of swelling, but amoeboid or other degenerate forms were not seen. The interfascicular oligodendroglia were swollen in all cases, but Greenfield (1942) has reported the normality of these cells in the presence of obvious oedema associated with cerebral tumour, granuloma, and abscess. The absence of any activation of the microglia confirmed the lack of damage to the myelin sheaths.

It must be concluded, then, that the honeycombing of the white matter together with the increased brain weight of one case must represent an increase in the inter-fibre fluid of the central white matter of such brief duration that myelin damage and its associated glial reactions have not yet occurred.

In view of the relationship between hepato-cellular disease and organic dementia (passing into coma) described by Sherlock (1955), the presence of extensive liver metastases in these three cases must raise the question of a possible connexion between the liver damage and the mental state. Such a connexion would imply that liver damage due to tumour deposits is to be regarded as a factor in the aetiology of the mental state distinct from the metabolic effects of the primary growth itself. Further, psychiatric disorders in malignant disease may be present in the absence of liver metastases (Brierley, unpublished cases; Meerloo, 1944).

The precise nature of the metabolic disorder associated with bronchogenic carcinoma remains elusive, and there is, as yet, little to replace the suggestion of Denny-Brown (1948) that carcinomas may produce some metabolite which interferes with the metabolism of vitamins. The very pleomorphism of the neurological and psychiatric manifestations of carcinoma of the bronchus, with a neuropathological picture ranging from apparent normality to severe cell loss—for example, cerebellum—must imply a complex pathogenesis. A factor of some importance here may be the normal involutional process. This is suggested by the fact that in Cases 1 and 2 the marginal, subependymal, and white-matter gliosis could well be regarded as typical involutional change occurring at a presenile age (43 and 53 years). The interrelationship of involutional change, metabolic disorder due to carcinoma, and liver damage, and their contributions to the genesis of the psychiatric picture, cannot be assessed, but it is possible that in the presence of carcinoma involutional changes could be accelerated, and in the present cases might have contributed some structural basis for the mental changes.

The various instances of the association of carcinoma with psychiatric symptomatology have been well reviewed by Fischer-Williams *et al.* (1955), and the above three cases show that mental symptoms can also occur in the absence of cerebral metastases, meningeal infiltration, peripheral neuropathy, or myopathy. In view of the higher incidence of carcinoma in the older age groups, the possibility of a hidden neoplasm deserves consideration in middle-aged and elderly subjects admitted to observation wards of mental hospitals suffering from a subacute organic reaction.

Summary

Three cases of carcinoma of the bronchus in patients aged 53, 43, and 63 years are presented.

In Cases 1 and 3 psychotic features preceded symptoms due to the growth, and in Case 2 they occurred 14 months after the initial symptom of haemoptysis.

The psychiatric symptoms were non-specific and resembled a fluctuating toxic confusional psychosis in which "lucid intervals" were well marked. There were no associated neurological signs.

In all cases cerebral metastases or meningeal infiltration were absent. Liver metastases occurred in all three.

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FAILURE TO PREVENT CONGENITAL SYPHILIS

BY

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Congenital syphilis is an eminently preventable disease provided the maternal infection is recognized in time to be adequately treated. As acquired syphilis in the expectant mother is so often clinically latent, its recognition must usually depend on the result of serological testing for syphilis. Amongst many others, Morton (1954) has stated that antenatal Wassermann-testing offers the best hope of the early eradication of congenital syphilis and has emphasized the need for close co-operation by all concerned in antenatal care if a high percentage of antenatal Wassermann-testing is to be achieved.

What progress has been made towards this goal? With venereologists in the lead persistent education over the past quarter-century has achieved much success in making a blood test for syphilis a routine measure in the majority of antenatal clinics of hospital and local public health authorities in England. The taking of this routine blood test for syphilis in expectant mothers was much facilitated by the introduction of rhesus-testing in 1947, and at that time it seemed that the goal of a blood test for syphilis as a routine in all expectant mothers would soon be realized. However, following the introduction of the National Health Service in 1948, the general practitioner has taken over the antenatal care of an increasing proportion of expectant mothers and, unfortunately, there is evidence that in few of such cases is antenatal blood-testing carried out. Thus in 1952, Macfarlane (quoted by Morton, 1954) found that on Tyneside, with an estimated 31,705 births (including stillbirths), of 15,812 (50%) antenatal Wassermann tests performed only 491 (3%) were made by general practitioners, who, according to the local executive councils, were remunerated for the care of 15,178 pregnancies.

In the area served by the Manchester Regional Hospital Board (Abstract of Statistics for the year ended December 31, 1954, p. 16 and Appendix Table vii) the 40,945 hospital births were 60% (Table I) of the total births in a home population estimated by the Registrar-General to be 4,379,760.

It might appear, therefore, that if, as at present, antenatal testing is seldom carried out in that proportion (about half) of all expectant mothers supervised by general practitioners, examples of congenital syphilis

TABLE I.—*Total Births in the Manchester Regional Hospital Board Area, Showing the Number and Percentage of These Births Taking Place in Hospitals*

Year	Total Births (Live and Still) Occurring in Area of Board	Live Births in Area of Board	Total Births (Live and Still) in Hospitals	Percentage of Hospital Births to Total Births
1949	74,182	71,489	40,535	55
1950	69,659	67,983	41,161	59
1951	68,813	67,053	40,057	59
1952	68,399	66,624	41,360	60
1953	69,330	67,558	41,820	60
1954	67,997	66,125	40,945	60

will continue to occur and be a reproach to the preventive aspects of the Health Service in general and the maternity service in particular. Is this conclusion justified or are there other factors involved in the continuing failures to prevent congenital syphilis? Answers to these questions have been sought by a study of the position in the area served by the Manchester Regional Hospital Board.

Present Study

The Manchester Regional Hospital Board area extends from Barrow-in-Furness in the north-west to Crewe in the south, a distance of about 120 miles (193 km.). The area is not more than 30 miles (48 km.) wide at any point, and the Census (1951) population was 4,398,306. More than 2,400,000 people live within a distance of 12 miles (19 km.) of Exchange Station, Manchester, and this is recognized as the most densely populated industrial area in Europe, not excluding the Ruhr. North of Preston the area is rural in character, with concentrations of population on the coast round Blackpool, in the vicinity of Lancaster, and at Barrow-in-Furness.

While some cases of infantile syphilis are still treated by paediatricians, the majority are known to the venereal diseases clinics and are consequently reported in the clinics' annual returns, which are sent through the Regional Hospital Board to the Ministry of Health. These statistical returns for the 22 clinics operating in the Manchester Regional Hospital Board area show that, during the five-year period 1950-4 inclusive, congenital syphilis was diagnosed in 75 infants under 1 year of age. In the four years 1951-4, inclusive, congenital syphilis was also diagnosed in 58 children aged 1 to 5 years. The records of these children and their mothers have provided the material for the present study, which has taken special account of the causes of failure to recognize the maternal syphilis in time to prevent or treat the foetal infection adequately. In addition, six cases in children between 1 and 5 years of age born just before 1951 are included, so that the total in the group studied is 139 (40 males, 99 females). Some 30 cases were rejected because it was felt that the original diagnosis of congenital syphilis was almost certainly mistaken, the two common errors being failure to allow for the "spill-over" of maternal reagin to the infant's circulation (blood taken in hospital from cord or soon after birth) and the practice of some obstetricians in giving "insurance" courses of penicillin to the infant immediately after birth where it was known that the mother had received antenatal treatment for syphilis. The remaining 109 cases were divided arbitrarily into two groups depending on whether or not the mother had had an antenatal blood test (Table II).

TABLE II

	No. of Cases of Diagnosed Congenital Syphilis	
	Under 1 Year	1-5 Years
No antenatal test	23	52
Antenatal test done	29	5
Diagnosis rejected	23	7
Total	75	64

Cases Without Antenatal Blood Test

This group of 75 cases was further analysed to discover by whom antenatal supervision, if any, had been carried out. It was known that certain local authorities had not established a routine blood test in their antenatal clinics until 1949, and this delay is obvious from Tables III and IV. Unfortunately, information was insufficient in 25 cases (Table III), including four children born abroad to displaced

TABLE III.—*Congenital Syphilis Diagnosed Between 1 and 5 Years of Age*

Year of Birth	Antenatal Care but No Blood Test				Total
	None	General Practitioner	Antenatal Clinic	No Information	
1944 ..				1	1
1945 ..				1	1
1946 ..	1	1	2	1	5
1947 ..	1	2	2	6	11
1948 ..		1	2	5	8
1949 ..	3	2	4	4	13
1950 ..	1	1	1	5	8
1951 ..	1	1	1	1	4
1952 ..				1	1
Total ..	7	8	12	25	52

TABLE IV.—*Congenital Syphilis Under 1 Year*

Year of Birth	Antenatal Care but No Blood Test				Total
	None	General Practitioner	Antenatal Clinic	No Information	
1950 ..	7	1	1	1	10
1951 ..	5	2	—	1	8
1952 ..	2	2	—	—	4
1953 ..	—	—	—	—	—
1954 ..	—	—	1	—	1
Total ..	14	5	2	2	23

persons and one foundling from an orphanage. The remainder include the children of mothers confined at home by midwife or medical practitioner and also cases diagnosed during the family investigation by the venereologist of expectant mothers, found to be seropositive in a further pregnancy, who had attended antenatal clinics before blood-testing was established as a routine. It is clear (Table IV), however, that during 1950-4 inclusive failure to prevent congenital syphilis arose most commonly because of failure of the expectant mother to seek any antenatal care or because the general practitioner failed to include a blood test in his antenatal supervision.

Infection was discovered in the 75 cases missed in the antenatal period, as follows:

Child developed physical signs of congenital syphilis ..	38
Mother had antenatal blood test in subsequent pregnancy ..	17
Examined as family contacts	14
Mother had blood test after admission in labour	6

The presenting clinical signs in the 38 cases, three of whom died in infancy from congenital syphilis, were:

Rash and/or snuffles, condylomata, and enlarged spleen ..	13
Periostitis (including one case of pseudo-paralysis) ..	3
Hydrocephalus	1
Neurosyphilis	1
Paroxysmal haemoglobinuria	1
Interstitial keratitis	14
Not specified	5

Of the 75 mothers who had had no antenatal blood test, 10 (13.3%) had defaulted from syphilis treatment at the V.D. clinic before pregnancy; the husband of one mother had been treated for secondary syphilis but refused to bring his wife to the V.D. clinic for examination; three mothers had each lost a previous child from syphilitic infection, but the obstetrician neglected to take any action; and another mother had had a previous stillbirth in hospital, the cause of which had not been investigated. Thus in 15 (20%) of these 75 expectant mothers the diagnosis could have been elicited or strongly suspected if a fuller case history had been taken, and, in fact, it is probable that 13 of these mothers knew that they had syphilis.

A faultless obstetric history in previous pregnancies is not a complete guarantee against congenital syphilis, usually due to infection of the mother immediately before or during the existing pregnancy (Case 1504).

Case 1504.—Child seen in 1953, aged 5 years, with interstitial keratitis. Born at home in 1948, after six previous healthy children. No antenatal blood test taken.

For the same reason the practice of omitting a blood test in subsequent pregnancies in cases in which the antenatal blood test was negative in a previous pregnancy is unsound. The blood test for syphilis should be a routine in each pregnancy.

Antenatal Blood Test Taken

There were 34 cases of congenital syphilis, 29 in infants under 1 year, where the mother had had a blood test taken during her antenatal supervision. Study of the records of these cases revealed the reasons for failure to obtain a healthy child (Table V).

TABLE V.—Reasons for Failure to Obtain a Healthy Child Where the Mother Had Had an Antenatal Blood Test (34 Cases)

Reason for Failure	No.	%
Positive blood test in antenatal clinic but no action taken	2	6
Positive blood test discovered too late to start treatment before delivery	1	3
Treatment of maternal syphilis begun less than 3 months before delivery	3	9
Treatment of maternal syphilis begun 3 or more months before delivery, but mother defaulted from treatment	16*	47
Antenatal blood test negative	6	18
	6	18

* Includes 3 in which premature labour reduced the time available for antenatal treatment.

Fallacies Due to Maternal Reagin

In most expectant mothers the syphilitic infection has passed the primary and secondary stages and is clinically latent. The positive serological tests are consequently slow to revert to negative during and after treatment, so that at delivery the mother's blood usually still contains reagin which "spills over" to the infant circulation and gives positive reactions to the serological tests for syphilis. This maternal reagin disappears from the infant's blood within a few weeks, and if the infant is not infected his tests soon become negative. In such cases tests taken from the umbilical cord or from the baby in the early neonatal period are very misleading, and have been responsible for many healthy infants being mistakenly diagnosed as congenitally syphilitic. In the absence of unequivocal clinical signs or radiological evidence of periostitis no infant should be diagnosed as suffering from congenital syphilis until quantitative blood tests, repeated weekly, show a definite and sustained rise in titre. These fallacies in infants arising from the "spill-over" of reagin from the mother, while well known to venereologists, still require wider recognition amongst obstetricians and paediatricians.

Discussion

Early Diagnosis.—It is believed that syphilitic infection of the foetus occurs only after placental function is established. Treatment of the mother with penicillin before the fifth month of pregnancy usually prevents infection of the foetus provided that the maternal infection does not relapse during the later months of pregnancy. If treatment is given before the fifth month and subsequently maintained throughout the pregnancy (to guard against relapse or reinfection), a healthy infant can virtually be guaranteed.

Delayed Diagnosis (16 cases, 47%).—When initial treatment is not started until the later months of pregnancy the foetus may be infected, but, by virtue of the mother's treatment, may be healthy at birth or show clinical, radiological, and/or serological evidence of resolving infection and proceed to cure without further independent therapy. The decision to institute or withhold treatment in such infants is often difficult, and the temptation to give an "insurance

course" of penicillin is understandable. However, if the latter is done the child should not automatically be diagnosed officially as a case of congenital syphilis, as otherwise the national figures will provide a distorted and artificially unfavourable picture of the true position.

Need for Greater Liaison Between Obstetrician, Paediatrician, and Venereologist.—These problems arise immediately after birth, while the infant is in the hospital care of the obstetrician or paediatrician, and, if close liaison exists, the venereologist can be of much assistance in such cases. Too often the venereologist sees the infant for the first time after several weeks, when it has been given much penicillin and an accurate diagnosis is no longer possible.

Effect of Prematurity (3 cases, 9%).—Syphilitic infection in mother and foetus may itself cause premature delivery, and such an event shortens the time available for antenatal treatment and reduces the prospects of obtaining a healthy infant (Case 436). Moreover, there is some evidence that the institution of antisyphilitic treatment may precipitate premature labour due to the Herxheimer reaction. These two factors again emphasize the importance of early diagnosis and treatment of the syphilitic mother.

Case 436.—Antenatal W.R. positive. Due September 10, 1951. Treatment started July 5, but infant born prematurely (weight 4 lb. 10 oz.—2.1 kg.) with congenital syphilis.

Default from Antenatal Treatment (6 cases, 18%).—Even where maternal infection is diagnosed early, failure may arise if the mother defaults from treatment. This problem of default is a perennial one to the venereologist, but normally the expectant mother is particularly amenable to encouragement and persuasion based on the benefits of treatment, particularly in relation to her unborn child. Such default is much less likely to occur if the expectant mother is offered treatment by the venereologist in a special session held in the antenatal clinic, but, in spite of the best efforts, it seems that some individuals will default before treatment is completed. In antenatal cases, especially towards full term, it often spares the patient much effort if her injections of penicillin are given by her own doctor, and where this step has been suggested I have always found the general practitioner fully co-operative.

False-Negative Blood Tests

In the present study there were six mothers (18%) with negative antenatal blood tests who nevertheless gave birth to congenitally syphilitic infants. Syphilis may be acquired only towards the end of pregnancy after a blood test taken at the beginning of antenatal supervision has given a genuinely negative result (Case 9724).

Case 9724.—A 2-para. Routine antenatal Kahn negative, August, 1952. Confined November 13. Child seen February, 1953, with infantile syphilis. Mother's W.R. and Kahn positive on March 3 and history indicated that she had secondary syphilis in October/November, 1952. Her husband refused to attend for examination.

In populations with a high incidence of infectious syphilis it is therefore necessary to insist on two blood tests during each pregnancy to detect those cases which become infected in the later months of pregnancy. With the present low incidence of infectious syphilis in England this repeated blood-testing is not justified as a routine but should still be considered in women known to be promiscuous. A syphilitic woman, without treatment, may become seronegative with the standard tests (W.R. and Kahn) and still infect the foetus (Case 3451). Again, the untreated infected mother may almost reach seronegativity and show fluctuating results, sometimes negative, sometimes doubtful or positive (Case E.64).

Case 3451.—A 4-para. Antenatal test negative. Child showed congenital syphilis and mother's test then found doubtful. Treponemal immobilization test (T.P.I.) positive in mother.

Case E.64.—A 3-para. Antenatal test negative in May, 1953. On July 2 tests positive. Confined July 4. Child showed signs of congenital syphilis on September 16. Then discovered that husband had been treated for primary syphilis in 1949.

These two possibilities could be guarded against only by the routine use of the T.P.I. test in all expectant mothers, and such a proposal is impracticable owing to the technical complexity of the test.

A woman who has had inadequate treatment for syphilis may be seronegative when tested antenatally but undergo serorelapse later in the pregnancy and infect her child (Case 52/385).

Case 52/385.—A 2-para. Treated May, 1950, during first pregnancy for secondary syphilis (6 mega units of penicillin, nine 0.45-g. doses of N.A.B., nine 0.2-g. doses of bismuth) and then defaulted. Antenatal test negative in September, 1951. Confined February, 1952, and child showed signs of congenital syphilis three months later. Mother's blood test positive on April 28.

Cases will be missed if the serological test is insufficiently sensitive (Case 1773).

Case 1773.—Child aged 2 seen in 1954 with infantile syphilis. Mother's antenatal Kahn test negative in 1952. Investigation of mother in 1954 revealed positive blood W.R. and positive changes in C.S.F. Also found that husband had been treated for neurosyphilis in 1950 by the neurologist of another hospital, but no action had been taken to notify husband's doctor of the diagnosis, to refer him to the V.D. clinic for further treatment and follow-up, or to have the wife examined.

The problem of insensitivity of the standard serological tests for syphilis (S.T.S.) is one of considerable technical complexity. If sensitivity is raised too far, specificity is sacrificed and false-positive reactions become more frequent. The best solution to this problem lies in the use of two serological tests on each specimen, one flocculation test—for example, standard Kahn test—and a complement-fixation test—for example, the Wassermann reaction: reliance on one flocculation test alone is condemned. There is also a strong case for concentrating the work of serological tests for syphilis in a few major serological laboratories in which the daily testing of adequate numbers of specimens and the experience and interest of a full-time serologist will ensure a much higher standard than that of the general laboratory, in which a few serological tests are performed only once or twice weekly, often by a junior technician.

Failure or Delay in Taking Action

There is little point in taking a blood test from antenatal cases if the laboratory report is not noted at once and effective action taken. In a busy antenatal clinic positive reports may be overlooked (Case 362) or action may be delayed (Case 468) unless a definite arrangement is in operation whereby the obstetrician's attention is drawn to the positive result without awaiting the patient's next visit. The widespread practice of awaiting the report on a second specimen of blood before arranging consultation with the venereologist is responsible for delays which in some cases may be vital. The venereologist may find definite clinical or historical evidence of syphilis which will justify immediate treatment without repetition of the blood test. When he finds no such evidence and requires to have the test repeated the venereologist may wish to divide the specimen and obtain the opinion of two serologists in different laboratories. Moreover, as valuable evidence can often be found by examination of the husband and any previous children, arrangements for such investigations can be made immediately.

I have experience of a system whereby my consultant colleagues at hospital authorized the serologist to send copies of positive reports direct to the venereologist, who then seeks out the consultant concerned for discussion of the case and agreement on the action to be taken. In this way no cases are overlooked and unnecessary delay is avoided. Such an arrangement has much to commend it for use in hospitals and antenatal clinics of local authorities, but would be laborious to organize for specimens sent to the laboratory by general practitioners owing to the need to approach them individually for their permission for the disclosure of the information to the venereologist.

Case 362.—Antenatal blood test positive. No action taken. Child showed signs of congenital syphilis two weeks after birth.

Case 468.—Antenatal test positive on December 17, 1953. Result overlooked in antenatal clinic until June 17, 1954, when test was repeated. Mother not seen by venereologist until one day after delivery. Child developed signs of congenital syphilis.

Infrequently, delay in starting antenatal treatment may arise in the V.D. clinic. This may be due to sins of omission (Case 7552) or to delaying treatment until the diagnosis in the mother has been fully confirmed. The former can be avoided in the busy clinic by maintaining a special list of pregnant patients to show their dates of future attendance. In this way their non-attendance is noted immediately and action can be taken by letter or visit to bring them back for treatment. The occurrence of false-positive results with the standard serological tests for syphilis makes the venereologist cautious in diagnosing syphilis in a patient who has no history or clinical signs of infection. Such cases demand full investigation, including family contacts, before a firm diagnosis is made and treatment is begun. In the pregnant woman, however, the delay occasioned by such investigation may jeopardize the chance of obtaining a healthy child and most venereologists agree that when such cases arise in pregnancy treatment should be given without delay and without awaiting the results of the full investigation.

Case 7552.—Mother referred to V.D. Clinic from antenatal clinic with positive antenatal blood test report some three and a half months before delivery. Husband found to have had syphilis in the Services. Mother defaulted and was brought back to start antenatal treatment only six weeks before confinement. Child developed condylomata lata 10 weeks after birth.

Conclusions

Although this study emphasizes the recent failures to prevent congenital syphilis, the real progress towards the elimination of this preventable disease recorded by the Chief Medical Officer's Annual Report to the Minister of Health (1955) must not be overlooked. Throughout England many infected women have been discovered and successfully treated as a result of careful antenatal supervision, which has included antenatal blood-testing. The study makes clear, however, that: (1) some pregnant women still come to confinement without antenatal care; (2) others receive antenatal supervision that does not include a routine blood test; (3) the maternal infection is diagnosed too late for treatment to prevent infection of the foetus; (4) premature labour reduces the time available for antenatal treatment; (5) some infected pregnant women default from treatment; (6) some pregnant women, in spite of a negative antenatal blood test, may still produce a child with congenital syphilis; and (7) there is need for greater liaison between the maternity services and the venereologist.

It must be concluded from this study that the routine antenatal blood test will not by itself lead to the complete elimination of congenital syphilis, although it can be instrumental in reducing greatly the incidence of this condition. This pessimistic conclusion, however, must not be used as an argument against the campaign for a blood test for syphilis as a routine in all expectant mothers. Other factors, which are now in operation and will eventually lead to the total elimination of congenital syphilis, will be discussed in a further communication.

Summary

The records of 139 cases of congenital syphilis in children under 5 years of age, reported by 22 venereal disease clinics in the Manchester Regional Hospital Board area during the five years 1950–4 inclusive, have been studied to determine the causes of failure to prevent what is widely stated to be a preventable disease. The causes of failure are discussed, and it is concluded that the practice of taking a routine antenatal blood test, whilst instrumental in greatly reducing the incidence of

foetal infection, will not by itself prevent completely the occurrence of congenital syphilis. Other factors which will lead to the achievement of this goal will be discussed in a further communication.

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BLOOD GROUPS IN DIABETES MELLITUS

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The finding by Aird, Bentall, and Roberts (1953) of an association between carcinoma of the stomach and blood group A and by Aird, Bentall, Mehigan, and Roberts (1954) between peptic ulcer and blood group O has made it desirable to search for similar associations in other diseases. We describe here the results of independent surveys in Liverpool and in Oxford of the ABO blood group distribution among 1,333 patients suffering from diabetes mellitus and compare them with control series.

Source of Material.—The Liverpool series was drawn from patients attending the diabetic clinic of the David Lewis Northern Hospital during a five-months period and comprises 833 cases. The Oxford series consists of 500 cases chosen at random from the patients attending the diabetic clinic at the Radcliffe Infirmary. The diagnosis of diabetes had been confirmed in all patients by high fasting-blood-sugar levels or by abnormal glucose-tolerance curves. The Rhesus and MN groupings of the Oxford patients were also determined.

Control Samples and the Subdivision of the Liverpool Area

The most suitable control samples available are those for the general population, based on consecutive registration of blood donors by the National Blood Transfusion Service. The figures used are shown in Table I. They were provided by the Nuffield Blood Group Centre of the Royal Anthropological Institute.

TABLE I.—Control Samples Used. (Supplied by the Nuffield Blood Group Centre)

	O	A	B	AB	Total
*Liverpool Postal District	1,673	1,374	303	101	3,451
*Remainder of S.W. Lancashire	1,473	1,274	243	69	3,059
West Cheshire	546	521	135	45	1,247
Oxford	2,888	2,839	557	208	6,492

* Added to give a single series.

As a control series for the Oxford group of diabetic patients 6,492 blood donors in Oxfordshire and neighbouring counties were used.

The choice of controls for the Liverpool series was not so straightforward. The patients' homes were situated as follows: Liverpool postal district, 533; remainder of S.W. Lancashire, 80; West Cheshire, 199; North Wales, 10; elsewhere in the United Kingdom, 11. The Nuffield Centre figures given in Table I do not show any significant difference between the Liverpool postal area and the rest of S.W. Lancashire; hence these patients could be added together, the control figures used being the sum of the first two lines of Table I. The available Nuffield Centre figures for North Wales (making no distinction of racial origin) are very similar to those of S.W. Lancashire, so the 10 patients have been added to that series. The 11 patients coming from outside the areas named were mostly from N.W. Lancashire, and they too have been added.

West Cheshire must be kept separate, as the control frequencies are quite different. Hence the whole material available for this paper has been divided into three series, the areas being S.W. Lancashire, West Cheshire, and Oxford.

It will be noted that the Liverpool controls are slightly lower in blood group A than those of the rest of S.W. Lancashire, though the difference is not significant. The numbers in the control series are fairly equal, whereas many more patients are drawn from the Liverpool postal district. Hence, addition of the two control series, which seems desirable in the interests of simplicity and numbers, has the effect of slightly reducing the difference between diabetics and controls which is described in this paper.

Results

The basic data, with subdivisions by area, sex, and age at onset of diabetes mellitus, are shown in Table II. If men and women of all ages are compared with the controls of Table I, the findings may be summarized as shown in Table III. The control figures are weighted according to the numbers of diabetic men and women drawn from each area. The one striking difference is that compared with the controls the men show a higher proportion of patients of group A and a lower proportion of patients of group O. On the other hand, there is no such difference in the women.

The relative differences in groups O and A, for which considerable numbers are available, were examined first. The method recommended by Aird *et al.* (1954) for examining the differences in blood-group proportions and the homogeneity of the areas was used, and the comparison is shown in Table IV. The relative increase in blood group A in men is shown to be fairly highly significant. A direct comparison of the men and women patients also yields a significant difference. The women are closely similar to the controls. The three areas are perfectly homogeneous.

The men patients are lower in blood group B than are the controls, but the numbers are small and the difference is not significant.

The women patients show a rather high proportion of group AB. This has been examined in two ways. First, a direct comparison has been made with the controls in regard to the percentage of group AB. With the method of Aird *et al.* (1954), χ^2 for the difference is 3.25 and so does not attain the 5% level of significance. χ^2 for the heterogeneity of the three areas is 2.88, which is not significant, but does to some extent reflect the fact that the excess of those of group AB is confined to two of the areas. Secondly, if the figures are added together, irrespective of area, Fisher's test for unreasonableness of group proportions (Dobson and Ikin, 1946) gives an expected number of those of group AB of 25.804 against the 38 observed, χ^2 for one degree of freedom being 3.99, which just exceeds the 5% level of significance. It may be concluded that, while the women are rather high