Whooping-cough.

This disease is caused by Bordet's bacillus, but very soon after the onset there appear, just as we see in influenza, Pfeiffer's bacillus and pneumococcus. For the treatment of the disease, therefore, a mixed vaccine should be given. The technical difficulties of isolating Bordet's bacillus make it almost imperative in practice to use a stock vaccine, and such a vaccine should contain all three of the bacteria mentioned above. This vaccine is very little toxic, so that even for small children comparatively large doses (1,000 or 2,000 million) can be given, and it is well to repeat the doses every two or three days instead of at the longer periods which are common with the other vaccines.

The administration of the vaccine cuts short the attack and prevents complications.

It is for prophylactic purposes that the whooping-cough vaccine will be found of greatest value to the community. Either a simple vaccine of Bordet's bacillus may be given or a mixed vaccine of this bacillus combined with Pfeiffer's bacillus and pneumococcus. Three doses of the vaccine should be given at intervals of a week, and it has been found that in some communities of children whooping-cough has been almost wiped out by this means. I should strongly advocate prophylactic vaccination in institutions where there are aggregated together numbers of children, and also in families where one of the children has become infected.

Chronic Rheumatic Conditions.

I include under this heading rheumatoid arthritis, fibrositis, neuritis, sciatica, myositis and similar complaints. These all seem to take their origin from some chronic infection, which is usually streptococcal. The site of the infection is usually in the mouth or the intestine, and the streptococcus which is responsible is very different from the *Streptococcus pyogenes*, which is the causative agent in acute septic infections such as erysipelas or acute septicaemia; it is of very much less virulence, so that it may infect a portion of the body for years without causing more than slight inconvenience. It is because of this that infections of this type are allowed to persist, maybe, for many years, and it is often only when some serious result, such as rheumatoid arthritis, is seen that any attention is paid to the original infection. A common history of a patient with rheumatoid arthritis when she comes to the out-patient department is that she had bad teeth for years, and when she consulted her doctor she was told to have all her teeth out. This was followed by only temporary improvement, after which the arthritis progressed as before. On examination of such a patient's stools, it will in all probability be found that there is an enormous preponderance of streptococci, and more especially of streptococci of the mouth type. Doubtless the infection commenced in the mouth, but some of the streptococci which were being continually swallowed escaped destruction by the gastric juice and bile and established themselves in the intestine, where they had continued to flourish.

The effect in such cases of the administration of vaccines, either autogenous or stock, has been that in almost all there is some alleviation of the condition, and in some there is apparently complete disappearance of the disease. In some few there is apparently no benefit, which is not surprising considering the difficulty in isolating the organisms from the intestine and the multiplicity of types of streptococci found there. Considering, also, that the source of the streptococci is the intestine, which is to all intents and purposes outside the body, it must be appreciated that the course of vaccine treatment must be long, and it is seldom that recovery will take place in less than a year. Owing to the multiplicity of types of streptococci in the mouth and intestine it is frequently better to commence treatment with a mixed stock vaccine such as the anti-rheumatic vaccine which we make at St. Mary's Hospital and which contains a very large number of strains of streptococci from rheumatic patients, and only to proceed with an autogenous vaccine if the stock vaccine fails. If this is done, only comparatively seldom will an autogenous vaccine be required.

Diphtheria Carriers.

Brownlie (*Lancet*, March 27th, 1920) showed that by the administration of a vaccine the diphtheria bacilli could be

got rid of in a very much shorter time than by any other means. Out of a series of 50 consecutive and unselected cases who received the vaccine in doses of 10 to 60 millions every four days 44 were free from bacilli after three doses, and all were free after eight doses of the vaccine. If these observations are confirmed it would seem that for public health purposes this vaccine of the diphtheria bacillus would be of the greatest value.

Other Conditions Suitable for Vaccine Treatment.

Vaccine therapy is applicable to very many conditions other than those on which I have touched, but time prevents my going into these. Local tubercle, acne, staphylococcal infections such as boils and carbuncles, streptococcal infections such as erysipelas or pyorrhoea, and many others have been successfully treated, and indeed vaccine therapy in these conditions seems to furnish the only direct means of combating the infection. Many publications have been made on these matters, and I need not weary you with recital of the merits of vaccines in these conditions which have been treated in this way for many years.

In conclusion, I wish to draw attention to the fact that patients may be inoculated with bacterial products not only from without, but also introduced into their circulation by some disturbance of the infected focus. It has been shown by means of blood examinations that any such disturbance is followed by a sequence of events which are the exact counterpart of those following the administration of vaccines by hypodermic injection.

It does not matter what form the disturbance takes—whether exercise, massage, forcible movement or the active hyperaemia induced by the application of a fomentation—the result is the same, the only difference being that, whereas the light forms of disturbance reproduce the effect of a small dose of vaccine, the more severe disturbances may be followed by the same events which follow a large dose of vaccine, and to which I have alluded above under the heading of "General Reaction"—namely, malaise, fever, or even collapse.

It follows from this that in the treatment of any patient by vaccines a satisfactory conclusion is only to be arrived at if this phenomenon of auto-inoculation is considered, and in most cases it is necessary that these auto-inoculations should be diminished or abolished by keeping the infected part as much as possible at rest by splinting or some other means.

In some conditions, such as phthisis, it is very difficult to control these auto-inoculations, and it is probable that the very indifferent results which have followed the administration of tuberculin in this condition in many cases have been due to this fact.

THE SEROLOGICAL CHARACTERS OF DISEASE-PRODUCING PNEUMOCOCCI.

BY

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RECENT investigations on several groups of micro-organisms, of which the meningococcus group may serve as an example, have proved the value of discrimination between disease-producing strains on the one hand and non-pathogenic saprophytes on the other. Such discrimination has been rendered possible by the general method of testing the agglutination reaction of a particular strain against specific serums, previously prepared by inoculation of rabbits with typical organisms from morbid lesions. By this means disease-producing micro-organisms have been gradually relegated to types.

The diversity of the clinical picture presented by pneumococcal pneumonia, the wide prevalence and severity of this disease, and the fact that the pneumococcus is a normal and usually harmless inhabitant of the upper respiratory passages, has suggested that distinct disease-producing types of the organism may exist.

Such has been shown to be the case by American workers at the Rockefeller Institute for Medical Research,¹

who have defined at least three serologically distinct types to which the great majority of pneumococci isolated from actual cases of pneumonia were found to belong; a number of strains from indifferent sources, such as saliva or nasal secretion, could not be grouped by the type serums.

Application of the American results to pneumonias occurring in this country was at once suggested, but having regard to our widely different climatic and social conditions, it did not seem sufficient to limit investigation to the typing of pneumococci by means of serums obtained from American sources only.

It was held that insufficient evidence of the relative prevalence of the three recognized American types in this country was available, nor was there proof that other types of pneumococcus, as fertile originators of disease as any recognized in America, might not exist here. Further, it was considered inconvenient that the serological test should depend on the availability of serums derived exclusively from American sources. The preparation at first hand of type-agglutinating serums appeared expedient therefore, both from the standpoint of excluding the necessity for importing supplies, and also in order to obtain agglutinating serums prepared against strains of pneumococci derived from home sources. Experiments have been carried out with these objectives in view, and the results obtained will be considered under two headings:

I. The serological characters of pneumococci isolated from a variety of cases of pneumococcal infection not only of the lungs, but of the respiratory tract in general.

II. The preparation of agglutinating serums by the inoculation of rabbits with pneumococci derived from British sources.

I.—SEROLOGICAL CHARACTERS OF PATHOGENIC PNEUMOCOCCI.

1. Identification of the *Pneumococcus*.

The identification of each strain of pneumococcus prior to investigation by the serological test has been based on the characters described below—namely:

1. Habitat. The source—for example, sputum or lung juice; or heart's blood culture in a fatal case of pneumonia.

2. The very characteristic appearance of colonies on solid media. These are ringed or discoid in shape, and have an appearance resembling ground glass.

3. Pneumococci, particularly of pathogenic strains, show extraordinary predilection for media enriched with fresh blood. Although the addition of other body fluids (ascitic, etc.) will promote growth, the haemophilic character of the pneumococcus appears characteristic, and herein the organism differs from streptococci; the size of streptococcus colonies does not appear to be quite so much affected by the presence of blood.

4. Uniform turbidity in blood broth and ascitic broth; relative absence of chains.

5. The shape of the pneumococcus is usually a valuable guide; the presence of a capsule when growing in material obtained from body fluids is of important diagnostic value.

6. Mair's modification of the bile-solubility test has been employed.²

One-tenth of a cubic centimetre of a 10 per cent. solution of sodium desoxycholate is added to a twenty-four-hours old culture in $\frac{1}{4}$ c.cm. of sugar-free broth enriched by the addition of half a cubic centimetre of ascitic fluid.

If a pneumococcus be present, the turbid culture almost immediately clarifies; on the other hand, control tests with similar cultures of *Streptococcus pyogenes*, *salivarius*, and *faecalis* are absolutely negative.

2. The Serological Test.

An epitome of the procedure employed in carrying out the serological test follows:

TECHNIQUE.

A. Preparation of the Standard Emulsion.

1. Single colony subcultures are made from first cultures of the material under investigation on—

2. Surface plates of legumin agar containing incorporated fresh human or rabbit's blood.

3. Plates are incubated at 37° C. overnight.

4. The growth is washed off in normal saline solution.

5. The suspension thus obtained is heated to 65° for half an hour.

6. Standardized to required strength—for example, 4,000 million cocci per cubic centimetre—and phenolated by the addition of 5 per cent. phenol solution requisite to produce a final concentration of 0.5 per cent. phenol.

B. Agglutination.

1. Small glass tubes $\frac{3}{16}$ in. by $\frac{1}{4}$ in. are arranged in racks for incubation at 55° C.

2. Required—control normal rabbit's serum, the three type serums, and suspensions of the three type cocci.

3. Dilutions of 1 in 10, 1 in 20, 1 in 40, 1 in 80 of serum, of each 0.5 c.cm. Add an equal amount of suspension to all tubes and incubate.

4. In marked cases results are easily readable within four hours, but as a routine twenty-four hours are given.

5. Agglutination when positive is generally complete in the case of typical specimens. Any supersensitiveness of coccal suspension to serum is betrayed by the control with normal serum.

For brevity and clearness results have been expressed as far as possible in the table on page 261, which summarizes the clinical features of each case, records the source from which coccus was derived, whether sputum, etc., during life or material obtained *post mortem*. The appearance of films of such material and of the primary cultures therefrom is noted, and also the serological type to which cultures from a selected single colony were found to belong.

The table of experimental results, giving the titre of each serum against the coccus examined, submitted in the full communication to the Science Committee of the British Medical Association, has been omitted from consideration of space.

It will be noted that dependence has been placed throughout on the isolation of the presumptive infecting strain of pneumococcus from sputum by culture methods. The alternative method of injection of sputum into the peritoneal cavity of a mouse and isolation of pathogenic strains by this means has not been employed, partly because it is felt that facilities for animal inoculation in this country are to a considerable extent restricted, and partly in order to ascertain how far sputal flora are representative of lung infections. That the sputum of cases of adult lobar pneumonia who acquire a massive infection of the lung is truly representative there can be no doubt; some uncertainty arises in the case of children, whose sputum, both in film and culture, differs very markedly from lobar sputum, most commonly showing a mixed flora, though usually containing pneumococci in excess. Coughing may always be induced, and a little sputum can thus be obtained, by swabbing the throat just above the upper opening of the larynx of a child suffering from bronchopneumonia.

Certain inferences appear justified from a study of the results recorded in the table.

1. The American type pneumococci are responsible for disease in this country and have a similar distribution.

2. Seeing that the Type I coccus is responsible for many typical cases of lobar pneumonia in adults, and that this infection must be widely distributed, it is remarkable that this type does not appear to cause disease in childhood. So far, the pneumococci responsible for disease in young children have been found to belong almost uniformly to Type II.

In four cases of bronchopneumonia examined *post mortem* a Type II coccus was obtained from the lungs, in the remaining eight cases from the sputum during life. From present observations it would seem that this type of coccus most frequently causes illness in children, as it has also been obtained from undoubted tissue sources—for example, empyemata or the meninges and heart's blood *post mortem*. At the same time the need for a confirmatory study of lung puncture fluid is indicated, while the sputum of normal healthy children may also repay investigation, particularly if it is found that type pneumococci are absent or relatively absent therefrom.

The passage of Type I infection from mother to child is exemplified by Cases G. and H., in which a boy, aged 12 years, developed a typical lobar pneumonia with crisis a week after his mother fell ill, her pneumonia being complicated by an empyema. On the other hand, in Cases E. and Z., a father and his son aged 4 were admitted to hospital simultaneously suffering from lobar- and bronchopneumonia respectively. A Type I coccus was isolated from the sputum of the father, a Type II from that of the child; this finding does not suggest a case-to-case infection.

In only one case, A.J., a girl aged 6 years, with empyema, has a Type I coccus been isolated from a child.

It would seem that a very different kind of susceptibility to the two types must exist in the case of children and adults, and the observed difference in the clinical aspect of pneumococcal lobar- and broncho-pneumonia is thus confirmed by the serological findings. So far as the writer is concerned this result was not anticipated.

Types of Pneumococci Occurring in Acute Infections of the Respiratory Tract.

Clinical and Serological Type.	Case Reference.	Age: Years.	Source.	Film or Culture.	Clinical and Serological Type.	Case Reference.	Age: Years.	Source.	Film or Culture.
LOBAR PNEUMONIA.	A.	Adult	Sputum	Dominant pneumococcus.	BRONCHOPNEUMONIA.	³ AB.	3	Sputum	<i>B. diphtheriae</i> , pneumococcus
A.-H., Type I.	B.	"	Empyema, pus	Pneumococcus.		AC.	2	"	Dom't pneumococcus
I.-O., Type II.	C.	"	Sputum	Dom't pneumococcus.		AD.	6	"	Mixed flora
P., Non-agglutinator.	D.	"	"	Dom't pneumococcus.		AE.	3½	"	Dom't pneumococcus
	E.	"	"	Dom't pneumococcus.	BRONCHITIS.	AF.	Adult	Sputum	Dom't pneumococcus
	F.	"	"	Dom't pneumococcus.	AF.-AH., Type II	AG.	"	"	Dom't pneumococcus
	G.	"	Empyema, pus	Pneumococcus.		AH.	"	"	Dom't pneumococcus
	H.	12	Sputum	Dom't pneumococcus.	EMPHYEMA.	AI.	Adult	Pus	Pneumococcus
	I.	Adult	Pleural exudate post mortem	Pneumococcus.	AI., AJ., Type I	AJ.	6	"	"
	J.	"	Heart's blood post mortem	Pneumococcus.	AK.-AM., Type II	AK.	Adult	Pus post mortem	"
	K.	"	Sputum	<i>B. influenzae</i> , dom't pneumococcus.		AL.	6	Pus	"
	L.	"	"	Pure culture pneumococcus.		AM.	6	"	"
	M.	"	"	Dom't pneumococcus.	SEPTICAEMIA.	⁴ AN.	Child	Heart's blood post mortem	Pneumococcus
	N.	"	Empyema, pus	Pneumococcus.	AN., Type III	⁵ AO.	1½	Pericardial fluid	"
	O.	"	Sputum	Dom't pneumococcus.	AO., AP., Type II	⁶ AP.	1½	Heart's blood post mortem	"
	P.	"	"	Dom't pneumococcus.	MENINGITIS.	AQ.	12	Pus post mortem	Pneumococcus
BRONCHOPNEUMONIA.	Q.	Adult	Sputum	Friedländer's bacillus, pneumococcus.	AQ.-AT., Type II	AR.	12	"	"
Q., Non-agglutinator.	² R.	"	Bronchial secretion post mortem	Dom't pneumococcus.		AS.	7	Lung juice post mortem	"
R.-AE., Type II.	S.	Child	Bronchial secretion post mortem.	Dom't pneumococcus.		AT.	Adult	Pus post mortem	"
	T.	"	Empyema, pus post mortem	Pneumococcus.	PERITONITIS.	AU.	Adult	Heart's blood post mortem	Pneumococcus
	U.	"	Lung puncture fluid	Dom't pneumococcus, streptococcus, <i>B. catarrhalis</i> .	UPPER RESPIRATORY PASSAGES: RHINITIS, etc.	AV.	Adult	Nasal discharge	Dom't pneumococcus
	V.	7 wks.	Sputum	Dom't pneumococcus.	AW.	"	"	"	Dom't pneumococcus
	W.	8 mos.	"	Dom't pneumococcus.	AX.	"	"	"	Dom't pneumococcus
	X.	2½	"	Dom't pneumococcus.	AY.	"	Post-nasal space secretion	Dom't pneumococcus	Pure pneumococcus
	Y.	1½	"	Dom't pneumococcus.	AZ.	"	Pharynx	Pure pneumococcus	Dom't pneumococcus
	Z.	4	"	Mixed flora, including pneumococci.	BB.	Child	Nasal discharge	Dom't pneumococcus	Pure pneumococcus
	AA.	3½	"	Pure growth pneumococci.	BC.	Adult	Empyema ethmoidalis pus	Pure pneumococcus	

¹ Complicated by morbus cordis.² Complicated by mitral stenosis.³ Post-diphtheritic bronchopneumonia.⁴ Primary focus, mastoid disease.⁵ General tuberculosis, terminal pneumonia.⁶ Pyopericarditis.

3. Of the other types, as already shown by American workers, Type III has a limited distribution in the upper respiratory tract in disease; it is interesting that the only specimen was derived from a mastoid abscess with pneumococcal meningitis.

4. Certain pneumococci, which there seemed every reason to believe responsible for a particular illness, did not agglutinate with the three type serums. These may possibly be referable to the heterogeneous Group IV.

Mair's modification of the bile solubility test has proved of very great value in separating off a few cocci morphologically resembling pneumococci and with similar cultural characters, but belonging to the group of salivary streptococci and on other grounds not to be regarded as belonging to the pneumococcus group.

In addition, organisms resembling pneumococci have been isolated from time to time which appear to be non-specific, although bile-soluble. Such are often exceedingly hard to emulsify from plate cultures for the purpose of testing their agglutinating properties; the explanation of this physical peculiarity is not fully understood. More than sixty strains of pneumococci have been investigated in the course of the inquiry.

II.—PREPARATION OF AGGLUTINATING SERUMS BY INOCULATION OF PNEUMOCOCCI DERIVED FROM ENGLISH SOURCES.

Living cultures of the only Type III coccus obtained (Case AN.) were unfortunately not kept, and an American Type III coccus—a stock culture obtained from Dr. St. John

Brook, Lister Institute—was utilized for the preparation of an agglutinating serum, a serum of good titre and keeping qualities being obtained from the first rabbit inoculated.

The stock Type I coccus from Dr. St. John Brook had but feeble agglutinogenic properties, but a satisfactory coccus "A" from a typical case of lobar pneumonia here has yielded good agglutinating serum. The preparation of a good Type II serum has presented very great difficulty, and caused delay and disappointment throughout the inquiry.

Of the Type II cocci investigated all are so far possessed of but feeble agglutinogenic power. Further, the wide distribution of the Type II coccus, and the variety of conditions to which pneumococci of this group give rise demands the production of a "catholic" serum of wide agglutinating scope.

Such a discovery might have been anticipated from the admittedly complex character of the Type II group. The difficulty of producing a Type II immune serum from horses has been recognized.

The principle adopted in the preparation of agglutinating serums has been the intravenous injection of standard phenolated suspensions of the selected coccus in increasing doses at intervals of forty-eight hours, and throughout only a single strain has been employed for each rabbit.

By this means satisfactory serums possessed of the property of completely agglutinating their homologous coccus, and subsequently other cocci belonging to the same group in dilutions of 1 in 80 in twenty-four hours

TABLE A.

Suspension.	Normal Serum.				"M." Serum.				"A.L." Serum.				"A.O." Serum.				"T." Serum.			
	1:20	1:40	1:80	1:160	1:20	1:40	1:80	1:160	1:20	1:40	1:80	1:160	1:20	1:40	1:80	1:160	1:20	1:40	1:80	1:160
"A." T.I. control ...	-	-	-	-	-	-	-	-	-	-	-	-	(+)	(+)	-	-	-	-	-	-
U.S.A. III control ...	-	-	-	-	+	(+)	-	-	+	(+)	-	-	++	++	+	(+)	+	-	-	-
"A.L." ...	-	-	-	-	+	+	+	-	++	+	+	tr	+	+	+	(+)	++	+	+	+
"A.O." ...	-	-	-	-	(+)	(+)	tr	-	+	(+)	tr	-	+	+	+	(+)	+	-	-	-
"J." ...	-	-	-	-	+	+	(+)	(+)	+	+	(+)	-	+	+	+	+	+	+	+	+
"M." ...	-	-	-	-	+	+	(+)	-	+	(+)	tr	tr	-	-	-	-	-	-	-	-

at 55° C., were obtained in the case of a Type I strain derived from a case of typical lobar pneumonia referred to as Type I "A" and in that of the American Type III coccus from the Lister Institute.

An example of the procedure followed when preparing a rabbit, and the result, at intervals, given by its serum, may be quoted.

A young animal weighing 1,300 grams was inoculated intravenously, at intervals varying from forty-eight to seventy-two hours, with five successive doses of an emulsion in 0.5 per cent. phenolated normal saline solution, increasing from 4,000 to 16,000 million Type I "A" cocci.

On the twelfth day from the beginning of the experiment a sample of the animal's serum was titrated against a standard emulsion of the homologous coccus. Complete agglutination in twenty-four hours at 55° C. occurred in dilution 1 in 10, distinct agglutination in dilution 1 in 20, a trace in 1 in 40.

Two further injections were given, the dose rising to 20,000 million cocci. A test of the agglutinating power of the serum six days later showed complete agglutination in dilution 1 in 40, slight in 1 in 80.

Doses of 16,000 million and 20,000 million cocci were repeated, and the animal, which had gained weight throughout the experiment, was finally bled out, exactly a month from the date of first inoculation. The final titration of the serum showed complete agglutination in 1 in 80, slight agglutination in 1 in 160.

The American Type II coccus proved a failure for agglutinogenic purposes, and recourse was had to a series of Type II cocci from definite tissue sources in cases of pneumococcal infection—for example, heart's blood, empyema pus, or lung exudate *post mortem*. These cocci were referred to type by titration against an American Type II serum prepared by the Mulford Company, Philadelphia. The strains employed are derived from the cases whose cipher they bear; the clinical features of each are noted in the table on p. 261.

The Case "I" Type II serum at first feebly agglutinated American Type II coccus, but, on keeping, this action became limited to its homologous coccus.

Case "M" and Case "J" cocci were next tried but without success, the titre attained by the Case "J" serum after sixteen injections over a period of six weeks being only 1 in 10.

It was thought that the animals employed might be in themselves poor agglutinin producers, but a result similar to the above was again obtained after repeated injection. In view of this lack of success the effect of *unheated* emulsion of cocci killed by the addition of 0.5 per cent. phenol and incubation at 37° was next tried, a rapid method of five injections at intervals of forty-eight hours being employed and the animal then bled out.

The titres of the two serums obtained were respectively:

	1:10	1:20	1:40	1:80
Case AL. ...	++	++	+	(+)
Case M. ...	+	+	(+)	-

++ = Complete agglutination, clear fluid.
+ = Distinct agglutination, fluid not clear.
(+) = Slight agglutination.
tr = Trace only.

Encouraged by the improved titre of the "AL." serum, two other rabbits were inoculated with the Case "AO." and Case "J." cocci, as before unheated but killed by phenol.

A sample of the blood of each rabbit taken from the ear prior to bleeding out yielded a serum with the following titre in twenty-four hours:

	1:10	1:20	1:40	1:80
Case J. ...	++	++	++	++
Case AO. ...	++	++	++	++

Three days later each of the four serums was titrated against its homologous coccus and the other cocci of the group, with the result shown in Table A. Some doubt was felt as to the accuracy of the readings owing to the fact that somewhat indifferent suspensions of cocci with tendency to auto-precipitation were employed and the experiment was therefore repeated a fortnight later, with the following result:

TABLE B.

Coccus.	T.			AL.			AO.			M.		
	1:10	1:20	1:40	1:10	1:20	1:40	1:10	1:20	1:40	1:10	1:20	1:40
J. ...	(+)	+	tr	(+)	-	-	(+)	tr	-	-	-	-
AL. ...	-	-	-	(+)	(+)	-	(+)	+	-	-	-	-
AO. ...	-	-	-	-	-	-	++	+	-	-	-	-
M. ...	-	-	-	(+)	-	-	-	-	-	(+)	-	-
A. ...	(+)	tr	-	-	-	-	-	-	-	-	-	-

No agglutination with normal serum control.

Rapid deterioration of all serums had obviously occurred, the reason for which has not yet been clearly defined; these serums were necessarily discounted and two more rabbits prepared against the AL. and M. cocci.

The AL. serum agglutinated its homologous coccus in dilution 1 in 20, and was thereupon tested against a group of cocci previously typed by the Mulford II serum to confirm the reactions of this serum. The result, Table C, indicated that the AL. serum was not only a feeble agglutinator, but insufficiently "catholic" as regards the Type II group.

TABLE C.

Type II Cocci.	AL. Serum.		Normal Serum.	Type II Cocci.	AL. Serum.		Normal Serum.
	1:10	1:20			1:10	1:20	
AL. ...	+	(+)	-	AA. ...	(+)	(+)	tr
AY. ...	(+)	-	-	AB. ...	+	(+)	tr
Y. ...	-	-	-	AM. ...	(+)	tr	+
Z. ...	+	+	+	"B." Type I	-	-	-

* Poor suspension.

† Control.

Meanwhile it was necessary to identify the type of a number of cocci which had been collected. A small quantity of Type II serum from the Rockefeller Institute became available from the pathological department, Charing Cross Hospital, and was tested against standard emulsions to ascertain its agglutinating properties. The serum proved so active that it agglutinated not only selected Type II cocci in all dilutions up to 1 in 80, but also reacted with a Type I and Type III coccus in dilutions of 1 in 10 and 1 in 20.

This cross-agglutination was found to be eliminated by using the serum in higher dilutions only. Finally, the serum was employed with satisfactory results in dilutions of 1 in 40, 1 in 80, and 1 in 160.

The problem presented by the preparation of a Type II serum cannot at present be considered solved. There remains to discover by repeated trial a Type II coccus of good agglutinogenic power and thoroughly representative of the group. Or, failing this, to investigate further the conditions which determine the production of agglutinins against the pneumococcus in the rabbit and lead to deterioration of agglutinin in serums when kept.

In conclusion, it may be said that the Type I pneumococcus is the most clear-cut and important of all. It is responsible for many of the severest cases here, while

American investigators have shown that Type I therapeutic serum has an appreciable effect in reducing mortality from lobar pneumonia; the serums prepared from Types II and III being up to the present far less successful.

In view of this practical aspect of the observations recorded in this report, it was necessary to determine whether the English strains of Type I cocci, identical with the American type on simple agglutination, are also indistinguishable when submitted to what is perhaps the most specific test available, the *absorption of agglutinin*.

The cocci compared in this respect were Type I American, English Type I "A," Type I "B" with Type II "M" as control. The serum used was the Type I "A," prepared as described.

The experimental procedure was as follows:

1 c.cm. of dilution 1 in 5 "A" serum was put up against equal amounts of suspensions containing 4,000 million per c.cm. of each of the above cocci.

Conditions.—Two hours in the water-bath at 37° C. Tubes then centrifuged and the supernatant fluid titrated against the Type I "A" coccus homologous to the serum.

Absorption Experiment.—Type I "A" serum absorbed with Type I "A" coccus, Type I, U.S.A. coccus, Type I "B" coccus, Type II "M" (control) coccus.

Result after Saturation V, Type I Coccus "A."

	Dilutions.			
	1:20	1:40	1:80	1:160
Control saline... ..	++	++	++	(+)
Control Type II "M"	++	++	++	(+)
Serum saturated with Type I "A"	+	(+)	—	—
Type I, U.S.A.	+	(+)	—	—
Type I "B"	+	(+)	—	—

Thus while Type II "M" completely failed to reduce the Type I agglutinin, the Type I cocci all caused its reduction by about three-quarters as shown in the accompanying table. In view of this result, there is no room for doubt that the two specimens of Type I coccus isolated from cases of typical lobar pneumonia in this country are identical with the stock specimen of Type I coccus obtained from America.

With a view to preparing Type I serum for therapeutic use, cultures of the organisms isolated from English cases have been forwarded to Dr. E. G. Murray, who is working at the Field Laboratories, Cambridge, on behalf of the Medical Research Council, at the production of therapeutic serum.

Throughout the inquiry I have been constantly indebted to the active assistance, encouragement, and advice of Dr. Mervyn H. Gordon, bacteriologist to St. Bartholomew's Hospital, and of his assistant, Mr. T. Heggerty, to both of whom I express my grateful thanks.

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EXOMPHALOS, OR HERNIA INTO THE UMBILICAL CORD.

BY

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THE condition of exomphalos, although somewhat rare, is of considerable interest, both from the point of view of origin and that of treatment.

It may present an abnormality of such extreme degree that the greater part of the abdominal organs are contained in a sac at the umbilical attachment of the cord or near that situation; but more commonly it consists of a globular swelling of about the size of a Tangerine orange. The former extreme cases are beyond surgical aid, but the more moderate degrees are eminently suitable for operation.

The literature, although fairly copious, contains few accounts of successful surgical treatment, the reason generally being that the cases were seen, or the operation performed, too late, when either infection or obstruction with gangrene of the contents of the sac had taken place. The appended cases, illustrative of the success of immediate operation, occurred in Mr. MacLennan's wards at the Royal Hospital for Sick Children, Glasgow.

Definition.—Exomphalos has been defined by Ballantyne¹ as a true hernia of abdominal contents into the umbilical cord. It is distinct, he says, from the deformity associated with a greater defect in the abdominal wall than merely in the neighbourhood of the attachment of the cord. To this condition he gives the name *gastroschisis*. A less pronounced form of this abnormality has been described by Nicaise as "amniotic umbilicus," and consists of a deficiency of skin around the umbilicus, the deficient space being covered by amnion from the cord. In a recent article Friend² describes a case of exomphalos and prefers the name of amniotic hernia, quoting Moschcowitz³ in support of the view that the term "hernia into the cord" is a misnomer. The undermentioned cases have all been clearly of the nature of hernia into the substance of the cord, and conform to Ballantyne's definition. Accepting this definition, it might at first appear that all cases of exomphalos would be amenable to early treatment, whereas cases of gastroschisis are beyond relief. This, however, is not so, for some of those hernias, although having but a narrow communication with the abdominal cavity, have nevertheless contained such proportions of the abdominal, and even thoracic, organs as to render replacement impossible.

Frequency.—Exomphalos is estimated by various authors to occur in from 1 in 2,000 births to 1 in 6,000 births.

Clinical Characteristics.—The abnormality usually takes the form of a globular, asymmetrical swelling situated at the abdominal attachment of the cord and extending into its substance. Sometimes there is a constriction between the swelling and the abdomen. In such a case a serious accident might happen, as in the case described by Victor Bonney,⁴ and quoted by Friend,² where the practitioner removed the hernial sac and its intestinal contents, consisting of small intestine, during the process of ligature and division of the cord at birth. In size it varies from a walnut to a large apple, but is commonly of an intermediate size. The coverings of a light grey colour are often quite transparent, and admit of inspection of the contents of the sac. In other cases the colour is darker and the sac opaque. The covering consists of three layers, namely, amnion, Wharton's jelly, and peritoneum, the former two constituents tapering at the summit of the swelling and passing along the cord. Occasionally the skin of the abdominal wall is continued some distance on to the swelling and forms a funnel-like cup into which the swelling fits. The swelling contains usually some part of the intestinal tract and—as would be expected—not infrequently a Meckel's diverticulum. In two of the cases the caecum and appendix were found in the sac, and in both the caecum had a well-marked mesentery. Rarely can the contents be reduced into the abdomen, and more often there is obstruction to the passage of bowel contents or even a complete strangulation of bowel. If treatment is delayed one of two conditions speedily causes the death of the child: It succumbs to intestinal obstruction, or the covering membranes are torn or slough off and peritonitis ends the case.

Treatment.

Operation at the earliest possible moment after birth is the only successful method. This statement is apparently at variance with some textbook teaching on the subject. One author⁵ states:

"Possibly in some of these less pronounced cases a radical operation may with safety be undertaken, especially if the infant has reached a few months of age."

And again:

"In certain favourable cases, where the child attains an age which will render operation justifiable, say six months or more, removal of the sac wall and suture of the edges of the gap may lead to a permanent cure."

Otherwise treatment would consist in the endeavour to prevent sepsis by appropriate dressings. Now, in the presence of the usual thin tissue-paper-like covering this is