of microphthalmic type. It is unprofitable to speculate as to the additional influences that determine such big differences in the mentality of affected persons. They are perhaps unlikely to be genetic, in view of the wide range of the effects and in view of the occurrence of very different mentalities in affected persons in the same sibship. It may be more reasonable to conclude that the organism during critical stages of its development is for genetic reasons abnormally sensitive to non-genetic influences and that these, entirely trivial in the case of normal persons, are on occasion capable of modifying the development of the brain and so of profoundly affecting its ultimate structure.

Summary

1. A family group is described in which microphthalmia is inherited as a sex-linked recessive condition.

2. The appearance of the eyes in six affected persons shows much variation.

3. The blind males may be of normal mentality or may exhibit any grade of mental deficiency from feeble-mindedness to profound idiocy. There is no mental deficiency in the family group apart from the blindness.

I am greatly indebted to Mr. A. E. Iles, consulting ophthalmologist to Stoke Park Colony, for the description given above of the eyes of the two patients at that institution (DII 21, 22) and for his advice on the examination of the other blind persons and on the preparation of this paper.

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MODERN CONTROL OF SCARLET FEVER*

BY

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This paper is written with a view to elucidating some of the problems with which the clinician is confronted when dealing with scarlet fever and haemolytic streptococcal pharyngitis. It is now generally accepted that scarlet fever occurs through certain types of *Streptococcus pyogenes* multiplying in the body and giving off an exotoxin which on gaining admission to the circulation causes the skin capillaries to dilate, the characteristic rash resulting. This toxin is neutralizable by its specific antitoxin.

Whilst working with Dr. F. Griffith some years ago I took thirteen strains of haemolytic streptococci obtained in epidemics of scarlet fever and pharyngitis from different parts of England, and tested their toxigenic power on patients with known skin reactions to standard Dick toxin. We found that the amount of toxin produced by the different strains was very variable, some filtrates giving a positive reaction when 0.1 c.cm. of a 1 in 4,000 solution was injected intradermally, others almost none when 0.1 c.cm. of a 1 in 50 solution was similarly used. When we correlated these findings with

the type of epidemic from which the strains had been cultured we found that:

1. In the epidemics caused by the powerful toxigenic strains were many cases of clinical scarlet fever and a few cases of simple pharyngitis.

2. Where medium toxigenic strains were the cause the number of cases of clinical scarlet fever and of pharyngitis were about equal.

3. Where a low toxigenic strain was the cause no clinical scarlet fever cases or only an occasional one appeared among many cases of pharyngitis.

It was clear that erythema, one important element of the clinical syndrome of scarlet fever, may be absent in cases of scarlatinal infection—that is to say, given an acute infection with haemolytic streptococcus a severe or transient erythema may develop or none at all. The conclusion that may be drawn from these observations is that scarlet fever cannot be considered as a specific disease like plague or cholera: it is one of the protean manifestations of streptococcal infection.

Further studies of the immunology of the haemolytic streptococcus show that the exotoxin is only one of its weapons of offence, among others being its lytic and invasive powers. Hence clinically acute pharyngitis caused by a haemolytic streptococcus can occur, without resulting rash, if: (1) the patient has sufficient antitoxin to neutralize the toxin produced by the invading streptococcus; (2) the organism has little or no toxigenic power. For these reasons the term scarlet fever, which was introduced before the aetiology of the disease was known, may be misleading. At present tonsillitis with erythema is called scarlet fever, and is a notifiable disease against which the most strict precautions must be taken—for example, hospitalization, isolation, etc.—while pharyngitis caused by the same organism but without erythema is regarded as a mild complaint for which no special measures are necessary. This attitude has caused the clinician much trouble in the past, particularly when dealing with epidemics of scarlet fever or pharyngitis in the wards of children's hospitals or in semi-isolated communities such as schools.

It has been found that the isolation of cases of clinical scarlet fever for six weeks does not stop the spread of the disease. Public health notification and hospitalization have not reduced the morbidity during the past twenty-five years. In several well-known schools outbreaks of scarlet fever have occurred term after term for over a year, often followed by severe complications, although the doctors in charge employed all the usual methods of control laid down in the textbooks. The best example is given by Glover and Griffith (1930), who described an outbreak of "scarlet fever" in a school of fifty boys which continued for three terms. They show how all the cases were caused by the same organism, the fresh outbreaks being brought about by patients whose throats still carried the germ when released after the usual isolation period.

Recently I have had the opportunity of testing clinically the validity of the above experiments and observations in an epidemic which occurred in a Dublin public school.

TABLE I.—Showing Time of Occurrence of Eleven Cases of Pharyngitis at a Public School

	June :	1	2	3	4	5	6	7	8	9	10	11
Pharyngitis	..	1		1				1				1
C. Erythema	..		1		1				1			
Carriers	..	..					4					

If Table I is examined it will be seen that on June 1 a case of acute pharyngitis occurred. More accurately it

* Read in the Section of Diseases of Children at the Annual Meeting of the British Medical Association, Belfast, 1937.

should be stated that a boy who had been "seedy" for some time was admitted to the sanatorium suffering from pharyngitis and cervical adenitis. The next day a boy was admitted with a very acute pharyngitis; he subsequently developed the typical erythema of scarlet fever. On the 3rd and 4th two other boys were admitted with acute pharyngitis, one developing erythema, the other not. Two days later the whole school had their throats swabbed. The previous four cases of pharyngitis showed pure growths of haemolytic streptococci, and four carriers were discovered. Strict isolation followed. During the following six days three more cases of pharyngitis appeared, one of them developing a rash. The school was Dick-tested, and anti-scarlatinal serum was given to all positive cases. No further cases of pharyngitis with or without erythema occurred.

Technique

In dealing with an epidemic of scarlet fever the problem of sorting out carriers of haemolytic streptococci is always one of considerable difficulty, since if a group of people have their throats swabbed a number of the resulting culture plates usually show colonies of haemolytic streptococci. The streptococci from the different persons often belong to different types, some of which are not of epidemic importance. Streptococcal strains can be differentiated to some extent by their cultural appearances, and definitely by precipitation and agglutination methods. The preparation of the culture plate is of importance if the individual colonies are studied, the double-layered plate (in which first a layer of plain agar is poured over the plate and allowed to set and then a thin layer of blood agar) being the best. Horses' blood is better than human blood in the preparation of the blood agar, as it does not contain specific antibodies to the haemolytic streptococcus, while human blood may.

In the epidemic reported here the causal organism had a characteristic appearance on the plates, being large and rough, and having a wide zone of haemolysis around. Other streptococci which were isolated were small and smooth, with small zones of haemolysis. Dr. Griffith typed the dominant strain and found it to be *Streptococcus pyogenes*, Type I. Altogether eleven of the boys (other than those clinically affected) had some colonies of haemolytic streptococci in their throat cultures; but with repeated cultures, following the above methods, seven were eliminated as non-pathogenic, leaving four definite carriers of the epidemic strain. The latter four are those mentioned above.

TABLE II.—Showing the Subsequent History of the Patients

Case	Type	Weeks Positive Haem. Str. in Throat Culture	Complications	Surgical Treatment
1	C. Erythema	8	Ethmoiditis	Ethmoidectomy
2	"	9	—	Tonsillectomy seventh week
3	"	10	Axillary abscess	Incision
4	Simple acute pharyngitis	6	—	—
5	"	8	—	Tonsillectomy sixth week
6	"	9	—	Tonsillectomy seventh week
7	"	22	—	Adenoidectomy third week
8	Carrier	2	—	—
9	"	3	—	—
10	"	5	—	Tonsillectomy third week
11	"	6	—	Tonsillectomy fourth week

The foregoing table shows the subsequent history of the three patients with clinical scarlet fever, the four with pharyngitis without rash, and the four carriers.

The organism was a highly toxic strain. All three cases showing erythema were very ill. Two of them developed further complications—in one an acute ethmoiditis, in the other a severe axillary abscess. Their throat cultures were positive for eight, nine, and ten weeks respectively.

The four cases of pharyngitis without rash were not nearly so ill; indeed, in two of them the temperature did not rise above 100° F., but their throat cultures remained positive for six, eight, nine, and twenty-two weeks respectively, the last case being that of the boy who had started the epidemic. Every form of treatment was tried for this boy: gargles, throat paints, etc.; adenoidectomy (his tonsils had been removed years previously); open-air holiday in the country. All failed, and he was not allowed to return at the beginning of the following term. In the end he cleared up spontaneously. In the case of the four carriers the throat cultures were positive for two, three, five, and six weeks respectively.

Local antiseptic treatment appeared to have little or no effect on the throat infection. Hence in five cases with persistent cultures associated with enlarged tonsils and adenoids tonsillectomy was performed. All these cases cleared up within ten days of the operation. It should be noted that the above epidemic occurred before the general acceptance of the specific action of prontosil on haemolytic streptococcal infection. It is possible that the whole course of the epidemic might have been shortened by its use, and complications and operations avoided.

Discussion

It is clear from the above analysis that if an epidemic of "scarlet fever" is to be stamped out in a community the old method of six weeks' isolation or waiting until peeling is complete is altogether inadequate, and should be replaced by one of control by throat cultures. Also, isolation must include not only clinical cases of haemolytic pharyngitis but also carriers of the specific organism. In the epidemic reported here it is impossible to say whether the administration of anti-scarlatinal serum had a preventive effect on the development of further cases of pharyngitis. It is noticeable that no further cases appeared after its administration, but against this we must place the fact that strict isolation of all positive cases was started at the same time. In addition the fact that pharyngitis occurred in four cases unassociated with erythema shows that the invasive power of the organism is not checked by the presence of circulating antitoxin in the patient.

Conclusion

Whilst the name scarlet fever is an unscientific term which may lead to misunderstanding it has been established by usage, and there would be many difficulties in replacing it by the more aetiological correct title "haemolytic streptococcal pharyngitis." No opportunity, however, should be neglected of emphasizing, both to members of our profession and to the laity, that an acute pharyngitis or tonsillitis may have the same causal agent as typical scarlet fever and may be a focus for the spread of scarlatinal infection. In applying modern knowledge on the epidemiology of streptococcal infections the practical problem of supplying a service for streptococcal throat cultures on a large scale will arise and the whole problem

of hospitalization and isolation will need revision. It should not be assumed from this that I am in favour of abolishing fever hospital treatment for clinical scarlet fever, but rather that accommodation should be provided also for acute pharyngitis caused by the same organism.

I wish to express my thanks to Dr. F. Griffith for his co-operation in this work and his help and advice in the composition of this paper.

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VITAMIN E IN THE TREATMENT OF HABITUAL ABORTION*

BY

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During the past few years the importance of the vitamins in the maintenance of the growing embryo has been repeatedly demonstrated. In 1922 Evans and Bishop discovered that rats when given a fairly normal diet failed to reproduce unless certain essential foodstuffs were present, while in all other respects they were normal. The females exhibited oestrus and even conceived, but they failed to deliver the young: either the foetus died *in utero* and was reabsorbed or the uterus aborted.

The Missing Factor

Other observers, working independently, came to similar conclusions. The essential missing factor was found in fresh green vegetables—for example, lettuces—but the most abundant yield was obtained from the embryo of seeds, especially the germ of wheat. Sure (1924) called this essential factor vitamin E. This vitamin is supplied for clinical purposes in wheat-germ oil, and animals deprived of it show definite defects in their ability to reproduce. The males suffer irreparable damage to the germinal epithelium of the testes, and whereas the sex glands in the female are unaffected, the vitamin deficiency leads to the death of the foetus, with subsequent abortion or reabsorption (Evans and Burr, 1927).

Vogt-Möller (1933) of Copenhagen first made use of the vitamins as a therapeutic agent in cases of sterility and abortion in domestic animals, and his results were such that he was tempted to apply the method as a means of cure in habitual abortion in women. He reported a series of nineteen patients treated with a preparation of wheat-germ oil called "fertilan," sixteen of whom gave birth to living children.

If we are correct in assuming that the vitamin has such an important action in aiding the growth of the foetus it is difficult to explain why women taking the varied and sufficient diet of to-day need any addition of an essential accessory food factor. It may be that those women who abort possess a personal idiosyncrasy; possibly, in them, the developing embryo demands a greater concentration of the vitamin, or perhaps they are unable to absorb the necessary amount from the normal diet.

Treatment with Wheat-germ Oil

It was Vogt-Möller's paper and the offer of wheat-germ oil from Glaxo Laboratories Ltd. that encouraged

me to treat habitual abortion with vitamin E, and the results obtained show similar satisfying figures to those published by Watson and Tew (1936) and Miles M'Gonigle (1935). Watson in his paper has pointed out that vitamin E bears more resemblance as regards clinical features, physiological properties, and clinical significance to the luteal hormone (progesterin) than to other hormones. This is a point of interest, because other observers (Johnson, Krohn, and Kane) have achieved satisfactory results in the treatment of habitual abortion with the use of the luteal hormone, and as James Young (1937) has pointed out it may be that the work of the vitamin is completed when the placenta is fully developed. Until recently it was the accepted view that the action of the corpus luteum ceased about the middle of pregnancy, and this statement was substantiated by the fact that women did not necessarily abort if the ovaries were removed after the twelfth week. We now know that the amount of luteal hormone continues to increase during pregnancy even though the corpus luteum diminishes in size, and it is believed that the hormone is supplied by the placenta during the later months and that a deficiency of it leads to toxic conditions such as albuminuria, eclampsia, and accidental haemorrhage. At present I am attempting to cure these conditions by the injection of Schering's proluton.

If this hypothesis be true, then vitamin E is only essential during the early months of pregnancy, and by reason of the aid it gives in the formation of the placenta it provides for the supply of luteal hormone in the later months.

These latter details were unknown to me three years ago when I began treating cases of habitual abortion with wheat-germ oil, and the majority of the cases here described have had no treatment other than vitamin E, save for the addition of vitamins A and D and calcium which were given to a small number of patients. Each case was examined for such accepted causes of abortion as fibroids, retroversion, torn cervix, syphilis, and other general diseases, and on only two occasions was the blood Wassermann reaction found to be positive. One capsule containing three minims of the oil extract was given daily from the first attendance until the day of delivery.

Results

Over fifty women have been given wheat-germ oil during pregnancy, but since habitual abortion implies that more than one pregnancy has failed to go to term I have included in Table I only those patients who have experienced more than one abortion. Having allowed for this we find that thirty-seven women who had had collectively 130 pregnancies gave birth to only sixteen viable children. Under treatment these women produced thirty-seven living children. Two of them aborted; there were two sets of twins; and four children died in hospital from prematurity.

The appearance of albuminuria of pregnancy to a severe degree was a new problem that arose during treatment. Five patients showed gross signs of toxæmia, in one it was necessary to induce labour by puncture of the membranes, and in two Caesarean section was carried out. Similar complications are now being treated by the injection of proluton.

Table I shows the results in detail. It will be noticed that in the great majority of cases treatment was not instituted until after the twelfth week of pregnancy—that is, until the placenta was fully formed—and yet the

* Read at a joint meeting of the Sections of Obstetrics and Gynaecology, and Nutrition at the Annual Meeting of the British Medical Association, Belfast, 1937.