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THE PROPHYLAXIS AND TREATMENT  
OF MILD CATARRHAL CONDITIONS  
OF THE UPPER RESPIRATORY  
PASSAGES, BY MEANS OF VACCINES.

By:- JAMES GOSSIP,  
M.B., Ch.B. (Edin. 1912).

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The inconstancy of the climate of this country is sufficiently noteworthy to be the subject of perennial unfavourable criticism. It is the most powerful ally of the coughs, colds and chills which are the bugbear of a large portion of the community for six months of the year.

The number of drugs (taken internally or applied locally) which have been tried and found wanting is legion. It is true that rest in bed will effect a cure in a few days, but patients object to this treatment, and naturally so, for, in the case of the more susceptible sufferers, such treatment would bid fair to lay them up for the greater part of the winter.

This is an unsatisfactory state of affairs, for, although Coryza is not, in itself, a serious disease, it is a most unpleasant one, and it induces a very distinct degree of debility in those who suffer from it acutely. Its local action upon the mucous membrane of the upper respiratory passages also paves the way for more grave infection.

Much attention is being paid to the earliest manifestations of chronic disease, and intestinal stasis leads the field at present. It is unlikely however that all chronic disease first emanates from the/

the lower bowel, and one has justification for believing that many diseases gain entrance to the body through catarrhal mucous membrane in the upper respiratory passages. A few notable examples are:- Influenza, Otitis Media, Sinusitis, Pneumonia, Rheumatism, Meningitis and the Exanthemata.

Enough has been said to show that Coryza is a disease which must not be disregarded, and any line of treatment which seems to give hopeful results should have a fair trial.

There are only four such to consider:-

1. Drug Treatment.
2. Treatment on general principles -  
improving the patient's mode of life  
and general health.
3. Change of climate.
4. Treatment with a view to increasing  
the patient's resistance to the  
organisms which cause the disease.

No. 1. has been considered.

No. 2. will be beneficial in certain cases. Deflected septa, tonsils and adenoids, enlarged turbinates, etc., should be dealt with. The patient may be taught how to breathe properly. The value of fresh air, day and night, should be brought home to/  
to/

to him.

No. 3. is outside the reach of the majority.

No. 4. is a vexed question. It is within the knowledge of the writer that many Practitioners who oppose this line of treatment are without practical experience in it. The commonest arguments used by its opponents are, firstly, that the causative germ is not known with certainty, and, secondly, that the results of vaccine treatment have been disappointing so far.

It is true that the germ lying at the root of the trouble may be a filter passer. But it is also the case that the infection is always mixed. By removing this secondary infection one has gone a long way towards curing the fundamental condition.

It is also unfortunately a fact that the results of Vaccine Treatment have been unsatisfactory so far. The only observation on this point which the writer wishes to make at this stage is that possibly the bad results, or rather the lack of any result at all, may be due to faulty administration on the part of the employers, and not due to any inherent fault in the treatment per se.

The writer has always been extremely susceptible to colds in the head and having tried

all the usual remedies, with no success, he began to experiment with vaccines in 1916. The results in his own case were so remarkable that he began the Vaccine Treatment of others on a small scale, with uniformly good results.

This will be gone into more fully in due course.

On approaching in theory the subject of immunization one is faced with five different courses:-

1. The conferring of passive immunity by means of sera.
2. The conferring of active immunity by means of -
  - (a) Sensitised Vaccines.
  - (b) Detoxiticated Vaccines.
  - (c) Stock Vaccines.
  - (d) Autogenous Vaccines.

In practice (c) and (d) only are of value so far, but (b) appears to hold great possibilities.

#### 1. PASSIVE IMMUNITY BY MEANS OF SERA.

As there is always a mixed infection in the upper respiratory passages a ready-made serum would not be procurable and a special serum would have to be prepared. This procedure would have no advantages not also gained by the use of an

autogenous/

autogenous vaccine, while it would have the added disadvantages of great expense, short-lived immunity and risk of anaphylaxis.

2.(a). ACTIVE IMMUNITY BY MEANS OF  
SENSITISED VACCINES.

Sensitised vaccines were introduced by Besredka and Broughton Alcock. They consist of bacilli combined with their specific antibodies, and are manufactured as follows :-

A suspension of bacteria and the corresponding antiserum are mixed and incubated until the bacilli and the antibodies are so firmly bound together that repeated washing, after removal of the supernatant serum, will not separate them. They are washed until all trace of serum has disappeared, suspended in salt solution and injected without being sterilized. These vaccines are said to have given excellent results in some acute conditions, but as a specific antiserum is necessary in their preparation they do not come within the domain of practical politics so far as Coryza is concerned.

2.(b). DETOXICATED VACCINES.

These vaccines have come into use very recently and have been used chiefly in the treatment of gonorrhoea. The results obtained in the treatment/

treatment of gonorrhoea have been extremely satisfactory. They have also been used, but to a much smaller extent, in the treatment of chronic nasal catarrh, and here also they appear to give good results.

The method of detoxication is too complicated to be gone into fully here. The literature on the subject is contained in the "Lancet" of June 28th, 1919, or it may be obtained from "Genatosan", Ltd., 12, Chenies Street, London, W.C.1., who manufacture these vaccines for the market.

The main facts are these:-

Germes may produce either an Exotoxin or or both.  
an Endotoxin. / The exotoxin is excreted by the germ into the surrounding tissues, while the germ is in a living state. All vaccines are washed free of this exotoxin before being injected into the patient.

The endotoxin is contained in the stroma of the germ and is only liberated after the germ has been destroyed. In ordinary vaccines this endotoxin is injected into the patient and sometimes causes a severe reaction. In detoxicated vaccines the endotoxin is removed before the vaccine is injected, with the result that a very large dose can

be/

be used without any untoward reaction taking place.

The method of detoxicating vaccines is as follows :-

The germ stroma is dissolved in a weak alkaline solution (N/10), the endotoxin being dissolved at the same time. The stroma is then precipitated by making the solution weakly acid, the endotoxin, however, remaining in solution. The supernatant fluid is then pipetted off and this process is repeated until no trace of endotoxin remains, and the resultant toxin-free stroma can be used as a vaccine.

This process only acts with certain germs - chiefly those which are gram-negative, and in a mixed infection it may not be possible to detoxicate all the different germs. However, the process is still in its infancy and it seems possible that it may prove very useful in the future. It has three advantages - it is safe in use, very large doses can be safely used, and the degree of immunity which results is very high.

#### 2.(c). STOCK VACCINES.

The most important development in the use of stock vaccines has been the use of the T.A.B. vaccine in the European war. The results obtained are/

are too well known to require further mention.

Stock vaccines were also used very largely as a prophylactic measure in the recent influenza epidemic, but here the results obtained were not nearly so satisfactory. The writer attempted to watch the results in the case of three hundred soldiers who were fully protected by a vaccine made by a competent Pathologist. Owing to many of the 300 men being drafted Overseas, no figures could be obtained, but the impression was formed that although a large number of the men so protected did contract the disease, the course of the influenza was not so severe as in unprotected cases, and pneumonia was not so common. Four of the men died of influenza and pneumonia.

The impression formed by many other observers seems to coincide with this, but some report no apparent result at all. On the other hand, R.W.Allen ("Practical Vaccine Treatment", page 99), reports 180 cases protected, none of whom contracted the disease, and Captain F.L.Armitage reports 247 persons protected none of whom were afterwards attacked. At West Meath Asylum Dr. Gavin reports that, among the Staff of the Asylum, of inoculated persons 3% were afterwards infected, while/

while of the unprotected persons 80% contracted the disease. Dr. W.H.Wynn (Lancet, Dec. 28th, 1918), states that among 112 inoculated persons two only had mild attacks, while among 53 unprotected persons 40 had attacks.

In view of these excellent results, it is apparent that there must be some fault in the technique of those who failed to protect their patients. The three most probable faults are:-

1. The causative germ was not included in the vaccine.
2. The right strain of the causative germ was not included.
3. The vaccine was administered in insufficient doses.

Probably more than one of these mistakes was made in many cases.

With regard to the milder infections of the upper respiratory passages, not so much information is available. The writer watched the result of the administration of Polyvalent Anti-Catarrhal Vaccine, as supplied by the well-known Manufacturing Chemists in London, in seven cases, and in no case could he observe any very marked improvement. The maximum dose given in any case (in/

(in accordance with the Makers' directions) was only 500,000,000 of the mixed vaccine. I consider this quite insufficient, but the question of dosage will be gone into later.

The Makers themselves claim good results from the use of their vaccines in the doses that they recommend for prophylactic purposes.

Messrs. Parke, Davis & Co., BEAK Street, Regent Street, London W.1., manufacture an Anti-catarrhal Vaccine containing :-

Pneumococcus,  
Streptococcus,  
Pfeiffers Bacillus,  
Micrococcus Catarrhalis.

The dose administered is 0.2 to 0.5 C.C.

Messrs. Burroughs, Wellcome & Co., Snow Hill Buildings, London E.C. manufacture four different Anticatarrhal Vaccines.

No.1. contains 100 million B.Septus in each C.C.

No.2. contains 100 million M.Catarrhalis in each C.C.

No.3. contains 100 million of both B.Septus and M.Catarrhalis in each C.C.

No. 4. contains :-

Each 1 C.C. phial contains	B. Septus	50,000,000 of each.
	B. Hoffman	
	B. Friedlander	
	M. Cataffhalis	
	Staphylococcus (mixed)	10,000,000 of each/
	Pneumococcus	
	Streptococcus (mixed)	

The doses recommended are :-

1/2 - 1-1/2 C.C.

Allen & Hanburys, Ltd., 7 Vere Street,  
Cavendish Square, London W.1., have placed on the  
market the Compound Catarrhal Vaccine containing in  
the first dose :-

B. Influenzae	10,000,000
Streptococcus	10,000,000
M. Catarrhalis	25,000,000
Pneumococcus	50,000,000
Staphylococcus	250,000,000.

The highest dose recommended is four  
times this amount.

W. Martindale, 10, New Cavendish Street,  
London, W., supplies a combined vaccine for colds.  
Five organisms are included in this vaccine and  
the Maker guarantees that many strains of each  
organism/

organism are included in the vaccine.

The doses recommended are :-

B. Influenzae	}	500,000,000
Pneumococcus		
Streptococcus		
M. Catarrhalis		
B. Septus.		

R.W.Allen (Practical Vaccine Treatment, page 95), gives the following scheme of dosage as a prophylactic measure against Coryza :-

Millions of	B. Influenzae.	Pneumococcus.	Streptococcus.	M. Catarrhalis.
1st Dose	500	250	250	250
2nd Dose	1,000	500	500	500
3rd Dose	2,000	1,000	1,000	1,000

The final dose contains, therefore, 5,000,000,000 mixed germs.

An analysis of the doses recommended by these different Makers yields the interesting information that while one considers a maximum dose of 15,000,000 Pneumococci or Streptococci sufficient, another recommends a final dose of 1,000,000,000. Similarly in the case of the B. Influenzae, one recommends/

recommends a maximum dose of 40,000,000, while another suggests that 2,000,000,000 is desirable.

In view of this enormous discrepancy one must seek for farther information on the subject. It is apparent that there is no inherent impossibility in the giving of such doses as the largest mentioned above.

The final T.A.B. dose used in the British Army contained 1,800,000,000 to 2,000,000,000 dead typhoid bacilli.

Castellani, (British Medical Journal of September 15th, 1917, page 356), in his hexavaccine for typhoid, plague, cholera and Malta fever (T.A.B. M.C.P.) used a final dose containing 6,500,000,000 mixed germs without obtaining an undue reaction.

It is admitted, however, that vaccines vary in toxicity according to the germs contained in them.

The writer has injected doses of 1,000,000,000 streptococci, 1,500,000,000 B. Influenzae and Pneumococci into himself and others on many occasions and has never yet obtained an undesirably strong reaction.

In America, Avery, Chickering & Cole, (Journal of Experimental Medicine, 1915, XXI), show that doses of 24,000,000,000 Pneumococci can be given/

given with safety.

Lister (Publications No. 2 & 8 of the S. African Institute for Medical Research) administered doses of 24,000 million pneumococci to African natives and found that these doses were necessary to secure immunity. He also states that these doses do not cause unduly severe reactions.

Borel employed doses of 30,000 million upon the Senegalese troops in France with good results.

At Camp Upton near New York, Cecil and Austin (Journal of Experimental Medicine, July 1st, 1918, Vol. XXVII, No.1., pp.19 - 41), employed three or four doses of 10 to 15 thousand million pneumococci upon 12,000 men. During the ten weeks subsequent to the inoculation, during which time the men were under observation, no case of pneumonia due to the three types of pneumococcus which were included in the vaccine occurred among the men who had received two or more doses of vaccine; while in a control of approximately 20,000 men there were twenty-six cases of pneumonia due to these three types during the same period.

In addition, the incidence rate of type 4 pneumonia (which was not contained in the vaccine) was much less among the vaccinated than among the unvaccinated.

The question of the different strains of organisms will be dealt with more fully in due course.

It is/

given with safety.

It is clear then that these large doses can be given. Whether they are actually necessary or not is not so easily proved. As they give rise to no ill effects it seems wise to give the vaccine every chance. There is a Gaelic proverb which says that there is no good in sending a boy to do a man's work. This is probably as true in the case of Vaccine Therapy as in any other case.

As regards the second possible fallacy in treatment by Stock Vaccines - that the causative germ may not be contained in the vaccine,

This is a possibility and by no means a remote one.

In R.W.Allen's "Bacterial Diseases of Respiration" (H.K.Lewis & Co.), the following list of organisms which may be found in the respiratory tract is given :-

Bacillus Influenzae

Bordet's Bacillus (Whooping Cough)

Bacillus of Friedländer

Pneumococcus

Streptococcus

Micrococcus Catarrhalis

Micrococcus Paratetragnus/

Micrococcus Paratetrigenus

Bacillus Septus.

More uncommonly :-

B.Ozenae

B.Diphtheria

B.Coli

B.Proteus

Staphylococcus

Hoffmann's Bacillus

B.Tetrigenus

B.Typhosus

B.Tuberculosis

Spirochaetes

Streptothrix Actinomycosis

Lepra Bacillus

B. of Rhinoscleroma

Meningococcus/

He considers that this list may be incomplete.

Although it is clear that many of the organisms mentioned above do not play any part in catarrhal conditions of the upper respiratory passages, the list remains, nevertheless, a long one, and as all the possible causative germs cannot be included in one mixed vaccine, the element of chance/

chance is always present to a most undesirable degree.

There is only one way by which the contingency of one of the organisms present being omitted can be excluded, and that is by having a thorough Bacteriological examination of the discharges made by a competent Bacteriologist, before the Vaccine Treatment is started. If this is done there is no adequate reason why the process should not be carried one step farther and an autogenous vaccine made at the same time.

The extra expense and time taken would not be great, and the third fallacy would be avoided.

The third fallacy which we have to consider is that the correct strains of the organisms present may not be included in the stock vaccine.

It is well known that there are at least three strains of the B. Typhosus and that several kinds of the B. Dysenteriae exist. Numerous types of the Streptococcus and Staphylococcus are recognised and there are believed to be several varieties of the B. Influenzae. It is permissible to suppose that farther varieties of these  
and/

and other organisms occur, although they have not been recognised yet.

In the case of the anti-typhoid vaccine, it was abundantly proved that inoculation with one type of the germ did not confer absolute immunity against the other two. In fact it appeared to have little or no effect on the patient's resistance to the germs which were not represented in the vaccine.

The researches of Avery, Dochez, Chickering Cole and others of the Rockefeller Institute (Monographs of the Rockefeller Institute for Medical Research, No. 7, October 16th, 1917, etc.), establish the following facts with regard to the vaccine and serum treatment and prophylaxis of pneumonia:-

(1) The pneumococcus group comprises a considerable number of closely allied members, which by means of suitable antisera and other methods can be differentiated from each other.

(2) A strain endemic or epidemic in one locality may differ markedly in certain directions from that of another locality, where indeed it may not even be represented.

(3) Usually more than one strain or type is represented in a given locality, though as a rule one type predominates.

(4) The immune bodies of one type may be entirely without influence upon the members of another type.

(5) An efficient vaccine must contain each and all of the strains or types peculiar to the locality in which it is going to be employed.

(6) The dosage necessary to produce high immunity differs with different races and with different individuals of the same race, but is in all cases far in excess of that commonly employed.

(7) These high dosages can be used with perfect safety and produce no ill-effects.

These rules are probably equally true in the case of many other germs, but the fact has not yet been proved. Here, then, we have our most serious stumbling-block in treatment by stock vaccines. It appears that antibodies are specific, not only to their own particular germ, but also to the precise strain of that particular germ.

Now it is sometimes difficult to differentiate by bacteriological examination all the organisms represented in a mixed infection. It is a much more intricate process to discriminate between different strains of the same germ, and by laboratory research alone this may be impossible.

The/

The only certain method of avoiding this impediment is by the use of autogenous vaccines. It can be minimised by employing a polyvalent stock vaccine, made from germs obtained from as many different sources as possible.

### AUTOGENOUS VACCINES

This is a subject on which it is not easy to collect much literature, but it appears to be a very hopeful line of treatment.

J. H. Horder (Index of Treatment by Hutchinson & Sherren, Specific Therapy) states that good results may be expected, but gives no particulars.

R. W. Allen (Vaccine Therapy, H. K. Lewis & Co.), considers that good results are obtained by the use of stock vaccines, but that the administration of autogenous vaccines makes success more certain.

The writer was informed by Dr. Logan of the Pathological Department, Royal Infirmary, Edinburgh, that he had made autogenous vaccines for coryza for several Doctors and Medical Students. He had been unable to follow up the cases but he believed that the results had been satisfactory.

The writer has watched the results of the administration of autogenous vaccines in what he considered adequate doses, in six cases. He has

also/

also been in communication with Practitioners who have used them in much smaller doses, in three cases.

The results obtained were as follows:-

In one case the vaccine was used during March and the disappearance of the catarrh coincided with an improvement in the weather conditions.

In one case there was a distinct improvement in the patient's condition, but complete cure could not be claimed.

In four cases the cure was complete and the patients experienced a most remarkable freedom from coryza for the rest of the winter.

In the three cases not seen by me one patient was completely cured, while the other two were very much benefited.

As these cases all showed the same salient features nothing would be gained by quoting them in extenso.

The writer's case was typical and will be given in full.

CASE - J.G. AGE - 28/ YEAR 1917.

For many years had been very susceptible to colds in the head, laryngitis and tracheitis. Usual history - would catch a severe cold about October or November. This would probably be accompanied/ .

accompanied by some laryngitis. In the course of a fortnight or so the condition would have spread down the trachea and would have become chronic. For the rest of the winter and well into the following spring the condition would be - some discharge from the nose with congestion of the mucous-membrane, slight laryngitis and some catarrh of the trachea, accompanied by a raw feeling behind the upper part of the sternum and the expectoration of about one ounce of sputum daily.

The systemic effect was a continual feeling of lassitude, mild frontal headache and slight pain in the lower dorsal region of the spine.

In addition two or three further attacks of acute coryza would be superimposed upon this condition.

In 1916 a stock vaccine was used. Three doses were taken, the final one containing 500 million mixed germs. No apparent result was obtained.

In 1917 an autogenous vaccine was manufactured, in November. This was injected as follows:-

Dose/

<u>DOSE</u>	<u>DATE</u>
50 million	24 November 1917
100 do.	27 November 1917
200 do.	30 November 1917
400 do.	3 December 1917.

Up to this point no result was apparent and in fact a fresh attack of coryza was contracted. It appeared that either the vaccine was valueless or the doses were too small. As a last hope the doses were increased to much beyond the original intention:-

<u>DOSE</u>	<u>DATE</u>
800 million	14 December 1917
1600 million	19 December 1917.

by this time all traces of catarrh had vanished, and the general health was greatly improved.

2,000 million	7 January 1918
2,000 million	3 February 1918
2,000 million	11 March 1918.

In December, 1918, a further attack of coryza was contracted for the first time that year. A second autogenous vaccine was prepared and this was injected as follows:-

Dose/

<u>DOSE</u>	<u>DATE</u>
500 Million	11 December 1918
1,000 Million	15 December 1918
2,000 Million	21 December 1918.

By this time the condition had cleared up completely.

2,000 Million	8 January 1919
3,000 Million	5 February 1919
4,500 Million	18 March 1919.

These larger doses were used, not because they appeared necessary, but for experimental purposes.

The systemic reactions after the larger doses were much the same as after the lesser ones, but the local reactions were more severe. In no case however was any transient incapacity caused.

Up to the present date there has been an entire freedom from catarrhal conditions of the upper respiratory passages and this relief is many times greater than the writer had dared to hope for in his most sanguine moments.

Before attempting to summarise the conclusions which may be drawn from these observations, a few further points in Vaccine Therapy in general will be considered. In particular some aspects of the

subject/

subject will be dealt with in such a way as might be helpful to the Practitioner who is taking up vaccine treatment of coryza for the first time:-

### 1. COST OF VACCINE

A supply of three or four graduated doses of stock vaccine from one of the Manufacturing Chemists costs from ten shillings to one pound. If the dosage is increased to about 2,000 million, the cost rises to from three pounds to five pounds.

An autogenous vaccine, and full report on the organisms found, may be obtained from Messrs. Evans, Sons, Lescher & Webb, Ltd., Higher Runcorn, Cheshire. They appear to be very thorough and skilled in their technique. The cost is about thirty shillings or two pounds.

W. Martindale, 10, New Cavendish Street, London, W., also manufactures autogenous vaccines. For the vaccine and report his charge is ten guineas.

### 2. CHOICE OF PATIENT

Unhappily a course of vaccine treatment is an expensive luxury and the first desideratum is that the patient should be able to pay for it.

To the cost of the vaccine itself must be added the Doctor's remuneration for the administration of several doses.

The/

The second point to consider in the choice of patient is whether or no he is likely to derive benefit from the administration of the vaccine.

It is useless trying to make a vaccine do the work which ought to be done by a surgeon. Such conditions as adenoids and large tonsils, deflected septum, enlarged turbinated bones, and sinusitis should be dealt with by operation. After this is done the vaccine may be used in addition, if required.

The writer considers that the opportunity of having a course of Vaccine Therapy should certainly be offered to all persons who are likely to suffer from chronic bronchitis. That is, persons persons who are susceptible to attacks of acute bronchitis, or who have a severe winter cough. Bronchitis and emphysema are all too common in this country, and once the lungs are in an emphysematous condition complete cure can never be expected. It is possible, however, that by increasing the patient's resistance early in the disease, by means of Vaccine Therapy, the progress of the condition may be arrested and the final disaster avoided.

Other cases, in which very material benefit may/

may be expected, are those in whom a susceptibility to tuberculosis of the lungs is suspected and who are also liable to attacks of catarrh of the upper respiratory passages.

Again, cases of persistent Eustachian catarrh may be cured by vaccine treatment, and possibly an attack of otitis media might be forestalled in this manner.

### 3. WHAT ONE IS JUSTIFIED IN TELLING THE PATIENT ABOUT VACCINES.

The laity appear to view inoculation with a certain amount of suspicion and one may have difficulty in prevailing on them to have it done.

One is justified in informing the patient that inoculation may entail a certain amount of discomfort, but that no real danger is incurred; that benefit will almost certainly ensue, and that a complete cure is by no means a remote possibility.

### 4. COLLECTION OF THE SPECIMEN FROM WHICH AN AUTOGENOUS VACCINE IS TO BE MADE.

The specimen must be obtained through either the mouth or the nose, in each case a contaminated channel. If the secretions are blown from the nostrils they are almost certain to be contaminated

by/

by the rapidly growing *B. Subtilis* which is nearly always found about the *vibrissae*. A better way is to take the specimen by means of a swab introduced through a sterilized speculum.

In collecting specimens from the post-nasal space and larynx, a swab should again be used, if possible. If this is not feasible, the discharges should be hawked down from behind the soft palate and expectorated; they should not be blown out through the nostrils.

When the specimen is obtained through the mouth, the mouth must be thoroughly prepared first. Antiseptics cannot be used, but boiled water or salt solution and a new toothbrush should be used freely.

The best time for the collection of the specimen is on awaking in the morning, and before the partaking of food. The mouth should be thoroughly cleansed, as directed, and a quantity of the water should be swallowed.

The sputum should be expectorated directly into a wide-necked, stoppered, sterilized bottle. The stopper should not have been removed prior to this stage.

In order to minimize the risk of missing one of the causative organisms, a second and third specimen/

specimen may be collected on successive mornings.

After collection, the specimen may be washed in sterilized salt solution to remove any contamination which may be present. It should then be placed in a second sterilized bottle and sealed up, for transmission to the Pathologist.

If several hours have to elapse before the specimen gets into the hands of the Bacteriologist, it may be well to inseminate a few culture tubes at once, in order to give the more delicate germs a better chance of life. If this is done, a few different media should be used in order that all the organisms in the mixed infection may be catered for. Blood Agar and Blood Serum may be used. The possibility of anaerobic germs being present should be kept in mind.

If there is any suspicion of whooping-cough playing any part in the infection, a tube of the appropriate medium should be prepared. When these inoculated culture tubes are sent to the pathologist, the specimen should be forwarded at the same time, in order that he may prepare his own tubes should he desire to do so.

The specimen may be collected either during an attack of coryza or at the beginning of Autumn,  
about/

about the time that colds commence - but at a time when the patient actually has not got a cold.

The writer favours the former course, as the germs found on the healthy mucosa may not be the same as those which cause the catarrh. The disadvantage of the first course is that the patient has to contract a cold before the process of immunization can be begun.

#### 5. DISPATCH OF THE SPECIMEN TO THE PATHOLOGIST.

The specimen should, of course, be forwarded as soon as possible. Along with the specimen a few notes on the case should be sent.

For example:-

<u>Name</u>	J. G.
<u>Age</u>	28 years.
<u>Disease</u>	Coryza and laryngitis.
<u>Material</u>	Mucous from larynx and naso-pharynx.
<u>How taken</u>	Expectorated after the mouth had been thoroughly cleansed with boiled water and a tooth-brush.
<u>History of Case</u>	Is very susceptible to catarrh and does not make progress/

progress under ordinary  
medical treatment.

Required Report on nature of organ-  
isms found, and a vaccine,  
if thought advisable.

Suggestions I would suggest that the  
vaccine be sent me in a rubber-  
capped bottle, and that the  
vaccine contain about 2,000  
million germs to the C.C.

All this information is of service to the  
Pathologist. It assures him that reasonable care  
has been taken in the collection of the specimen,  
and it also shows him the reason why an expensive  
vaccine is required. The suggestion as to dosage  
I have found necessary as many pathologists are  
liable to make up vaccines with 500 million or less  
germs to the C.C. If the vaccine is put up in a  
rubber-capped bottle it is easy to dilute it after-  
wards, if necessary. The bottle has the additional  
advantage that only the quantity desired need be  
withdrawn; whereas if a portion of the contents of  
an AMPOULE be used the rest is wasted. The  
disadvantage of the bottle is that unsatisfactory  
aseptic technique may infect the vaccine and give rise to  
to/

to trouble when the vaccine is next used.

If reasonable care is used this should not occur. The fact that vaccines are made with a small quantity of antiseptic in the suspending fluid makes the danger even more remote.

#### 6. PREPARATION OF THE VACCINE.

Unless the practitioner is an experienced bacteriologist, he will be well advised to send the specimen to a specialist to have the vaccine made. Should he decide to manufacture the vaccine himself, special attention should be paid to the following points:-

Subcultures should be used as little as possible, as, the resulting diminution in the virulence of the organism usually entails an equal decrease in its immunizing power. For the same reason incubation should be as short as possible.

In sterilizing the vaccine, great care should be taken to avoid heating the vaccine to a higher temperature than is absolutely necessary. Heat also diminishes the immunizing power of the vaccine in most cases.

R. W. Allen recommends that heat should not be used at all, but that reliance should be placed on the 0.5% carbolic acid or 0.04% iodine  
which/

which is introduced. Whichever method is used great care must be taken to ensure that the vaccine is sterile, and that no pathogenic spores are still alive.

The finished product should be a smooth emulsion, free from clumps of bacteria and free from all exotoxin.

In the case of a mixed infection, nothing seems to be gained by having the different bacteria made up separately, while there are obvious advantages in having them combined. As a general rule it is probably wisest to combine the different germs in equal amounts.

#### 7. STORAGE OF VACCINES.

Vaccines should be stored in a cool, dark place. In the writer's opinion they deteriorate after about six months and become unreliable.

#### 8. ADMINISTRATION OF THE VACCINE.

Vaccines may be given:-

1. by the mouth.
2. per rectum.
3. Intravenously.
4. Intramuscularly.
5. Subcutaneously.

Nos. 1 & 2 are unreliable.

No. 3 increases all the risks of vaccine administration, with no apparent advantages, except that the local reaction is diminished and smaller doses can be given, <sup>with</sup> without diminishing the degree of immunity conferred.

Nos. 4 & 5 are probably the best. The subcutaneous method causes slower absorption, while the intramuscular route is more painful when the local reaction commences.

The syringe should be in perfect working order and the needle sharp and free from rust. The needle should be plunged in boldly, not pushed in slowly.

The writer formed the impression that the local reaction was much more painful and that a tingling pain came on almost immediately after inoculation when the vaccine was administered near a large subcutaneous nerve. He therefore formed the habit of inserting the needle near a landmark, such as a mole, whenever possible. This enabled him to avoid the same spot on subsequent occasions if the reaction seemed too painful; or to use the same spot again if the reaction was slight.

#### 9. DOSAGE AND INTERVALS BETWEEN DOSES.

No hard and fast rules can be laid down, except this - that we must always be guided by the severity/

severity of the reactions. This assists us on every occasion after the first. We will begin, therefore, by considering what is a desirable reaction and what a severe one.

Reactions are three in number:-

1. Local/.
2. Focal.
3. General.

#### 1. LOCAL.

A local reaction always occurs, even after small doses. About 6 - 10 hours after inoculation the area round the needle track becomes swollen, red, hot and tender. This should pass off within 48 hours, and should cause no disability whatever. Sometimes, especially if a large bulk of vaccine is used, the reaction is much more severe and the nearest group of glands may enlarge. The local reaction is not a good test of the suitability of the dose.

#### 2. FOCAL.

The focal reaction consists in a slight aggravation of the signs of the disease which we are treating. It usually commences about twelve hours after inoculation and passes off in about 24 to 36 hours. If the dose is too small it does not/

not occur.

In the cases such as we are considering the signs that the dose is high enough are an exacerbation of the symptoms, a feeling as if a fresh cold had been contracted. When this passes off it should be followed by a feeling of relief from the catarrh and an increased sense of physical well-being.

An unduly severe focal reaction is unlikely in cases of mild disease. In more grave cases it consists of an alarming increase in the severity of the symptoms.

### 3. GENERAL .

The fact that a general reaction does not take place is not necessarily a sign that the dose is too small. The reaction commences about 5 to 8 hours after inoculation, reaches its maximum within 18 hours and should disappear within 24 to 36 hours. A reasonably strong reaction, which need cause no alarm, is a rise of temperature to about 100 F. with slight acceleration of the pulse and breathing rate. This will be accompanied by a feeling of being out-of-sorts - malaise and slight headache. A reaction, more severe than this, indicates that the dose is too large.

Occasionally/

Occasionally the reaction reaches alarming dimensions, with nausea, rigors, vomiting, erythema or diarrhoea. This, however, is rare.

We have seen that the reactions reach their maximum within 12 - 18 hours. Therefore the best time to inoculate is in the afternoon, so that the patient may spend the time when he feels most poorly in bed. If this is done, he may have recovered completely by the following morning. If there is any reason to believe that the patient is incubating a fresh cold, or any other disease, the administration of the vaccine should be deferred for a day or two. Any mishap to the patient's health, occurring within a few days of being inoculated, will almost certainly be attributed to the vaccine.

Armed with the knowledge of reactions, we can now return to our first dose. A general rule is that the more acute the infection, the smaller should be the dose. In inoculation for prophylactic purposes, then, the initial dose will be larger than it will be when injected for therapeutic reasons.

Suppose that in the case of a vaccine containing three or four different germs we

consider/

consider 250 million mixed germs a fairly large therapeutic dose, we can adopt one of two courses. Either warn the patient that the reaction may be somewhat severe - and inject 250 million forthwith - or else begin with a much smaller dose - say, 50 million, and double the dose on every subsequent inoculation until a suitable reaction is obtained. In the treatment of mild infections, such as coryza, the writer prefers the bolder course, as little or no real harm can be done, even if the dose is much too large.

The objections to the second course are that time is wasted and that the patient is subjected to two extra injections.

For prophylactic purposes the initial dose may be 500 million, if the bolder alternative be chosen.

Provided that the general reaction has been slight or absent altogether, the dose may be doubled on the next occasion, without incurring any risk, and this process can be continued until either a severe reaction occurs, or cure is complete, or the dose has reached 2,000 to 4,000 million without any improvement taking place. Even if cure is complete, it may be wise to continue until a dose of 2,000 million

has/

has been administered. If 4,000 million has been injected without a severe reaction having occurred, and with no evident improvement in the patient's condition, the advisability of increasing the dose to 8,000 or 16,000 million should be considered. The writer has never seen such a case, but there appears to be no reason why this course should not be adopted. For prophylactic purposes a dose of 2,000 million may be assumed to be sufficient, unless the patient, by catching a cold, proves that this is not so. In this case again the dose may be increased. If a severe reaction occurs, before cure is complete, again one of two courses may be adopted: either the dose may be diminished and afterwards cautiously increased again, or the interval between the two doses may be increased and the same dose again administered. If the reaction is very severe indeed the interval should be lengthened and the dose decreased as well.

This leads us to the consideration of the interval which is desirable between doses.

Sir A. Wright has shown that for a day or two after the injection of a vaccine, the resistance of the blood is diminished, and that thereafter it increases steadily.

Dreyer/

Dreyer has shown (Lancet, April 6th, 1918, p. 498), that the maximum is reached in about three weeks, and thereafter slowly falls. The usual custom is to inject doses every 7 to 10 days, until the largest dose which is desired has been given. The writer, with a view to obtaining results as soon as possible, used an interval of only four days, with quite satisfactory results.

Once the dose aimed at has been given, one of two alternatives may be chosen, when injecting for prophylactic purposes. A course of treatment can be given in September - when the cold weather is about to commence - and repeated in February, to make up the leeway which the patient's immunity has lost in the meantime. This will only be possible if a stock vaccine is used.

The second course is to have the vaccine made when the patient catches his first cold, and give the largest dose desired once a month or so throughout the Winter and Spring. This is the course adopted by the writer with very satisfactory results.

#### CONCLUSIONS

Provided that the vaccine contains the correct organisms and is administered in sufficient doses/

doses, there can be no doubt that sufficient immunity against catarrhal organisms can be obtained.

If vaccine treatment fails, it does so for one of the following five reasons:-

1. The vaccine was badly made and its immunizing power destroyed.
2. The vaccine has deteriorated through being kept too long.
3. The causative organisms were not all represented in the vaccine.
4. The correct strains of the causative organism were not included in the vaccine.
5. The vaccine was not administered in adequate doses.

Unfortunately, as there is always a mixed infection, the third and fourth requirements are difficult of attainment.

The only way in which these essentials can be accomplished with reasonable certainty is by means of an autogenous vaccine, made by an expert bacteriologist. If this fails, when administered in adequate doses, it may be presumed that one or more of the causative germs has escaped detection and a further bacteriological examination is necessary.

Autogenous vaccines have two disadvantages:-

1. They cannot be prepared until an attack of coryza has actually been contracted.
2. They take a week or so to prepare.

Stock vaccines are less reliable than Autogenous vaccines, but they have given excellent results in many hands. They have the advantage of being ready for use at any time. If it is decided that a stock vaccine is to be used, one which is polyvalent should be chosen. Probably the best is that manufactured by W. Martindale, New Cavendish Street, London, W.

Detoxicated vaccines are not yet sufficiently tested. If a patient were found, whose power of manufacturing antibodies were so abnormally low that he could not be given sufficiently large doses of ordinary vaccines, it might be well to endeavour to detoxicate the vaccine. Detoxicated vaccines are put on the market by "Genatosan". Ltd. 12, Chenies Street, London, W.C. 1.

#### DOSAGE.

It is clear that vaccines, like drugs, must be given in sufficient doses if benefit is to

be gained. Many users of vaccines do not administer them in adequate quantity. It seems probable that doses of 1,000 million or even less mixed germs may be sufficient to secure immunity, but that doses of double this amount, or more, are better, and do not cause harmful results.