A CLASSIFICATION OF MENINGOCOCCI BASED ON GROUP AGGLUTINATION OBTAINED WITH MONOVALENT IMMUNE RABBIT SERUMS.

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THAT all strains of meningococci are not affected equally by an immune serum prepared against any one strain has long been known. This has led to the conception that there are within the meningococcus group types of organisms which are more or less immunologically independent. This conception, borne out by the practical results in the treatment of human cases, has led to the universal adoption of a polyvalent serum in the treatment of cerebro-spinal fever. Though this conception of variant types of meningococcus has long existed, the number of types which occur and the degree of specificity which exists within these types has never been determined. It is for this reason that, in the preparation of the therapeutic serums, as many strains as possible have been used and the strains obtained from widely varying geographical sources. In this way it was hoped to include representatives of all existing types.

The purpose of this communication is to show that, by means of a specific immune reaction, two types of organism causing cerebro-spinal fever can be demonstrated, and that of forty-six organisms studied all belonged to one or other of these types. It will be shown, moreover, that both types are widely distributed, representatives of each type having been found in six different epidemic foci; that they occur in some epidemics with nearly equal frequency; and that the differentiation obtained is such as to suggest the probable complete immunological independence of the two types.

The earliest attempts made to differentiate types of meningococci were mainly directed towards establishing points of difference between the organism isolated in cases of epidemic meningitis and those from the sporadic cases of this disease, the so-called posterior basic meningitis. These attempts were unsuccessful.

In 1909 Elser and Huntoon¹ described an organism indistinguishable from the meningococcus except by means of agglutinin absorption tests. To this organism they gave the name "pseudomeningococcus." In their article the source from which these organisms were obtained is not very clearly stated, but apparently they were all isolated from the naso-pharynx. They speak of the pseudomeningococcus as "only rarely encountered in the throats of normal and diseased subjects," and do not consider that it interferes with the practical identification of the meningococcus or of meningococcus carriers. They do not seem to look upon the pseudomeningococcus as a causative agent of cerebro-spinal fever.

In the same year Dopter² studied and described a similar organism, also obtained from the upper air passages, to which he gave the name "parameningococcus." This organism, probably identical with the pseudomeningococcus of Elser and Huntoon, has since been found by Dopter and other French workers to invade the blood and meninges, and is looked upon by them as one of the causative agents in epidemic meningitis. An anti-serum against this organism has been prepared by Dopter and successfully used in the treatment of human patients.

Recently Wollstein³ has made a careful comparative study of the immune reactions of the meningococcus and the parameningococcus of Dopter. From her investigations she came to the conclusion that "the parameningococci of Dopter are culturally indistinguishable from true or normal meningococci, but serologically they exhibit differences as regards agglutination, opsonization, and complement fixation. Because of the variations and irregularities of serum reactions existing amongst otherwise normal strains of meningococcus it does not seem either possible or desirable to separate the parameningococci into a strictly definite class. It appears desirable to

consider them as constituting a special class among meningococci, not, however, wholly consistent in itself." It will be seen, therefore, that, though there is apparently some variation in the reaction to immune serums of certain organisms isolated from cases of cerebro-spinal fever, no sharp-cut differentiation of meningococci has as yet been made and no record of the frequency with which these aberrant or parameningococcal strains occur is available.

In reviewing the literature of meningococcus agglutination two facts immediately impress themselves—first, the wide variation in agglutinability of different strains of meningococci, and, second, the susceptibility of certain strains to agglutination by any serum, normal or immune, that is, susceptibility to non-specific agglutination. Thus Atkwright,⁴ and also Elser and Huntoon,⁵ have shown that gonococcus-immune serum will agglutinate certain strains of meningococcus in as high dilutions as will meningococcus-immune serum. Elser and Huntoon, however, noticed that in such cases, while the final result with gonococcus and meningococcus serum was the same, the rate at which the reaction occurred in the two instances varied widely, the reaction being much more rapid with meningococcus serum.

In all previous work upon the agglutination of the meningococcus the agglutinations have been studied with increasing dilution of serum, and the highest dilution in which agglutination has occurred at the end of twenty-four hours has been taken as the standard of agglutination. In the light of the above results, it seemed possible that when a period of twenty-four hours was allowed to elapse before readings were made, a more slowly occurring non-specific agglutination might frequently mask all specific results. It seemed advisable, therefore, to see if, by allowing a powerful serum to act over a short period of time, specific differences could be demonstrated which were missed when the ordinary method of diluted serum acting for twenty-four hours was used. Undiluted serum was therefore employed and the agglutinations which immediately ensued noted. It was at once determined that with this method marked differences between strains of meningococci could be demonstrated.

Method.

Monovalent serums were prepared by immunizing rabbits against single strains of meningococcus. The rabbits were immunized by intravenous injections given at weekly intervals, the dose consisting usually of half a slant culture of twenty-four to seventy-two hours' growth. The first two or three injections were made with organisms killed by heating at 60° C. for thirty minutes; subsequent injections were of living organisms. Five injections usually produced a satisfactory agglutinating serum.

Agglutinations were all done macroscopically, equal quantities of undiluted serum and of rather thin bacterial emulsions being drawn into a capillary pipette, thoroughly mixed on a glass slide and the mixture again drawn into the pipette, the tip of which was then sealed in the flame. In the case of a prompt reaction, agglutination takes place before the mixing is completed, all the organisms becoming almost instantaneously tightly clumped, leaving a clear supernatant fluid. The tubes were read immediately and then left at room temperature, readings being again made at the end of an hour and on the following morning. In recording the results of agglutinations the following designations were employed: C, complete clumping of the organisms, leaving a clear or faintly opalescent fluid; I, majority of organisms clumped, the supernatant fluid remaining opalescent; L, slight clumping; and O, no clumping, though in the course of twenty-four hours slight sedimentation may occur.

Experimental.

Rabbits were immunized against eight different strains of meningococci. Unfortunately four of these eight strains were lost before their agglutination reactions could be tested, so that cross agglutinations between the whole eight strains and their corresponding serums could not be carried out. They were, however, done with the four remaining strains. The results are shown in Table I. It is to be understood that these results were not all obtained on one day, but represent the combined protocols of three separate experiments.

TABLE I.—Agglutination of Meningococcus Strains by Homologous and Heterologous Monovalent Immune Rabbit Serums.

SERUMS.	MENINGOCOCCUS STRAINS.											
	M. 4.			M. 7.			M. 9.			M. 13.		
	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.
Rabbit 53, M. 3...	0	I	C	L	C	C	0	0	L	I	I	I
Rabbit 76, M. 4...	C	C	C	C	C	C	0	0	0	C	C	C
Rabbit 83, M. 5...	0	I	C	L	L	I	0	0	0	L	L	I
Rabbit 56, M. 6...	0	0	I	0	0	L	C	C	C	0	0	0
Rabbit 58, M. 7...	0	I	C	I	C	C	0	0	I	I	I	I
Rabbit 15, M. 9...	0	0	C	0	0	I	C	C	C	0	0	I
Rabbit 84, M. 11	0	0	C	0	0	I	C	C	C	0	0	I
Rabbit 69, M. 13	I	C	C	C	C	C	0	0	I	C	C	C

C = Complete agglutination. I = Incomplete agglutination. L = Least degree of agglutination. 0 = Negative result.

It will be seen that the three strains M. 4, M. 7, and M. 13 were agglutinated by five of the eight serums employed (M. 3, M. 4, M. 5, M. 7, M. 13), though in the case of three of these (serums M. 3, M. 5, M. 7) the agglutination was feeble. Three serums (M. 6, M. 9, M. 11) failed entirely to agglutinate these organisms. The reactions with strain M. 9 were, on the other hand, exactly opposite, the five serums (M. 3, M. 4, M. 5, M. 7, M. 13) failing to agglutinate this strain, while prompt agglutination occurred with the three (M. 6, M. 9, M. 11) which failed to agglutinate the other three organisms. That the feeble agglutination in the case of the serums M. 3, M. 5, and M. 7 was due to a simple lack of potency of these serums, and not to difference in the organisms, seems probable, since in the only case where it could be tested (M. 7) agglutination was equally feeble with the homologous organism.

On the basis of these results it would seem that two types of meningococci can be differentiated according to their reaction to monovalent immune rabbit serums. These we shall designate Types I and II. To Type I belong M. 4, M. 7, M. 13, and since serums prepared by immunizing rabbits to strains M. 3 and M. 5 agglutinate these organisms, it is evident that they also are of this type. Similarly M. 6, M. 9, and M. 11 are evidently another type, which we shall designate Type II. A second point which is brought out in Table I is, perhaps, worthy of mention. This is the well known variation in the agglutinability of different strains of meningococci. It will be seen that M. 7 and M. 13 show almost identical reactions, while with M. 4, though qualitatively the same, they are quantitatively weaker, the three weak serums failing to give any immediate reaction, and showing, only at the end of an hour, agglutinations comparable to the immediate reactions obtained with the more agglutinable strains.

A preliminary classification into two types having been thus obtained, it was necessary to determine whether such results would hold when applied to a large number of strains of meningococci. All available strains were therefore tested with strongly agglutinating serums of both types. The results are shown in Table II. The Type II serum which was at first employed was not as powerful as one which was afterwards produced, so that the reactions of this group were not at first quite as sharp as those later obtained. In Table II strain M. 33 marks the beginning in the use of more powerful Type II serum.

Table II shows clearly the sharp differentiation of two types of meningococci, all the strains tested with three exceptions (M. 18, M. 39, M. 49) belonging clearly to one or other type. These three inagglutinable strains will be considered later. Excepting them we see that in no case did immediate agglutination fail to occur with the proper type serum. Cross agglutination between types was never seen immediately, but did occur three times at the end of an hour (M. 28, M. 32, M. 56). In two of these three instances, however (M. 32, M. 56), the strains showed agglutination of equal extent with normal serum. Only one example of true cross agglutination therefore occurred (M. 28), and here the reaction was so slight that it could not possibly interfere in the differentiation of the type to which this strain belonged. As will be seen by Table II, three strains could not be classified (M. 18, M. 39, M. 49), failing to agglutinate with serums of either type. Further investigation showed that the inagglutinability of these

TABLE II.—Agglutination of Meningococcus Strains by Monovalent Serums, Types I and II.

STRAINS.	SERUMS.								
	Type I.			Type II.			Normal Rabbit.		
	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.
M. 10	C	C	C	0	0	0	0	0	0
M. 12	0	0	I	C	C	C	0	0	I
M. 18	0	0	I	0	0	I	0	0	I
M. 19	C	C	C	0	0	0	0	0	0
M. 20	C	C	C	0	0	I	0	0	I
M. 21	C	C	C	0	0	I	0	0	I
M. 22	C	C	C	0	0	0	0	0	0
M. 23	C	C	C	0	0	0	0	0	0
M. 24	C	C	C	0	0	L	0	0	L
M. 25	C	C	C	0	0	0	0	0	L
M. 26	0	0	I	L	I	C	0	0	C
M. 27	C	C	C	0	0	I	0	0	0
M. 28	0	L	C	I	C	C	0	0	C
M. 29	C	C	C	0	0	I	0	0	C
M. 30	0	0	I	I	C	C	0	0	L
M. 31	C	C	C	0	0	L	0	0	L
M. 32	C	C	C	0	I	C	0	C	C
M. 33	0	0	L	C	C	C	0	0	I
M. 34	C	C	C	0	0	I	0	0	C
M. 35	0	0	0	C	C	C	0	0	I
M. 36	C	C	C	0	0	I	0	0	C
M. 37	0	0	I	C	C	C	0	0	0
M. 38	C	C	C	0	0	I	0	I	C
M. 39	0	0	L	0	0	I	0	0	0
M. 40	0	0	C	C	C	C	0	0	C
M. 41	C	C	C	0	0	0	0	0	C
M. 42	0	0	L	C	C	C	0	0	L
M. 43	C	C	C	0	0	L	0	0	C
M. 45	C	C	C	0	0	0	0	0	L
M. 46	C	C	C	0	0	L	0	0	0
M. 47	C	C	C	0	0	L	0	0	C
M. 48	C	C	C	0	0	L	0	0	I
M. 49	0	0	0	0	0	I	0	0	0
M. 50	C	C	C	0	0	0	0	0	L
M. 51	C	C	C	0	0	I	0	0	C
M. 53	0	0	I	C	C	C	0	0	I
M. 55	0	0	I	C	C	C	0	0	L
M. 56	C	C	C	0	L	C	0	L	C

TABLE III.—Agglutination Reactions of Relatively Inagglutinable Meningococcus Strains and their Monovalent Antiserums.

SERUMS.	MENINGOCOCCUS STRAINS.														
	Type I, M. 20.			Type II, M. 37.			M. 18.			M. 39.			M. 49.		
	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.
Type I, Rabbit 76, M. 4...	C	C	C	0	0	I	0	0	L	0	0	L	0	0	0
Type II, Rabbit 66, M. 12...	0	0	0	C	C	C	L	L	I	I	C	C	C	C	C
Rabbit 4, M. 18 ...	0	0	0	C	C	C	0	0	L	0	L	I	L	I	C
Rabbit 21, M. 39 ...	0	0	0	C	C	C	0	0	L	0	0	L	0	I	C
Rabbit 90, M. 49 ...	0	0	0	C	C	C	0	0	L	0	I	I	L	I	C
Normal rabbit ...	0	0	0	0	0	L	0	0	L	0	0	L	0	0	L

three strains was only a relative affair, and that when more potent Type II serum—for example, rabbit 66, M. 12, obtained by more prolonged immunization of rabbits—was used, some degree of agglutination of even these resistant strains occurred (Table III). It was noticed, moreover, that the agglutinability of these strains varied from day to day, an organism which had failed to agglutinate one day showing typical prompt agglutination the next. In order to prove definitely the relationship of these exceptional strains monovalent serums were prepared against all three, and cross agglutinations were then carried out between these serums, their homologous organisms, and known representatives of Types I and II. The results are shown in Table III.

It will be seen that all three strains are certainly representatives of Type II, since their antisera give typical agglutination of a known Type II organism (M. 37) and fail to show any reaction with an organism of Type I (M. 20). It will be noticed that the three show a graded variation in their degree of inagglutinability—M. 18 the most inagglutinable, M. 39 next, and finally M. 49, which, with a powerful Type II serum, shows immediate agglutination. It is clearly shown that the failure of these organisms to react is due to their inherent inagglutinability and not to any difference in type, since in every case their antisera agglutinate an agglutinable Type II organism more strongly than they do their homologous organism. Moreover, within the group the reactions take place according to the evident potency of the serums and agglutinability of the organisms, and not according to whether homologous or heterologous serum is employed. Thus rabbit 21, M. 39, fails entirely to agglutinate its homologous organism, while it agglutinates strongly the agglutinable Type II organism (M. 37) and weakly the relatively inagglutinable strain, M. 49. The same phenomenon is seen with the serum of rabbit 4, M. 18.

In Table II the results of exposing a number of strains of meningococcus to Type I and Type II serum were shown. By way of confirming these results the effects of exposing organisms of Types I and II to the action of serums prepared against a number of the strains tabulated in Table II have been studied. These results are shown in Table IV.

It will be seen that these results are in every case confirmatory, the antisera prepared against the two organisms of Type I alone agglutinating the Type I strain,

while the Type II organism is agglutinated only by antisera of organisms previously determined as of Type II.

TABLE IV.

Agglutination of meningococcus strains Type I (M. 4) and Type II (M. 12) by monovalent rabbit serums produced by immunizing with various meningococcus strains M. 4 and M. 48, Type I, the remainder Type II. Normal rabbit serum control.

SERUMS.	MENINGOCOCCUS STRAINS.					
	Type I, M. 4.			Type II, M. 12.		
	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.
Rabbit 76, M. 4...	C	C	C	0	0	L
Rabbit 56, M. 6...	0	0	L	C	C	C
Rabbit 15, M. 9...	0	0	L	C	C	C
Rabbit 66, M. 12	0	0	C	C	C	C
Rabbit 27, M. 18	0	0	I	I	C	C
Rabbit 22, M. 39	0	L	C	C	C	C
Rabbit 87, M. 42	0	0	C	C	C	C
Rabbit 11, M. 48	C	C	C	0	0	L
Rabbit 90, M. 49	0	0	C	C	C	C
Normal rabbit...	0	0	L	0	0	L

Distribution and Relationships.

It has thus been shown that without exception all strains of meningococci, so far met with in this investigation, can be placed in one or other of two types. There remains to be considered the distribution of these types and their relations to the parameningococcus of Doptre.

The strains of meningococcus which have been studied were isolated from patients in six different epidemic foci. For those from the Tidworth, Reading, Woolwich and London epidemics I am indebted to Dr. J. A. Arkwright of the Lister Institute, and for some of the strains isolated in France to Captain J. W. McNee, No. 3 Mobile Laboratory. In Table V is shown the epidemic focus from which individual strains were obtained, and the number of each type found in the strains from these various sources.

Organisms of both types were found in all six epidemic foci. Type I was more common than Type II, but in the

TABLE V.—Classification of Meningococci Isolated from the Spinal Fluid of Patients from various Epidemic Foci. Classification obtained by Agglutination with Monovalent Rabbit Serums.

British Expeditionary Force, France.		First Canadian Contingent, Salisbury Plain.		Tidworth.		Reading.		Woolwich.		London.	
Type I.	Type II.	Type I.	Type II.	Type I.	Type II.	Type I.	Type II.	Type I.	Type II.	Type I.	Type II.
M. 3	M. 6	M. 7	M. 9	M. 27	M. 26	M. 29	M. 30	M. 31	M. 33	M. 41	M. 42
4	18	10	11		28			32	35	43	49
5	39	13	12					34	37	45	
20	40	19						36		46	
21	53	22						38		47	
50	55	23								48	
51		24									
56		25									
8	6	8	3	1	2	1	1	5	3	6	2

Type I ... 29 = 63 per cent.
Type II ... 17 = 37 ..
Total ... 46 = 100 per cent.

case of the British army in France the difference was negligible. It is perhaps of some significance that this group in which the proportion is more nearly equal, embraces the largest number of organisms, the widest distribution in area, and the most nearly constant conditions of isolation and subsequent growth of the organisms. It will readily be seen that in a heterogeneous collection, such as these forty-six strains represent, a slight variation in ease of isolation or in subsequent viability of one type as compared with the other might completely upset all calculations. In contradistinction to the greater frequency of Type I in these strains isolated from the spinal fluid, we have found in five strains of meningococci isolated from the naso-pharynx of healthy carriers Type II four times and Type I once. The exact frequency with which the two types of meningococci occur can, then, only be determined by a study of the infecting organism in every case of a large series. It will probably be found to vary in different places and in different years. It seems obvious, however, that both types are widely distributed, and must be held equally responsible as causative agents of cerebro-spinal fever.

The relation of the parameningococcus of Dopter to the types above described has been determined for one strain of parameningococcus. This strain, known as "parameningococcus St. Quay," was obtained through the kindness of Dr. Arnaud Netter of Paris, and was isolated by Dr. Matthias Pierre Weil. Its reactions are shown in Tables VI and VII; they are identical with an organism of Type II.

TABLE VI.—Agglutination Reactions of Parameningococcus.

Monovalent rabbit serums of Types I (Rabbit 76, M. 4) and II (Rabbit 66, M. 12) vs. parameningococcus (P.M. St. Quay). Monovalent rabbit anti-parameningococcus serum (Rabbit 42, E.M. St. Quay) vs. organisms Type I (M. 20) and Type II (M. 37). Normal rabbit serum control.

SERUMS.	MENINGOCOCCUS AND PARAMENINGOCOCCUS STRAINS.								
	Type I, M. 20.			Type II, M. 37.			Parameningo. P.M. St. Quay.		
	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.	Imm.	1 hr.	24 hrs.
Type I, Rab. 76 (M. 4)	C	C	C	0	0	0	0	0	0
Type II, Rab. 66 (M. 12)	0	0	I	C	C	C	C	C	C
Antipara., Rab. 42 (P.M. St. Quay)	0	0	0	C	C	C	C	C	C
Normal rabbit	0	0	L	0	0	L	0	0	0

TABLE VII.—Agglutination Reactions of Parameningococcus.

Monovalent rabbit serums Types I and II vs. parameningococcus strain P.M. St. Quay. Normal rabbit serum control.

SERUMS.	P.M. St. Quay.			
	Imm.	1 hr.	24 hrs.	
Type I, Rabbit 76, M. 4	0	0	0	
Type I, Rabbit 11, M. 48	0	0	I	
Type II, Rabbit 66, M. 12	C	C	C	
Type II, Rabbit 90, M. 49	C	C	C	
Type II, Rabbit 15, M. 9	C	C	C	
Type II, Rabbit 27, M. 18	I	C	C	
Type II, Rabbit 87, M. 42	C	C	C	
Normal rabbit	0	0	0	

Another strain of parameningococcus, obtained from the Pasteur Institute, has also been studied. Unfortunately, this organism possessed such a high degree of non-specific agglutinability and such low antigenic properties that its exact relations could not be determined. It, too, however, appeared to be a member of Type II.

It would seem probable, therefore, that our Type II meningococcus and the parameningococcus of Dopter are identical. In view of the apparent frequency with which this organism causes cerebro-spinal fever, the identical character of the disease caused by the two types, and, if we except immune reactions, the exact similarity of the two organisms, it would seem desirable to call both types

of organism the meningococcus, and to drop the use of such terms as "parameningococcus" and "pseudomeningococcus," which are only complicating and misleading. In this connexion it may be interesting to point out that the occurrence of types of meningococci differing only in their immune reactions has an exact parallel in the types of pneumococci demonstrated by Dochez and Gillespie,⁶ by whom four types of pneumococci causing lobar pneumonia have been established.

The Bearing of these Observations.

The occurrence of two types of meningococci and the fact that all organisms so far tested will react to a monovalent immune serum of one or other type suggests at once the possibility of the treatment of human cases of cerebro-spinal fever with such monovalent serums. It is probable that in this way more powerful antisera could be prepared than by the haphazard choice of strains for the immunization of horses such as at present obtains. In the preparation of monovalent type serums the most powerful antigenic strain of each type would, of course, be used. For the first treatment of the patient a mixture of the two serums could be used, to be followed as soon as the type of the infecting organism is determined by the appropriate monovalent serum. Such a scheme would seem to put the serum treatment of cerebro-spinal fever on a much sounder basis and would prevent the occurrence of situations, such as were common in England last winter, where patients were treated with serums which, even *in vitro*, showed no effect on the organism causing the disease. Here we may again point to the parallelism with pneumonia, where the use of a similar method⁷ has led to a much clearer understanding of the difficulties and possibilities of serum-therapy.

SUMMARY.

1. The causative agent of cerebro-spinal fever, the meningococcus, is of at least two types.
2. These two types are, as regards the one immune reaction tested, agglutination, absolutely independent.
3. In a study of forty-six strains of meningococci, obtained from various sources, all were of one or other of these two types.
4. Both types are widely distributed, having been found in each of six epidemic foci. They may occur with equal frequency.
5. Both types have been found in the naso-pharynx of healthy carriers.
6. We have designated these two types, Types I and II.
7. In so far as evidence is available, Type I has been more frequently the cause of the disease in the recent epidemics than has Type II. In view of the wide distribution of the two types, both must, however, be held equally responsible as causative agents of cerebro-spinal fever.
8. The organism herein described as Type II is probably identical with the parameningococcus of Dopter.
9. It is suggested that in the treatment of cerebro-spinal fever better results might be obtained, and more exact knowledge of the adequacy of serum treatment gained, if monovalent horse serum of appropriate type, and therefore known to be active against the infecting organism, were employed in place of the polyvalent serums at present in use.

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THE Paris Municipal Council has voted a sum of £2,400 in aid of the scheme of sanitary stations created by the Minister of the Interior for the temporary accommodation of tuberculous soldiers.

THE first National Medical Congress of the Republic of Uruguay will be held at Montevideo in April, 1916 (9th to 16th), under the presidency of Professor José Brito Foresti. Among the members of the honorary committee are the President of the Republic, the Ministers of the Interior and Public Instruction, the Rector of the University, the Dean and Professors of the Medical Faculty, and the officers of the leading medical and scientific societies of Uruguay. Among the subjects proposed for discussion are syphilis, alcoholism, the means of checking the prevalence of abortion, cancer in Uruguay, and the hospital question in that country.