dentine. It is interesting to note that even in sections of teeth in which caries appears to be completely arrested the dentinal tubules may contain micro-organisms. These, however, are apparently inactive. For instance, some Gram-positive bacteria were found in the dentinal tubules of the teeth ground sections of which are seen in Figs. 2 and 3.

The production of secondary dentine in puppies by artificial stimuli has been related to the intake of vitamin D.^{8,9} With an abundance of this vitamin much well-calcified secondary dentine is formed as the result of a given stimulus, whereas with little of the vitamin there is little or no reaction. The arrest of caries in children obtained in the present investigation as the result of giving abundant vitamin D in the diet is, therefore, just what would be expected on the basis of the animal experiments.

That other factors play a part in the arrest of caries seems certain, but at present little is known concerning these. It has been shown by one of us⁹ that calcifying diets which tend to assist the arrest of caries also result in a high calcium content of saliva, which may be of significance.

Summary.

In a batch of 21 children whose average age was about 5½ years the addition of vitamin D in the form of

irradiated ergosterol (radiostol) checked the initiation of new carious points, diminished the spread of old carious points, and arrested the infective process in many carious teeth.

This investigation corroborates those previously made, in which it was found that the carious process in the teeth of children could often be inhibited by increasing the intake of fat-soluble vitamins by the addition to the diet of cod-liver oil, egg yolk, and extra milk. The present work shows that vitamin D is a most powerful agent in these inhibitory processes.

Our thanks are due to the Medical Research Council and the Dental Board of the United Kingdom for their financial support of these investigations, and to the British Drug Houses, Ltd., for preparing and supplying the radiostol and the vitamin A oil used.

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THE UTILITY OF STREPTOCOCCAL VACCINES IN THE TREATMENT OF PUERPERAL SEPSIS.

BY

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THE following paper describes an investigation carried out (1) on clinical lines, (2) by laboratory experiments on animals, to decide the utility of vaccines in the treatment of puerperal sepsis.

Clinical Investigation.

It is generally accepted that the *Streptococcus pyogenes* haemolyticus is by far the commonest cause of puerperal septicaemia. The majority of morbid puerperia are also due to this organism. At St. Bartholomew's Hospital, London, trust has been placed, during some years past, in the use of *Streptococcus pyogenes* vaccine, both as a prophylactic and for treatment in the severer forms of streptococcal infection, including puerperal fever. Vaccine "sensitized" by suspension in Pasteur Institute anti-streptococcal immunizing serum has been used. The mere fact that there has been constant demand over a long period of years for this vaccine implies a belief in its therapeutic value. But nothing is more difficult than to estimate the worth of a particular method of treatment in an infective disease naturally liable to spontaneous recovery.

The conditions under which the maternity and lying-in practice of St. Bartholomew's Hospital extern midwifery district are conducted favoured a large scale inquiry designed to test the value of vaccination as a preventive of morbid complications. Every woman has been delivered in her own home. During the first month of our inquiry each patient received a dose of sensitized killed *Streptococcus pyogenes* vaccine, containing 250 million organisms, on the day of delivery. If the patient's temperature rose, 500 million vaccine was given, followed the next day by 1,000 million vaccine, this latter dose being continued daily till the temperature fell. During the second month no prophylactic dose was given, but pyrexia was treated by 250 million vaccine on the day of onset, 500 million the next day, and then 1,000 million vaccine daily till the temperature fell. During the third month vaccine was not given in any circumstances, so that women confined during this month served as controls to the other cases. The same routine was observed in the following quarter, and so the changes were rung until, in the course of two years, the results of two thousand cases were available for analysis.

The women were visited and treated in their own homes by such means as were available in a district of the poorest class. The only technical refinement has been the consistent use by the midwifery clerks of sterilized rubber gloves and the employment at each case of a "drum" containing the following sterilized dressings, etc.: a sterilized gown, four small towels, two large pieces of wool, six small surgical wool swabs, two long strips of folded gauze, 1½ yards in length (for plugging the cervix if required), six gauze eye swabs; this in addition to the fully equipped midwifery bag such as is in universal use.

Such apparatus betokens more than an attempt at surgical cleanliness. It is to be considered an outward and visible sign of inward and spiritual grace, a recognition by the midwifery student, even in his novitiate, of the essential need to avoid contamination by employing cleanliness, care, and conservatism in the management of labour. We believe it is to this that the satisfactory results as regards morbidity and fatalities are due.

The vaccines used have been described above as "sensitized." Sensitization implies the conjugation of bacteria with specific antibodies contained in the homologous immunizing serum. It is doubtful whether the streptococcal vaccines used in the inquiry were truly sensitized in this sense. A suspension of pneumococci or typhoid bacilli, in contact with their corresponding antiserum, is agglutinated and precipitated in a coagulum consisting of bacteria surrounded by a gelatinous capsule; this may be stained and clearly seen under the microscope. Such a vaccine is actively chemotactic, and is rapidly ingested by leucocytes. The *Streptococcus pyogenes* vaccine supplied for use did not behave in this manner, and it is therefore doubtful if it were truly "sensitized." Experiments described by one of us¹ seem to prove that, at least in the case of the pneumococcus, sensitized vaccines are less rapid and less efficient antigens than "raw" vaccines. It is probable, therefore, that nothing was lost to treatment by the inoculation of simple vaccine. In any event it must be pointed out that the investigation here described was not so much a progressive and reasoned attempt to establish new treatment as a test of the validity of existing practice and beliefs.

In classifying the cases the British Medical Association standard of "morbidity" has been adopted—namely, a rise of temperature from any cause whatever, not necessarily streptococcal infection, to 100.4° F., on two occasions at least between the second and tenth days of the lying-in period. By "clinically septic" is meant the occurrence of offensive lochia, subinvolution of the uterus, and characteristic fever. The temperature shows a rise on the third day, a maximum on the fifth day, and fever persisting for an average of five days. "Septicaemia" indicates the severest form of infection with the demonstration of *Streptococcus pyogenes* in blood culture.

Results.

The cases may be grouped as follows; it is to be understood that the category "morbid" also includes all the clinically septic cases and any case of septicaemia.

GROUP A.—250 million *S. pyogenes* vaccine on day of delivery in any event, followed, if a rise of temperature occurred, by a further dose of 500 million, the next day 1,000 million, this dose being continued daily until the temperature fell.

Date.	No. of Cases.	Morbid.	Clinically Septic.	Septicaemia.
July, 1925	81	5	3	—
October, 1925	74	5	2	1
January, 1926	59	4	3	—
May, 1926	84	1	1	—
July, 1926	75	2	2	—
October, 1925	85	5	5	—
January, 1927	78	4	3	—
April, 1927	63	0	0	—
July, 1927	69	1	0	—
Total	668	27	19	1

Percentage: Morbid 4.04; Clinically septic 2.8.

GROUP B.—No prophylactic dose on day of delivery. If a rise of temperature occurred 250 million *S. pyogenes* vaccine was given on the day of onset, followed by 500 million the next day, and by 1,000 million on each succeeding day till the temperature fell.

Date.	No. of Cases.	Morbid.	Clinically Septic.	Septicaemia.
August, 1925	76	6	4	—
November, 1925	71	2	1	—
February, 1926	79	4	3	—
April, 1926	69	2	2	1
August, 1926	64	2	2	—
November, 1926	60	2	2	—
March, 1927	68	2	2	1 death
May, 1927	56	3	3	—
August, 1927	75	3	2	—
Total	618	26	21	2

Percentage: Morbid 4.20; Clinically septic 3.69.

GROUP C.—No vaccine in any circumstances, whether the temperature rose or not.

Date.	No. of Cases.	Morbid.	Clinically Septic.	Septicaemia.
September, 1925... ..	72	6	3	—
December, 1925	79	2	2	1
March, 1925	69	3	2	—
June, 1926	69	2	2	—
September, 1926... ..	74	1	1	—
December, 1925	76	3	1	—
February, 1927	62	1	1	—
June, 1927	59	3	3	—
September, 1927... ..	54	2	1	—
October, 1927	53	1	0	—
November, 1927	54	4	3	—
Total	721	28	19	1

Percentage: Morbid 3.89; Clinically septic 2.6.

A comparison of the summaries at the foot of each table makes clear that there is little to choose between the three groups of cases. The morbidity rate is low in each group, and, as it chances, lowest in the unvaccinated. In fact,

had this all-important control group been omitted, it would have been tempting to argue that prophylactic vaccination had proved highly beneficial.

The experience during the whole period may be summarized briefly. In all 2,007 cases were delivered; 81, or 4 per cent., became morbid, and of these 61, or 3 per cent., are recorded as clinically septic also. There were 4 cases of septicaemia, one of which proved fatal. In addition, one fatal case of icterus gravis gravidarum and one of pneumococcal peritonitis occurred, making a total of three deaths in all.

Operations and Morbidity.

A study of the individual case records, particular details of which there is no space to include, makes the close correlation of morbid temperatures with operations abundantly clear. The following operations were performed:

Replacement of cord	1
Bipolar version	2
Internal version	1
Episiotomy	1
Craniotomy	2
Manual removal of placenta	13
Forceps delivery	40
Total	60

The two latter operations were most often associated with morbidity, manual removal in particular.

The total morbidity among the operation cases was 18, or 31 per cent., as compared with a gross morbidity rate of only 4 per cent. over the whole series, or, deducting operation cases, a net rate of 3.23 per cent. Operative intervention, therefore, increased the rate of sepsis tenfold. It will be noted that the forceps rate was only 2 per cent.

The low incidence of cases requiring operation is to be attributed in part to conservative tradition and practice in the district. In the main it must be recognized to be due to careful ante-natal supervision. As a result, cases which would inevitably have proved complicated have been eliminated from among the women treated in their own homes. Thus the conditions perceived and postulated by James Young of Edinburgh in his admirable survey of the problem of puerperal sepsis, published in the *British Medical Journal* (June 9th, 1928, p. 967), have been to some extent realized. On the one hand there is convincing proof of the close causal interrelationship of morbidity and operative intervention—inevitable, apparently, no matter what patience be exercised in confinement to avoid forceps delivery. On the other hand, ante-natal supervision has fulfilled its proper function in segregating cases likely to be complicated, for appropriate institutional treatment in the best possible surroundings.

The day of onset of pyrexia during the puerperium is of interest.

Day of Puerperium.	No. of Cases.	Day of Puerperium.	No. of Cases.
1	6	6	2
2	14	7	3
3	24	8	1
4	13	9	4
5	7	10	0

Thus in one-third of the febrile cases a rise of temperature occurred on the third day, and in two-thirds from the second to the fourth day inclusive.

A bacteriological study by one of us of the uterine flora day by day after delivery, the results of which are in course of publication, indicates that the uterus becomes invaded very early in the puerperium by bacteria from contiguous surfaces. This growth rapidly increases from the third to the fifth day, after which it diminishes, practically to disappear by the tenth day. The frequency of raised temperature on the third day of the puerperium therefore receives explanation.

Literature.

Turning now to results published elsewhere, we are largely indebted to the chapter by Sigwart in the recently published *Biologie und Pathologie des Weibes* (Berlin, 1927, vol. 8, Part 1, p. 719 et seq.) for references to results of the use of streptococcal vaccine in the prevention and treatment of puerperal sepsis. The published observations

fall under two headings: (1) large scale experiments; (2) treatment of relatively small numbers of women in the wards of lying-in hospitals.

In the former category Toltens (1917) inoculated some 1,600 women shortly before labour and found that the larger the dose of vaccine administered the lower the morbidity rate. No control group was studied. Thus:

No. of Cases.	Dose of Vaccine (millions).	Morbidity (per cent.).
819	25.50	16.0
433	100	13.3
300	250	10.6
126	500	7.1

The methods employed by Louros (1923) have served as a model for several investigators. Louros gave 250 million polyvalent streptococcal vaccine twenty days before confinement was to be expected, and a further dose of 500 million vaccine ten days before. The concurrence of a negative phase, following vaccination, with the time of delivery was thus avoided and active immunity was supposedly established. Of a group of 151 women so treated, 33 sustained complications in subsequent childbirth; only in one case did the temperature rise above 104° F. But all the women were carefully watched and treated in the maternity clinic before and during their labours and puerperia; the low incidence of sepsis might as well have been ascribed to this as to the vaccine.

In another series of 3,215 births and abortions 522 cases were immunized, some actively and some both actively by vaccines and passively by administration of anti-streptococcal serum before and during labour. All of these cases were either febrile or, being complicated, were likely to develop fever; 163 actually ran temperatures, 4 of these were cases of septicaemia and 4 deaths occurred from various causes, not necessarily the result of streptococcal infection.

Maroudis (1923) applied Louros's methods in the maternity clinic at Athens. Despite adverse conditions and overcrowding, the results among vaccinated women were better than among the untreated.

Of 1,229 vaccinated women 367 received two doses of vaccine before labour, and 862 received 500 million vaccine and anti-streptococcal serum during labour. Among these women there was no death from streptococcal infection and only 2 had local streptococcal infections. Among 786 untreated women there were 7 deaths, and 8 suffered from local infections.

In the second category, treatment of groups of women in hospitals, the published descriptions scarcely merit individual mention, for the results are equally divided for and against vaccination. No results are claimed in highly virulent infection; unhappily, in such cases death invariably supervenes before time has elapsed sufficiently for the dose of vaccine to have established adequate protection. Indeed, a woman surviving long enough to be fully treated by Louros's standard might be expected to recover unaided.

Summary of Clinical Evidence.

The clinical evidence, then, in favour of the use of streptococcal vaccine, if not negative, is indefinite, whether the vaccines be used in prophylaxis or for treatment. In making this assertion we do not presume to express an opinion on the efficacy of bacterial vaccines in general. Amongst experienced clinicians the feeling that vaccines are of service is too strong for the subject to be lightly dismissed. Nevertheless, in our opinion, the scale, both clinical and experimental, on which our observations have been carried out justifies our conclusion.

Non-specific Protein Therapy.

Against the claim that the alleged protective effects exercised by streptococcal vaccines in puerperal sepsis are specific is the fact that similar results have been obtained by the use of heterologous vaccine such as *B. coli*. In fact, Louros himself suggests that the vaccine acts by protein shock.

It is not opportune to discuss here how far non-specific vaccine therapy is of value, whether the reagent be administered in homoeopathic doses of a few million organisms or in mass sufficient to produce protein shock. Such

observations as favour vaccine treatment of puerperal sepsis tend rather in the direction of non-specific protein therapy—the larger the dose of foreign protein administered and the more severe the “shock” produced, the greater the apparent effect on the course of the disease. Under the heading of protein therapy, treatment by “colloidal” metals (for example, silver) must undoubtedly be included, as the effect produced must likewise be attributed to the protective colloid rather than to the metal component. The phenomena of shock and recovery are undoubtedly in some way bound up with leucocytic activity.

Experiments with Animals.

It is very remarkable that so common an organism as the *Streptococcus pyogenes* should have baffled experimental investigation. At first sight the efficacy of streptococcal vaccines would appear readily ascertainable by experiment with animals, but this is not the case in practice. The susceptibility of laboratory animals—rabbits, rats, and mice—to streptococcal infection is not only low, but varies greatly; furthermore, difficulties constantly arise owing to change and depreciation in the virulence of streptococcus strains.

The method of intradermal inoculation of the shaven back of rabbits, first described by Birkhaug² in 1925, but initiated independently by one of us,³ has proved, within limits, of value in studying antistreptococcal immunity. Unfortunately, considerable doubt has been thrown on much of Birkhaug's work, and his results have not been successfully repeated in this country.

Intradermal inoculation of shaven rabbits with a culture of a recently isolated strain of *S. pyogenes*, the virulence of which has been well maintained by animal passage, is followed by the appearance of local lesions proportionate in severity to the size of dose and resistance of the animal. Three doses—1/10 c.cm., 1/100 c.cm., and 1/1,000 c.cm.—of a sixteen-hour broth culture, 1 c.cm. of which is fatal to a mouse within twenty-four hours, are inoculated alongside each other. The characteristic lesion is a local erysipeloid patch, sometimes also surrounded by a bright scarlet erythema. Local suppuration usually follows, or actual necrosis of tissue may occur with formation of a deep ulcer.

In resistant animals the lesions may not progress beyond the stage of cellular infiltration. Almost without exception lesions are fully developed by the fifth day, after which recovery sets in and is complete by the tenth day, in the sense that streptococci disappear and active inflammation ceases, although mechanical damage may persist and heal but slowly. It seems reasonable to conclude that, taking a batch of rabbits of about the same weight and age, the severity of the lesions may be accepted as an index of the balance between virulence of infection and vigour of defence.

The experiments were originally planned to determine the prophylactic value of the products of streptococcal growth, “toxins” as well as vaccines. Two rabbits were immunized with each of the prophylactic agents under test; a pair was likewise inoculated with living virulent streptococcus culture; a pair was reserved as blank control. In a long series of experiments three intradermal inoculations of the homologous strain of streptococcus in living culture were administered, as described, at intervals of from five to ten days after completion of the prophylactic course. The degree of immunity possessed by each animal was apparent on comparing the lesions on the third and successive days; a survey of the whole batch enabled a just estimate to be formed of the significance of each experiment.

In general terms, the method failed to differentiate the relative prophylactic efficiency of broth filtrates (toxin) and vaccine; it was often a matter of difficulty to decide whether unprotected animals or those which had received killed vaccines were more susceptible. There was no ambiguity, however, in deciding the merits of living culture, as the animals so protected were completely resistant to subsequent infection in every instance. Laboratory experiments, therefore, support the clinical evidence that streptococcal vaccines are of doubtful value as a safeguard against living virulent streptococci.

Conclusion.

Summarizing the position, morbidity in the puerperium is in the main due to a single cause, the *Streptococcus pyogenes*; the failure of vaccines, a specific means of treatment, is, therefore, the more disappointing.

It appears that all but a few of our morbid cases recovered spontaneously. This being so, the conclusion follows that special remedies, such as vaccines, are of subsidiary importance in the prevention of sepsis as compared with conservative and aseptic midwifery. Puerperal sepsis, being a specific disease, must be recognized as a definite clinical process to be treated like any other infectious or contagious malady.

We are particularly indebted to Dr. Malcolm Donaldson for assistance and advice throughout the inquiry. The inauguration of the experiment on the extern district and the details of treatment were due in the first instance to him, and were carried out under his direction. To Donaldson also is due the introduction of the systematic use of sterile dressings and towels on the district, and insistence on conservative methods in the management of labour; his name in particular must therefore be associated with this paper. The extern midwifery department is grateful to Dr. Mervyn Gordon, consulting bacteriologist to the hospital, for large supplies of vaccine, and for much helpful advice on its application.

Acknowledgement is due to the Medical Research Council for assistance in the conduct of the experimental side of the inquiry.

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OBSERVATIONS ON BREAST-FEEDING.*

BY

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It is customary in this Branch for the incoming president to deliver an address or read a paper, a task which I, as a general practitioner, have viewed with some dismay. I have chosen, however, a subject which I think is interesting to all general practitioners, and particularly to

CHART 1.—Showing superiority of breast-feeding over artificial feeding in good and bad conditions of home. B1, Breast-fed by careful mothers. B2, Breast-fed by careless mothers. A1, Artificially fed by careful mothers. A2, Artificially fed by careless mothers.

TABLE I.—Showing the average weights at 1 year of infants grouped according to the income of individual members of the family after rent is paid.

	Average weekly income up to—					Over 5s.
	1s.	2s.	3s.	4s.	5s.	
Entirely breast-fed to 6 months.	1b. oz. 17 13	1b. oz. 18 0	1b. oz. 18 13	1b. oz. 18 7	1b. oz. 18 12½	20 2½
Not entirely breast-fed to 6 months.	15 11	16 6	15 14	16 6½	17 3	17 9

those who, like myself, have been engaged in the work of infant welfare for many years. To such the question of breast-feeding is paramount, whether we consider it from the point of view of the mortality or well-being of the infant, or even from that of the comfort and happiness of its parents. Chart 1 and Table I illustrate this; the type

* Being the presidential address delivered to the Midland Branch on July 13th, 1928 (abridged).

of home or of mother, or the wage of the father, makes no difference to the comparative results. Breast-feeding, then, being of prime importance, why is it that so many women do not continue to suckle for the necessary period? I propose to discuss a few of the reasons which so often lead to the abandonment of breast-feeding.

The mammary secretion depends almost wholly on one vital factor—the efficiency of the suction stimulus of the infant, acting probably through the sympathetic system, with a centre in the medulla. As the milk is formed it accumulates in the enlarged galactophorous ducts, and after the tension has reached a certain point further secretion is inhibited. If the ducts are emptied a new secretion begins. The emptying of the ducts seems to constitute the normal physiological stimulus to the gland cells, and any condition in mother or child interfering with this stimulus will cause difficulty in the establishment and maintenance of breast-feeding. In the case of the child interference with suction may be due to:

1. *Prematurity or immaturity or some cerebral injury at birth*, often resulting in somnolence. In some of these infants suction is ill controlled and inco-ordinated, or the act of swallowing may be bungled, so that the milk escapes by the mouth or sets up fits of coughing. Apart from actual injury, infants who have suffered severely at birth from the effects of a difficult labour are apt to be inert, lax, and feeble in suction for a few weeks.

2. *Various infective disorders*, such as sepsis neonatorum, icterus, eclampsia, and haemorrhagic disease, which cause loss of appetite and refusal to suck.

3. *Indigestion*, often brought about by injudicious purgation or irregular or too frequent feeds, is usually of a simple type due to too frequent feeding. It has been stated that there may also be a fat indigestion, brought about by the ingestion of excess fat in the frequent small feeds; the child is being fed practically on "strippings" always carrying a high percentage of fat. I think, however, this is extremely doubtful. Some of the wet-nurses at the Paris Maternité frequently give from 30 to 40 feeds a day, and the infants under their care do not appear to suffer from fat indigestion at all.

4. *Morbid conditions of the child's nose, mouth, and upper air passages*, such as thrush, Bednar's aphthae, nasal catarrh, adenoids, bronchitis, cleft palate, etc.

5. *Congenital dyspepsia*, a constitutional condition characterized by indigestion from the outset.

6. *A neurotic temperament.*

In the case of the mother there may be:

7. *Local conditions*, such as depression, excoriation or cracking of the nipples, and abscess of the breast.

8. *General conditions*, such as malnutrition from deficient nourishment; carious teeth; dyspepsia, etc.; and

9. *Psychological causes*, as anxiety, excitement, over-exertion, want of sleep, etc. Budin describes a serious setback to three or four infants in the Paris Maternité due to a violent fit of passion in their wet-nurse.

Many of the difficulties I have enumerated can be obviated by simple hygiene of the breasts before or after delivery; and other troubles, and their treatment, are matters of everyday experience. I do not propose to dwell further on these, but rather to discuss the more serious conditions which interfere with the establishment and maintenance of lactation, and, incidentally, certain theories and speculations of my own concerning some of them.

CONDITIONS AFFECTING THE MOTHER.

Delayed Lactation.

In some cases the full supply of milk may not be forthcoming for three or four days after labour, and may even be postponed for three weeks. If there is delay this is one of our most difficult periods; the mother is getting very anxious about her child, and must be encouraged and reassured in every possible way. It is well to avoid any form of artificial feeding. If this is not possible, a little boiled water sweetened with saccharine, or an ounce of whey, may be given for the first three days. We should, however, strictly limit the amount—the child must be kept hungry till lactation is established.

Underfeeding of the Mother.

Underfeeding of the nursing mother has, I am sure, some effect, not perhaps on the actual development of lactation, but certainly on its efficiency. I have had the