

A THESIS
ON THE
TREATMENT OF
BACTERIAL INFECTIONS
BY
INTRADERMAL MEDICATION.

Nutting Stuart Fraser, M.B., C.M.

M. D. 1926



A General Practitioner is not capable of scientific observation. He is easily prejudiced in favour of any new treatment, and has not the means at hand to test out results, using controls &c. But his greatest interest is in treatment. If any method of treatment will relieve his patients of their suffering, either mental or physical, he is justified in adopting it.

The following suggestions regarding treatment of infections is made with the full knowledge of the fact that they may not stand scientific observation. The number of cases is necessarily limited.

POINT OF ENTRY OF INFECTION

How did the patient become infected; how did the infection enter the system; how did it spread?

Sir Robt. Philip states that "the tubercle bacillus can pass into the body by a variety of channels ----- it may occur through the mucous membrane at almost any point and whatever channel the bacillus enters the body,----- its further passage throughout the system is effected for the most part by lymphatic spread. There is a moment of time when the bacillus passes the protecting barrier - the mucous membrane most commonly. This is followed by a latent period (primary incubation) while the bacillus is establishing itself within the lymphatic circulation. After an interval ----- objective evidence may be found in glandular enlargement." (I.)

HUDACK and McMaster⁽²⁾ have shown that in the lymphatics the spread is remarkably quick and they found that dye introduced into the resting forearm reached the axilla in a few minutes.

Case 1. A medical man cut his little finger Jan. 29th. 1912. Next day his temperature was 103° and he was delirious. There was some oedema over the shoulder and left clavicle, and it was necessary to make an incision and evacuate the pus which was found to contain streptococci. From this the infection spread through the whole system, forming abscesses on the chest wall and even down in the knee-joint, so that only amputation saved the life of the patient, thus bearing out the observation on the rapidity of the spread through the lymphatics.

IMMUNITY.

All inoculated cases do not result in this wide-spread infection. In many cases, nature deals with the infection and the general health does not suffer. How is this accomplished?

In an Editorial on Allergy and Immunity in Tuberculosis,⁽³⁾ the Editor of the British Medical Journal states "the preliminary sensitization, mechanical clumping, and sometimes lysis of the bacteria, appear to be dependent on antibodies which are either free in the circulation or are concentrated on the surface of the tissue cells, while the ingestion of the bacteria, their removal from the circulation, and their subsequent disintegration are accomplished mainly by phagocytic cells of various types."

In Medical practice it would seem that it is only through the stimulation effected intradermally that the defences of the organism are stimulated.

the organism are set in motion. For example, an infected scratch is followed by inflamed lymphatics, enlarged lymph-nodes and leucocytosis - nature's effort to deal with the infection, and it is evident that this must occur successfully in many cases, particularly in the case of tuberculosis. We are so constantly exposed to the infection of tuberculosis, and so many of us prove to be immune, that it is evident that we have been able to fight the infection successfully.

Case 2. A young girl, P.M. aged 18 consulted me December 1934, suffering from tuberculosis to which she afterwards succumbed, and her family history was suggestive in this respect. She was one of a family of seven, the father still living and healthy, the mother died of T.B. several years ago, and four of the children also died from the same cause. P.M. then is the fifth case in the family, but two are healthy and the father is still healthy, thus three have been able to deal successfully with the infection, while the remainder have died, yet all were exposed to the same infection, had the same surroundings, and the same food and comforts.

It is evident then that in many cases of infection, and particularly of tubercular infection, nature throws off the poison - they are immune to that particular poison.

TREATMENT.

How shall we apply these principles in our treatment of cases? Our object must be to stimulate nature's defences, and if any serum or virus is used it must be in such doses that will stimulate these defences, and not overcome them. The difficulty is to establish immunity quickly enough to deal with the infection. By hypodermic inoculation immunity can be established for diphtheria and scarlet fever, but only slowly, the inoculation must be months before exposure to infection.

Hudack and McMaster (2) have demonstrated the rapidity of the lymph flow in the lymphatics of living human skin, and the Editor of the Journal of the American Medical Association states "the peculiar biochemical mechanism of intracutaneous vaccination has not been yet determined. Apparently initial or secondary interactions between an injected vaccine and local tissues so modify the vaccine as to alter qualitatively the subsequent antibody response" (4) In Dr. DuBois' (5) monograph it is termed "the reticulo-endothelial system" and the function of certain of its cells as phagocytes explained. My own observation leads me to believe that the "antibody response" is rapid, almost immediate, and by using the lymphatic inoculation (intra-dermal vaccine) we start this response almost immediately, as evidenced by the leucocytosis which so quickly follows. In this way we would explain the difference in the rapidity of establishing

immunity in cases of diphtheria or scarlet fever by hypodermic medication with the immediate effect of the intradermal small-pox vaccination. The established custom in the case of small-pox vaccination has been to break the epidermis and apply the virus to the abrasion. It is a crude method and personally I have not used it for years as I find the intradermal method more sure of success, more easily kept free from secondary infection, and more easily and quickly applied. In cases of exposure to the infection of small-pox it has always been the custom to apply vaccination immediately, and the immunity is established at once if the disease is not already in the system.

If a virulent disease like small-pox can be controlled in this way it would seem reasonable to apply it in all other infections, such as tuberculosis, typhoid, streptococcal, staphylococcal, and colon bacillus infections, and of these tuberculosis gives the best opportunity of checking up the effect of treatment. In the few cases under observation the treatment seems to have had a beneficial effect, and helped nature to fight the disease. Tuberculosis can be followed, not alone by the physical signs in the chest, but by the X-ray and especially by the effect upon the blood-tests commonly made in such cases.

In cases of tuberculosis, free from secondary infection with a low leucocyte count, it is found that the leucocytes are quickly increased, but, as in all other methods of treatment, the effect largely depends upon the amount of infection already present before treatment commences. In this respect the artificial pneumothorax and thoracoplasty are valuable aids in limiting the amount of infection. Further the method is safe, will not light up a latent focus, does not cause a general reaction and does not necessitate confinement to bed in ~~in~~ ⁱⁿ ~~safe~~ febrile cases. The bovine type of tuberculin has been found the most satisfactory.

This method of treatment was commenced in 1929, and at first was used like a Von Pirquet test, that is, the pure tuberculine was used, but in the smallest quantity possible. Later experience showed that equally good results could be obtained by using dilutions, and our custom now is, to use the third dilution, that is one-tenth of a milligram, for many months or a year, and then the stronger dose. One point noticed in these cases is the fact that even after years of treatment the same weak dose will cause a local reaction.

This method of treatment has been carried on since 1929 and in the year 1932 a paper was published by Dr. Corbus of Chicago on "Intradermal immunization in gonorrhoea" (6) in which he advocates a similar method of treating gonorrhoea, with excellent results.

The following are a few of the cases of tuberculosis treated in this way:

Case 3. F.W. a young man, aged 23 years, seen March 28th 1828 and who had been ill many months. The temperature ranged from 99° to over 100°. The physical signs were, on the right, high-pitched bronchial breathing, loudest at the apex, with increased vocal resonance and whispering pectoriloquy. At the left base there were crepitations with cough, and increased vocal resonance. An X-ray taken April 26th. showed a cavity well defined between the first and second ribs. The apex was

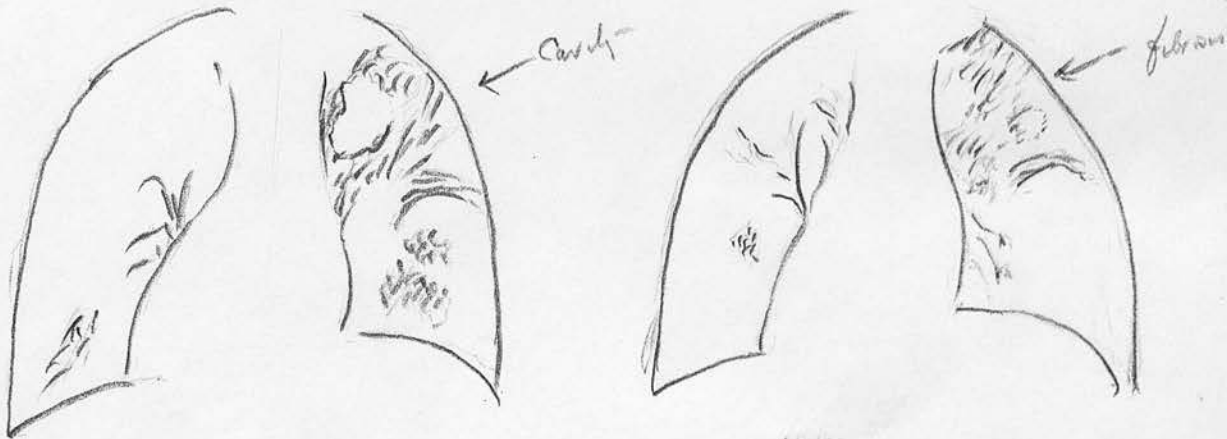
dense.

Artificial pneumothorax was induced, beginning May 5th. and continuing until the summer, when he went to the country, and the pneumothorax was discontinued.

Dec. 8th., on return to town it was found impossible to continue the pneumothorax, owing to pleuritic adhesions. Intra-dermal injection of pure tuberculin caused a reaction about an inch and a half in diameter. It was repeated on the 15th. and then not until Jan. 1st. 1929. The treatment was continued at about ten days intervals for four months when he seemed convalescent and the X-ray was satisfactory.

March 29th. 1929 he was examined again and found free from physical signs.

In this case only the leucocytes were counted and found to be 16,000. No recurrence of the disease has occurred in the seven years that have elapsed since then.



April 27. 1928.

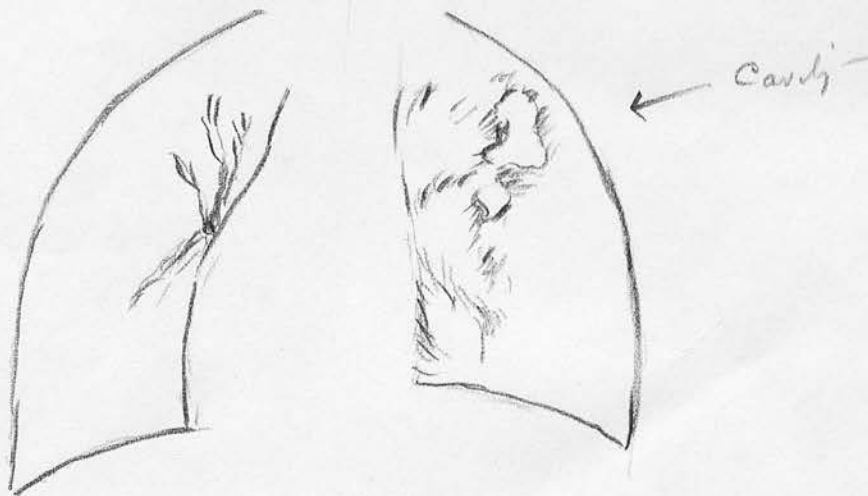
March 29. 1929

Case 4. Jan. 4th. 1928.

A.F. female, aged 25 years, complained of cough, debility and loss of flesh. On examination it was found that she had a temperature of 101°, pulse 90. The right apex was dull, high-pitch bronchial breathing and crepitations, particularly heard on coughing.

The X-ray showed a cavity at the right apex and considerable infiltration.

Pneumothorax was started Jan. 19th., beginning with 250 c.c. and was continued until May 4th., during which time she seemed to be making good progress, but an attack of pleurisy supervened with an increase of temperature, and subsequently it was found impossible to continue the pneumothorax. She continued about the same until Jan. 6th. 1929 when inoculations with bovine tuberculin were commenced. They were continued regularly until May when she returned to her home and treatment was stopped, but from reports received she has been leading a normal life since that time. The only blood examination was a leucocyte count and this continued high, from 17,000 to 29,000.



Case 5.

Feb 23rd. 1929.

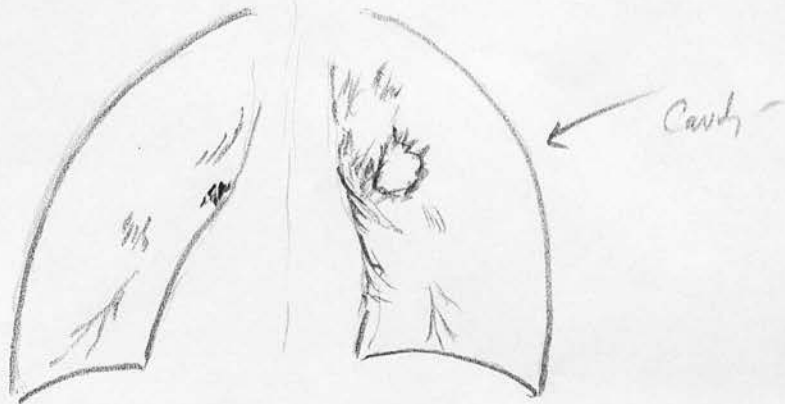
C.N. a young man 22 years, who reported having coughed up blood-stained sputum. He had always been in good health and had a good family history. The physical signs were confined to the ~~right~~ **right** apex at which the breathing was bronchial, and the vocal resonance increased.

X-ray showed a low lying area of density at the left apex and a radiolucent area between the ribs.

X-ray showed a localized area of density at the **right** apex and a radio-lucent area between the 2nd. and 3rd. ribs. Increased density at the hilus and peribronchial thickening extending to the base. On the **left** side a calcified gland at the hilus. The leucocytes were 4,800.

Feb. 23rd. inoculated bovine tuberculin and five days later it was noted that the local reaction was considerable, and the leucocytes increased to 10,000.

March 4th. they had increased to 13,800. The treatment was continued at two weeks intervals for three months, and he has continued in good health since that time.



During the last two years an attempt has been made to keep check on the progress of the cases by blood examinations, and I have to acknowledge my indebtedness to Prof. Lyle Cummins of Cardiff for instruction in these methods. Taken collectively the three blood-examinations described by Prof. Cummins at⁽⁵⁾ the meeting of the Canadian Medical Association in 1933, have proved very reliable in prognosis, and a sure guide to the progress of the cases under treatment.

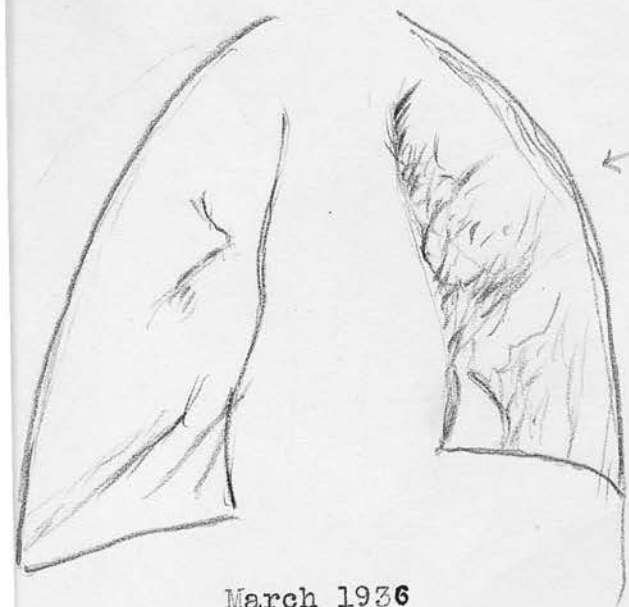
Case 6. M.L. female, several years ill with cough and the usual symptoms of tubercular disease of the lung.

Feb. 1935 there were the physical signs of a cavity at the right apex, and a deposit at the left base. The pulse was 90 and the temperature a little over 99° in the evening.

The X-ray showed an adhesion in the centre of the right diaphragm, a heavy deposit at the hilus extending out along the inter-lobar pleura. A parenchymatous involvement at the base, and a cavity at the apex. The blood examination was: sedimentation 36 % Von Bonsdorf modification of the Arneth count 156, the lymphocyte-monocyte 88-12.

She was given pneumothorax several times and the adhesions showed up in the X-ray, but prevented compression of the cavity and was given up. Inoculation intradermally was used regularly from May 1935 to the end of the year. The blood-picture now is : leucocytes 14,200., sedimentation 4 % , nuclear divisions 189 and lymphocyte-monocyte 89-11. Guided by the blood counts she has been allowed free exercise and lives a normal life without any set-back.

Case 6. M.L.



March 1936

← Fibrosis



Feb. 1935

← Carls-

While it has been found that this method of treatment is helpful in cases of moderate severity and in recent cases, it would be foolish to expect any benefit in a well established case. It depends upon the extent of the infection, for in some cases the system seems to be overwhelmed almost immediately, while others go on for years showing very little systemic infection. Those cases with a sedimentation ~~count~~ ^{rate} up to 50 and 60 % in one hour are not promising cases for this or any other treatment. Of the 12 cases now reported, four had a sedimentation rate over 50 % and bilateral disease. One died in eight months, one will probably die within the year, the other two cases are progressing towards a cure. While the sedimentation rate was over 50 % in these four, the lymphocyte-monocyte ratio differed. In the fatal case the monocyte percentage was 58 %; the hopeless case 34 %; the two favourable cases 16 % and 17% respectively, showing the value of including all the counts in making a prognosis. In eight of the cases treatment has been stopped for months, the other ~~three~~ cases are still under treatment and doing well, so that one feels that something has been accomplished in helping nature to fight the disease.

TYPHOID FEVER.

As already stated the same method should aid us in treating other infections, and so seven cases of Typhoid have been so treated, using the stock vaccine, antityphoid, for the purpose. In these cases the temperature is the only record that we have been able to keep. All the cases gave positive Widal reaction but this is not of value because the inoculation would be sufficient to cause a positive Widal. The other symptoms were unmistakable, -rose spots and enlarged spleen in each of the cases. The charts give the record of treatment and the response to the inoculations is almost immediate. In two of the cases one inoculation was sufficient. The local reaction was decided in each one, being an area at least two and a half inches in diameter.

Case 7.

Rita C. female, 16 years, seen Sept. 5th. 1935, complaining of pain in th lower abdomen, with vomiting and diarrhoea. This continued three days and she was examined for appendicitis, but no local signs and the rectal temperature was only one degree higher than the mouth. Sep. 11th. splenic dulness increased and several spots on the abdomen, and the case diagnosed as Typhoid. The ordinary typhoid vaccine was used intra-dermally and caused a marked reaction, about two inches in diameter and by the 14th. the temperature was normal and all symptoms had subsided. The further convalescence was uninterrupted.

Regⁿ No. _____

NAME RITA CHRISTOPHER 16 yrs. WARD _____

MONTH	Sept 1935														
DAY OF MONTH	7	8	11	12	14	15	16	17							
DAY OF DISEASE															
MEMORANDA	107	MEM	MEM	MEM	MEM	MEM	MEM	MEM	MEM	MEM	MEM	MEM	MEM	MEM	C°
	106														41°
	105														40°
	104														39°
	103														38°
	102														37°
	101														36°
	100														
	99														
	98														
	97														
	96														
	PULSE	M	120	132	130	96	92	84	84						M PULSE
	RESPIRATION	M													M RESP
	AMOUNT OF URINE	M													M MOTIONS
VOMIT	E													E	

Diarr

8 P.M. 8 A.M. M
MOTIONS
8 A.M. 8 P.M. E
*AMOUNT OF URINE
ENDING AT 8 P.M.
- EACH 24 HOURS.
VOMIT

Case 8

Mrs. C., mother of Rita and nursed her .

Sept. 13th. complained of abdominal pain, vomiting and constipation. Castor oil was taken and acted well, but continued sick and high fever.

Typhoid vaccine was given intra-dermally, and reacted locally so that an area of two inches diameter resulted. The chest was free, no sign of pneumonia or other disease.

Nov. 16. still vomiting, bowels constipated.

Nov. 17th. vomiting stopped and feeling well. The further progress was satisfactory.

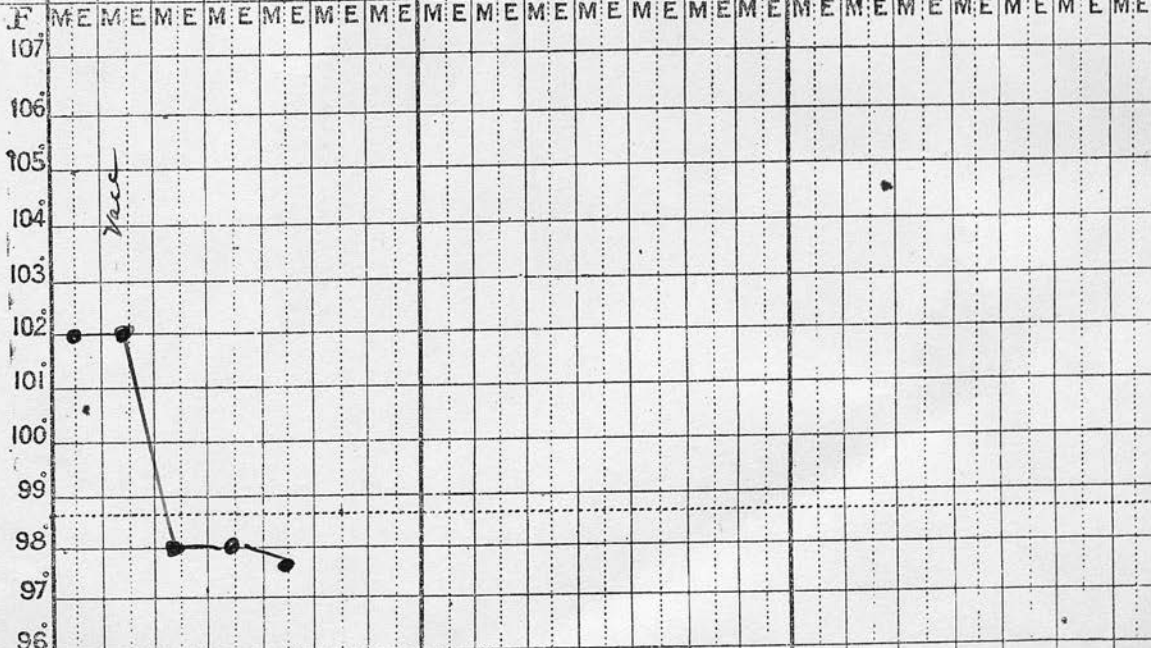
REG. IV.

NAME MRS. CHRISTOPHER

WARD

MONTH		Sept 1935																				
DAY OF MONTH		13	14	15	16	17																
DAY OF DISEASE																						
MEMORANDA		F	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	C°
		102	102																			39
																						38
																						37
																						36
PULSE			88	80	80	72														M PULSE		
RESPIRATION																	M RESPN					
MOTIONS																	M MOTIONS					
AMOUNT OF URINE																	AMT OF URINE					
VOMIT																	VOMIT					

Vaccine



*AMOUNT OF URINE ENDING AT 8 P.M. EACH 24 HOURS.

Case 9.

W.B. male 20 years. brother of C.B.
 Sept. 20th has been sick a week with loss of appetite
 weakness and diarrhoea. Has a temoerature but slow
 pulse. Four rose-spots were noticed on the abdomen
 and the splenic dulness was increased. The Typhoid
 vaccine gave a positive reaction and he expressed himself
 as feeling well a few days later.

Regⁿ No.

NAME W. Bowman 2074 WARD

MONTH	Sep 1935										Oct.								
DAY OF MONTH	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5			
DAY OF DISEASE																			
MEMORANDA																			
PULSE	80	90	80	72	76	72	72	76	80	72	80	72	80	76	80	84	84	76	M PULSE E
RESPIRATION				18	18	18													M RESPN E
6 P.M. 8 A.M. M MOTIONS 8 P.M. 8 P.M. E	2	0	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	M MOTIONS E	
*AMOUNT OF URINE ENDING AT 8 P.M. -EACH 24 HOURS.																		AMT OF URINE	
VOMIT																		VOMIT	

Case 12.

Mrs. M. in whose house the girl M.F. worked was the most severe case of those seen, but although she went through a four weeks illness, and was very weak afterwards, the treatment by vaccination seemed to help each time it was given, but it failed to cut short the disease. Seen first Dec. 6th. and had been sick for a week. Her symptoms were weakness, loss of appetite, insomnia, and constipation. By Dec. 11th spots had appeared and the spleen definitely enlarged. The urine contained acetone and a trace of albumen. The patient was drowsy, weak pulse, and delirium. The vaccine was used four times, with diminishing reaction locally, until at the fourth injection it was negative. The progress is shown by the temperature chart.

Regⁿ No.

NAME MRS MARTIN

WARD

MONTH	Dec 1935																				JAN																				
DAY OF MONTH	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2													
DAY OF DISEASE																																									
MEMORANDA	F	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M													
			Vacc +++			Vacc ++				Vacc +				Vacc -																											
	104	101	104	101	103	100	102	101	102	101	103	100	103	100	102	101	102	101	100	101	100	99	100	101	100	99	100	99													
PULSE	M 104	E 96	M 116	E 112				M 108	E 116	M 124	E 112	M 104	E 104	M 112	E 108	M 108	E 108	M 108	E 108	M 98	E 96	M 96	E 96	M 96	E 96	M 96	E 96	M 98	E 98	M 96	E 96	M 96	E 96	M 92	E 88	M 88	E 88	M 88	E 88		
RESPIRATION																																									
MOTIONS	0	0		1	2	1	1	1	1			2			3	1						2	1	1																	
AMOUNT OF URINE	0	0	E 1		E 1			1	1	2	E 1		2	1	1	1	2	2	4			1																			

INFLUENZA.

Many cases of influenza have been successfully treated, using a stock vaccine, and nothing is so effectual for the chronic cough following an attack of influenza, as an example of which the following case may be quoted:

Case 14.

Mrs. A.G., 34 years. April 16th. 1935. Good family history but complains of persistent cough and pain in the chest at the level of the nipple. Medicines failed to give relief and she consulted different doctors and had thorough examinations, but always with negative result. The heart and lungs were reported normal, as was also the blood-pressure and the nervous system. Examination of the blood included the differential count, and sedimentation, which were found to be normal. The sputum was negative to T.B. showed a greyish-white tenacious mucus, with large round cells and coarse granules, no pus cells. July 27th. the same condition continued without any improvement in the cough or pain, it was decided to try the vaccine treatment. A stock vaccine for "colds" was used and caused a well-marked reaction at the site of the injection, but the effect was rapid, the cough and pain disappeared, and she was able to resume her usual games of golf and tennis. Oct. 8th. there was a recurrence of the symptoms and the injection was repeated, and again eight days later, after which there was no more trouble.

In this case treatment by various doctors in Newfoundland and in Boston failed to give relief, until the inoculation, but the latter was entirely successful. Probably a latent focus of influenza was there, which the vaccine stimulated the system to throw off.

RESUME.

It is claimed that stimulation of the lymphatics (reticulo-endothelial system, DuBois) causes an immediate "antibody response" helping the system to fight any bacterial infection. Cases have been quoted to prove the benefit of such treatment in Tuberculosis, Typhoid Fever and Influenza.

REFERENCES.

1. Philip, Sir Robt. : Musings in the Garden, fifty years association with tubercle bacillus. B.M.J. June 23rd. 1934.
2. Hudack S.S. and McMaster P.D. : The lymphatic participation in human cutaneous phenomena. Jour. Exper. Med. 57: 751, May 1933
3. Editorial B.M.J. June 2nd. 1934.
4. Edit. Jour. A.M.A. May 16th. 1931, quotes Jordon and Falk. " the newer knowledge of bacteriology and Immunology. Univ. Press Chicago, 1928 Chap. 28 Page 1078.
5. Edit. B.M.J. Aug. 3rd. 1935.
6. Corbus, B.C. : Intradermal immunization in Gonorrhoea, Jour. A.M.A. Feb 13th. 1932.



18. VIII. 36