence was 1 in 580 deliveries. This high figure is due to the fact that a number of the patients were referred to the Obstetric Unit from the Diabetic Clinic of the hospital. Pregnancy in the diabetic is an infrequent occurrence, and is in part due to the decreased fertility of the diabetic patient and in part to the fact that diabetes is much commoner in women during the latter portion of the child-bearing period, when pregnancy is less frequent (Barns, 1941).

In 48 of the pregnancies diabetes had been diagnosed and treated by a physician before the onset of the pregnancy. In the remaining 10 pregnancies the diagnosis was made during the pregnancy on the strength of a fasting blood sugar of 130 mg. per 100 ml. or over, a typical blood-sugar curve, and history of diabetic symptoms. The diagnosis was subsequently confirmed after the pregnancy. Hence in approximately one-quarter of the patients pregnancy appeared to unmask the condition of diabetes by precipitating the onset of symptoms or actually to initiate the clinical onset of the disease, which persisted, although usually in a milder form, after the pregnancy in question.

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Insulin Requirements During Pregnancy

In this series of 58 pregnancies treatment was with diet alone in 7 cases and with diet and insulin in 51. Of 19 cases under insulin treatment in which the diet remained unchanged throughout the pregnancy and the puerperium (alteration being made only during the labour), nine required more insulin as the pregnancy advanced up to the time of delivery; nine required more up to two to four weeks before delivery, after which a gradual and slight fall in insulin requirements occurred until delivery; and the remaining patient needed no alteration in the insulin dosage throughout pregnancy. Of the 19 patients 17 showed a marked fall in the insulin requirements after delivery; the other two showed no change. These figures support the contention that carbohydrate tolerance usually diminishes as pregnancy advances (Duncan and Fetter, 1934; Skipper, 1933).

It has been thought that any increase in the carbohydrate tolerance acquired during pregnancy was due to the transference of insulin from the foetus to the mother. Skipper (1933) reviewed the evidence and concluded that there was no good reason to believe that such improvement in the carbohydrate tolerance was due to this cause. It should be mentioned that eight of the nine patients who showed this improvement just before delivery were receiving oestrogen therapy at the time, and this may have some significance. Some writers claim that oestrogens improve the glucose tolerance in women developing diabetes at about the menopause (Gessler, Halsted, and Stetson, 1939; Spiegelman, 1940). Lawrence and Madders (1941), using small doses of stilboestrol on a few patients of menopausal age, failed to confirm these findings. In the present series the pregnant diabetics who were treated with oestrogens received ten times the amount of stilboestrol given to the patients of Lawrence and Madders.

The marked and abrupt fall in the insulin requirements after delivery in the majority of patients must be emphasized, for there is the obvious danger that the patient will develop hypoglycaemic coma if this fact is neglected.

Complications of Pregnancy

Hydramnios.—There appears to be a definite and pronounced tendency for the pregnant diabetic to develop hydramnios of the chronic variety with its added complications. In 17 of the pregnancies of this series clinical hydramnios developed—an incidence of 29%.

Coma.—One patient developed diabetic coma in the 33rd week of pregnancy and was successfully treated. Another was admitted with diabetic intoxication at the 29th week. This patient was never in diabetic coma, but her diabetes was exceedingly difficult to balance on account of repeated vomiting. She died a few days after admission. Her blood pressure was 170/100 one day before death, and on the day of death she developed epileptiform convulsions which were not hypoglycaemic in nature. At necropsy there was no evidence of eclampsia or nephritis. In some patients ketosis was precipitated by the onset of urinary infection.

Two patients developed hypoglycaemic coma, and there were others who experienced hypoglycaemic symptoms in the early stage of pregnancy. This may have been related to the development of renal glycosuria, which is often found in normal pregnancy and which may be superimposed on the diabetic condition, or to the prevalence of hyperemesis in early pregnancy or to overdosage with insulin. It cannot be stressed too strongly that the care of the pregnant diabetic should be shared with a physician who will supervise the treatment of the diabetes as soon as it is recognized.

Toxaemia of Late Pregnancy.—There is general agreement that the diabetic is more liable to develop late pregnancy toxaemia than the non-diabetic. The degree of this greater liability varies from three times (Mengert and Laughlin, 1939) to fifty times (White, 1937), according to different observers. On the strict standards for the classification of late pregnancy toxaemia adopted at University College Hospital, and previously outlined (Barns, 1941), there were 25 diabetic pregnancies with this complication. This gives an incidence of 43% as compared with the usual incidence of 35% obtained at University College Hospital for the non-diabetic pregnancies. The toxaemia in 12 of these 25 cases was severe enough to warrant admission to hospital, according to the standards laid down by Browne (1946). Hence the incidence of toxaemia of this severity is 20.7%, which is similar to that in diabetic pregnancies quoted by Herrick and Tillman (1938). The incidence of this severe toxaemia for all patients delivered at University College Hospital during the year 1939 was 5%. White (1935) found that the incidence of eclampsia in the diabetic was nearly 17 times that for the non-diabetic. It would therefore appear that the relative incidence of toxaemia of late pregnancy varies with the standard of severity taken for comparison, and that there is a predisposition for the pregnant diabetic to develop the more severe type of toxaemia.

Prognosis for the Mother

In the pre-insulin era a quarter of the mothers died during delivery or the puerperium and a further quarter died within two years of delivery (Williams, 1909; Offergeld, 1908). Diabetic coma was usually responsible for the maternal death. The prognosis for the mother has been considerably improved since the introduction of insulin. Skipper (1933) gave the immediate maternal mortality as 9.3%, with an additional mortality of 3.4% for the next two years. In the present series of 58 pregnancies in 45 diabetic patients there was one immediate death, to which reference has already been made above.

The diabetic is especially liable to infection of one kind or another. Provided that the diabetes is kept under proper control this tendency is reduced to a minimum. There were four pregnancies which were followed by puerperal pyrexia: two were due to urinary infection and one to pleurisy; the fourth was probably due to puerperal sepsis, but this was not definitely established by bacteriological investigation.

Walker (1927), like Skipper (1933), is of the opinion that if the diabetes is adequately controlled pregnancy does not produce a permanent increase in the severity of the condition. Observations made in this series of patients support that view. In 34 pregnancies the carbohydrate tolerance, as judged by the diet and insulin requirements before and after pregnancy, is known; in 28 (82%) it was unchanged and in six it was decreased. It is to be noted that the onset of the diabetes in these six patients occurred either within a few months of the beginning of the pregnancy or during the pregnancy (two patients).

Prognosis for the Foetus

The foetal mortality for pregnancies complicated by diabetes mellitus has remained persistently high in spite of the great advance made in the treatment of diabetes with insulin. In the pre-insulin era it was 41% (Williams, 1909). Since the introduction of insulin it has remained at approximately the same figure.

The obstetrical histories of the patients of the present series show that of 64 diabetic pregnancies 7 ended in abortion—an incidence of 10.9%. As judged from this small series it would appear that the incidence of abortion

in the pregnant diabetic is no greater than that in the non-diabetic (11.8%, Barns, 1947) or that in the woman who subsequently develops diabetes (Barns and Morgans, 1948). The high foetal mortality in the pregnant diabetic is therefore due to some unknown factor or factors which cause the death of the viable foetus and the newborn infant.

The 58 diabetic pregnancies have been divided into a first series of 43 and a second series of 15 because of a radical change in the treatment of the latter. Of the first 43 diabetic pregnancies two resulted in abortion, and in a third case the patient was evacuated (during the war years) whilst pregnant, and lost sight of. There are therefore 40 diabetic pregnancies which were followed throughout pregnancy and which continued beyond the 28th week. Of these 40 pregnancies 18 resulted in live infants, 13 ended in the birth of stillborn or macerated foetuses, and in the remaining 9 neonatal death occurred. The total late foetal mortality is therefore 55%. The cause of this high foetal mortality, consisting of intrauterine death of the viable foetus, stillbirths, and neonatal deaths, is little understood, and none of the hypotheses presented to explain it is wholly satisfactory.

Late pregnancy toxæmia in the mother, with its associated hormonal changes in the serum, has been considered by Smith *et al.* (1944) to be the cause of these foetal catastrophes. In the present series it was found that intrauterine death of the viable foetus did occur without the association of late pregnancy toxæmia, and also that neonatal death was infrequently associated with this complication in the mother. Conversely, Lawrence and Oakley (1942) found that toxæmia could exist without any accompanying foetal catastrophe. They found no support for the view that toxæmia was an important factor in the causation of the high foetal mortality in diabetic pregnancies. The foetal mortality for non-diabetic pregnancies complicated by late pregnancy toxæmia is approximately only half that for diabetic pregnancies with this complication (Barns, 1941). It would therefore appear that late pregnancy toxæmia cannot be regarded as the primary factor in the production of the high foetal mortality. The presence of this complication in the diabetic pregnancy cannot, however, be regarded as unimportant, for it may weigh the scales against a successful outcome.

Coma, diabetic or hypoglycaemic, has been incriminated in the past as a cause of intrauterine death of the viable foetus. Studies of pregnancies in women who subsequently develop diabetes have shown that there is a high foetal mortality in these pre-diabetic pregnancies which increases as the clinical onset of the diabetes is approached (Barns and Morgans, 1948; Miller, 1946). Presumably the factor responsible for these foetal deaths is the same but differs in degree before and after the onset of the diabetes, and it has been suggested that this factor might arise from the anterior pituitary lobe of the mother. It is therefore clear that if such is the case these diabetic complications cannot be the primary cause of the foetal catastrophe, for such occurs with undue frequency before diabetes develops.

Hypoglycaemia in the newborn infant has been suggested as an important cause of the high neonatal death rate in diabetic pregnancies. In six cases of the present series blood-sugar estimations of the newborn were carried out. In no case was the blood-sugar level below the normal range for newborn infants given by Ketteringham and Austin (1938), and in three of the infants so investigated neonatal death occurred. Hypoglycaemia therefore seems unlikely to be the cause of the high neonatal mortality rate, particularly as it is difficult to see why this condition should occur in the infant of the pre-diabetic, in whom there is also a high neonatal mortality rate. The blood-sugar level of the

infant of the diabetic is higher than normal when *in utero* and at birth by virtue of the raised blood sugar of the mother. There is therefore an appreciable drop in the blood sugar to the normal range in the first few hours of life, and this fall is greater than is usual in infants of non-diabetic mothers. It therefore seems reasonable, and at least can do no harm, to give the infant glucose to allow this fall to be accomplished more slowly.

Infants of diabetic mothers are larger than normal; but so, too, are those born during the pre-diabetic period of the mother, hence hyperglycaemia in the mother cannot be the cause of the gigantism, as has been suggested. The abnormal hormone picture of high serum gonadotrophin, low serum oestrin, and diminished pregnandiol excretion sometimes found in these pregnant diabetics has been thought by White *et al.* (1939) to be related to the large size of the infant. This abnormal hormone picture had been claimed by Smith and Smith (1935a, 1935b, 1937, 1940) to precede the onset of, and to accompany, late pregnancy toxæmia. Since, however, the non-diabetic pregnancy with late pregnancy toxæmia does not produce the large infant characteristic of the diabetic mother, it seems unlikely that the abnormal hormone picture is directly related to the production of the large infant. Recently the importance of the pituitary gland in this connexion has been stressed, and it has been suggested that there might be an excess of the growth hormone from the maternal anterior pituitary lobe which causes the infant of the diabetic and the pre-diabetic mother to be large (Barns and Morgans, 1948).

The incidence of congenital defects of the foetus of the diabetic mother is greater than in the non-diabetic. Comyns Berkeley *et al.* (1938) state that the incidence for pregnancies in general is 3%. There were four infants with congenital defects out of the 40 diabetic pregnancies of the first series.

In view of the good results claimed by White (1947) for hormone therapy in the diabetic pregnancies it was decided to treat a series of diabetic pregnancies with oestrogens. The therapy was used on the assumption that oestrogens might act as an anterior pituitary lobe depressant. In the past it has been the custom at University College Hospital to terminate the pregnancy just after the 36th week in order to avoid intrauterine death. Although the infants obtained were large, they were immature. This immaturity cannot be neglected as a factor likely to increase the chances of neonatal death. The first series of 40 diabetic pregnancies were so treated.

The second series of 15 diabetic pregnancies have been treated with oestrogens, and early artificial termination of the pregnancy was avoided in all but the first two cases. There was one stillbirth due to cerebral haemorrhage which occurred in one of the pregnancies terminated early, one intrauterine death, and one neonatal death. Although the series is small, the results suggest that the outlook for the foetus of the pregnant diabetic is improved by the above procedures. It is hoped to present a detailed analysis of these cases in the near future.

Summary

A series of 58 diabetic pregnancies in 45 patients is reviewed.

In the majority of patients the carbohydrate tolerance was found to diminish as pregnancy advanced. In some, however, it increased prior to delivery, and it is possible that oestrogens given therapeutically may have been a factor in this improvement.

The tendency of the pregnant diabetic to develop hydramnios is confirmed.

It was found that hypoglycaemic symptoms and coma tend to occur in early pregnancy, and ketosis and diabetic coma in the latter part of pregnancy.

There is a greater tendency for the diabetic to develop late pregnancy toxæmia than the non-diabetic, and the relative incidence varies with the standard of severity of the toxæmia taken for comparison.

The maternal prognosis is good, and pregnancy does not make the diabetes worse provided that it is well treated.

The late foetal mortality was 55% in a first series of 43 pregnancies. In a second series of 15 pregnancies in which oestrogens were given there were only three deaths. The cause of the foetal mortality is discussed, and it is suggested that the factor affecting the viability of the foetus probably arises in the maternal anterior pituitary lobe. The incidence of abortion does not appear to differ from that for non-diabetic pregnancies, and suggests, first, that diabetes mellitus is not a cause of abortion, and, secondly, that the factor which reduces foetal viability exerts its strongest influence towards the end of pregnancy.

Congenital deformities, gigantism, and hypoglycaemia of the newborn are briefly discussed, and it is suggested that the tendency to gigantism is due to an excess of the growth hormone from the maternal pituitary gland.

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REFERENCES

- Barns, H. H. Fouracre (1941). *J. Obstet. Gynaec. Brit. Emp.*, **48**, 707.
 — (1947). *British Medical Journal*, **1**, 169.
 — and Morgans, M. E. (1948). *J. Obstet. Gynaec. Brit. Emp.*, **55**, 449.
 Berkeley, Sir C., Bonney, V., and MacLeod, D. (1938). *The Abnormal in Obstetrics*, p. 103. Arnold, London.
 Browne, F. J. (1946). *Antenatal and Postnatal Care*, 6th ed., p. 384. Churchill, London.
 Duncan, G. G., and Fetter, F. (1934). *Amer. J. med. Sci.*, **187**, 347.
 Gessler, C. J., Halsted, J. A., and Stetson, R. P. (1939). *J. clin. Invest.*, **18**, 715.
 Herrick, W. W., and Tillman, A. J. B. (1938). *Surg. Gynec. Obstet.*, **66**, 37.
 Ketteringham, R. C., and Austin, B. R. (1938). *Amer. J. med. Sci.*, **195**, 318.
 Lawrence, R. D., and Madders, K. (1941). *Lancet*, **1**, 601.
 — and Oakley, W. (1942). *Quart. J. Med.*, **11** (Pt. 41), 45.
 Mengert, W. F., and Laughlin, K. A. (1939). *Surg. Gynec. Obstet.*, **69**, 615.
 Miller, H. C. (1946). *J. Pediat.*, **29**, 455.
 Offergeld, H. (1908). *Arch. Gynäk.*, **86**, 106.
 Skipper, E. (1933). *Quart. J. Med.*, **26**, 353.
 Smith, G. van S., and Smith, O. W. (1935a). *Surg. Gynec. Obstet.*, **61**, 27.
 — (1935b). *Ibid.*, **61**, 175.
 — (1937). *Amer. J. Obstet. Gynec.*, **33**, 365.
 — (1940). *Ibid.*, **39**, 405.
 — and Hurwitz, D. (1944). *Amer. J. med. Sci.*, **208**, 25.
 Spiegelman, A. R. (1940). *Ibid.*, **200**, 228.
 Walker, A. (1927). *Proc. R. Soc. Med.*, **21**, 377.
 White, P. (1935). *Surg. Gynec. Obstet.*, **61**, 324.
 — (1937). *Amer. J. Obstet. Gynec.*, **33**, 380.
 — (1947). *Penn. med. J.*, **50**, 705.
 — Titus, R. S., Joslin, E. P., and Hunt, H. (1939). *Amer. J. med. Sci.*, **198**, 482.
 Williams, J. Whitridge (1909). *Ibid.*, **137**, 1.

Another step towards closing the wartime gap in the issue of vital statistics by the Registrar-General has been taken with the publication of Part II of the *Statistical Review* for 1943. During that year in England and Wales the improvement in the birth rate following the record low figure in 1941 was maintained, the fall in the still-birth rate continued, and the number of marriages was the lowest for seventeen years. There were 684,334 live births during 1943, representing a birth rate of 16.2 per 1,000 total population. This maintained the improvement seen in 1942, when the corresponding figures were 651,503 and 15.6, and compared favourably with the record low figures of 579,091 and 13.9 for 1941. The birth rate for 1943 was the highest since 1930, when the corresponding figure was 16.3. Later figures showed that the birth rate further increased to 17.7 in 1944, fell to 15.9 in 1945, and again increased to 19.2 in 1946 and 20.6 (provisional) in 1947. Of the live births in 1943, 43,709 or 6.4% were illegitimate compared with 36,467 and 5.6% in 1942 and an average of 4.3% for the ten years 1930-9. In 1945 this proportion was 9.3%; in 1946 it was 6.6%, and in 1947 it was 5.3%.

THE RELATION OF STAPH. PYOGENES TO DENTAL CARIES

BY

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Appleton (1944), in his review of the bacteria occurring in dental caries, mentioned several workers who have isolated *Staphylococcus aureus* from carious cavities. Among them were Miller, Goadby, Kantorowicz, and Niedergesaeß, but although they had established the presence of this organism in both the superficial and the deep layers of carious cavities it was only rarely and then in small numbers.

Nord (1946) stated that Gottlieb, in a private communication, said he had "discovered the micro-organism causing dental caries to be *Staph. aureus*, and that a perfectly sound tooth in a pure culture of this organism will in two months show caries which cannot be distinguished from true caries."

Gottlieb (1947) headed a paragraph of his book "*Staphylococcus aureus* produces dental caries," and referred to the work of Crawford (1946), who stated that *Staph. aureus* was isolated from carious cavities and that sterile extracted teeth, when placed in a culture of that organism, developed yellow spots and real cavities within two months. Ground sections of these teeth revealed exactly the same picture as that found in naturally carious teeth.

This paper reports the results of a collaborative investigation to test the claims of Gottlieb and Crawford and to find out if the presence of *Staph. aureus* in the mouth could be correlated with caries.

Bacteriological Technique

Material to be examined was incubated for twenty-four hours in a salt-meat medium specially selective for staphylococcus.* A loopful of this culture was spread on a horse-blood agar plate, incubated for twenty-four hours, and then allowed to age on the bench for two or three days so that colonies would have ample time to develop pigment. All varieties of colonies suspected of being staphylococcus were picked off and tested for the production of coagulase. Only "coagulase-positive" strains—i.e., *Staph. pyogenes*—were considered in the results which follow. These strains were all haemolytic. Most of them produced golden-yellow pigment (*Staph. aureus*), but some had white or nearly white colonies (*Staph. albus*). It has been well established that *Staph. pyogenes* nearly always liquefies gelatin and produces toxin and is potentially pathogenic for man. *Staph. pyogenes* should be regarded as including virtually all the strains which, on the basis of colour of colony, were formerly classed as *Staph. aureus*.

It has been shown that by the technique adopted it was usually possible to obtain a nearly pure plate culture of staphylococci when 300 staphylococci were mixed with 1,000,000 other bacteria in 1 ml. of a prepared mixture used as original inoculum. It follows that this method of culture gives no information about the presence or absence

*A full account of work on selective media for staphylococci is being published from the Department of Bacteriology.