days. He always took his food well, consequently his motions were very large. He constantly passed his urine in bed, and seemed to have very little control over the acts of micturition and defaecation.

Having recovered from his first attack of diarrhoea, and the abdominal distension having returned, the patient remained in the same condition for about eighteen months, when he developed a second attack of diarrhoea and vomiting, the distension again disappearing, only to return in a couple of days when the diarrhoea had ceased. It was noted that he did not feel so well until he regained his distended condition.

He now remained in his usual health for about nine months and then began to get gradually worse. His abdomen became enormously distended, absolutely tense and of highly glazed appearance. This stage lasted about three or four months. Finally breathing became so difficult and the heart's action so much impeded that he died. There was also severe vomiting before death. The condition was diagnosed independently by several of his medical attendants as idiopathic dilatation of the colon.

Necropsy.

A post-mortem examination was performed, when the following pathological conditions were noticed:

There was great oedema of the legs and scrotum, the abdomen being distended to an extreme degree. On opening the latter the small intestine immediately bulged out; and on extending the incision, a quantity of pale greenish fluid flowed out of the abdominal cavity.

The alimentary tract from rectum to stomach was greatly dilated and contained practically nothing but gas. Dilatation was greatest in the descending and transverse colon. Commencing at the sigmoid flexure, it rapidly increased so that the lumen of the descending colon measured about four times its normal diameter after being deflated. At the splenic flexure the bowel was constricted, and dilatation again occurred in the transverse colon, which was between three and four times its normal diameter. Another constriction was found at the hepatic flexure, and the bowel again became dilated. Dilatation, however, was not nearly so extreme in the ascending colon and caecum.

The appendix was normal. The small intestine and stomach were considerably distended and filled with gas. The diaphragm was abnormally high and arched, the liver small, nodular, and freely movable, and showed some fatty degeneration. The spleen was normal in appearance; the kidneys showed some congestion and interstitial changes.

The heart was markedly displaced upwards and very small; the valves appeared healthy, but the pericardium contained excess of fluid. The lungs were pushed upwards, but appeared healthy.

SOME EXPERIMENTS ON COLD-CHAMBER TREATMENT.

BY

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With Prefatory Note by

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PREFATORY NOTE.

SOME years ago Sir Edwin Durning-Lawrence, Bart., offered funds to the Liverpool School of Tropical Medicine for the purpose of experimenting on the effect of cold on yellow fever, a subject in which he had long been interested owing to various reports which had come to his knowledge. The school found it difficult to give effect to his wishes, and the matter was allowed to drop. For a long time I have felt that much experimental work remains to be done on various possible therapeutic agencies, such as cold and heat, and in 1909 I therefore asked Sir Edwin Durning-Lawrence whether he would not assist us to commence such studies in Liverpool. He assented at once, and very generously gave a considerable sum of money for the purpose of making the required cold chamber and for maintaining the cost of the investigation. The chamber was made by the Haslam Engineering Company, Derby, and the researches were in full progress at the beginning of 1910. At first Major Williams, I.M.S. (retired), conducted them under myself; but in April Mr. J. G. Thomson, M.B., Ch.B., took up the work, and has continued it to date. He reports the total results in the following paper. I may add that there are considerable difficulties in the way of such researches, many of the experiments being rendered invalid by the death of the animals owing to various causes. Experiments with many diseases is almost impossible owing to several small difficulties.

I think, however, that some evidence has been obtained the effect that a cold dry air may retard certain

infections, and will therefore probably have some beneficial effect in disease. In such an important matter as treatment, this may be looked upon as of value, and also as an indication for work in the same line in connexion with human patients. We should therefore like to advocate the construction of cold chambers in connexion with hospitals—that is, chambers where human patients suffering from various disorders, such as phthisis, could be kept under observation; and I hope that efforts may be made to carry out this idea. We should like cases for trial.

R. R.

PRELIMINARY.

No noticeable change can be observed in a patient's body as a consequence of alteration of external temperature; but nevertheless changes may be produced in his blood and tissues which may be inimical to the parasites living in him.

It is common to send patients suffering from malaria to temperate climates, for example the hills of India, and it is easier to treat such patients in England than in the tropics. Again, from a careful study of the statistics in India it has been noted that a sudden rise in the malaria-rate occurs at the end of the cold season before any new brood of *Anophelines* has been hatched out. This may be due to relapses caused by the greater heat.

In discussing relapses in malaria, R. Ross (1910) puts forward as a hypothesis that external heat probably tends to encourage these. Although the temperature of the body remains much the same, the parasites may be stimulated by the heat in some way, owing to the fact that warm climates are specially suitable to them and to their dissemination by mosquitos. The same observer, while conducting experiments in India with birds, noted when he took these to a cold climate, such as the Himalayas, that the parasites in their blood greatly diminished in numbers. Many observers, especially in Italy, have noted that season affects the plasmodia, especially the sexual forms, quite apart from the proliferation of the carrying agents.

Not many years ago phthisical patients were shut up in hot rooms, and now such patients go to the hills of Switzerland, where they are subjected to a cold dry atmosphere. In fact, there is good reason to believe that the cold acts in these cases as a tonic to the whole animal organism, and without doubt acts almost as beneficially as the purity of the air inhaled.

It has been shown by Raubitschek (1910) that white rats fed on buckwheat and exposed to the sunlight develop a disease which has been called fagopyriemus, a condition which in many respects simulates pellagra, whereas those kept in the dark remain quite healthy. Before this experiment, a suggestion that sunlight was capable of aiding disease would have been regarded as most improbable, but here we have absolute and direct proof of the influence of such natural agencies.

It is usually admitted that people who live in cold climates have more vitality and energy than those who live in the tropics. More work is done and greater energy displayed in cold climates. Too much heat and too much cold will both lower vitality. In suggesting cold treatment, however, we do not mean exposure, and we did not in any way lower the vitality of the animals observed by us. It has been well proved, after about eighteen months' experimental work with rats and guinea-pigs, that the animals in the cold chamber are livelier and take their food better than those in the varying atmosphere of the animal house, the temperature of which in the summer months was often very high. A cold moist atmosphere or exposure to a sudden change of temperature may be exceedingly dangerous to the vitality of an organism, but this is quite a different thing to the cold dry bracing atmosphere of Switzerland and Canada during the winter. All visitors to the cold chamber here admitted the efficacy of a short sojourn in it, and this was most noticeable during the heat of summer. One feels more vigorous in this chamber, and this probably better than anything else may suggest the possible value of treatment in it.

Very little seems to be known of the physiological action of cold air on the living organism. It is known that cold causes constriction of the peripheral arterioles of the skin, and that a cold bath stimulates leucocytosis. We know that animals which are homoithermal, if anaesthetized with ether, become poikilothermal, but have

little precise knowledge what exactly are the changes produced by heat and cold in the blood and tissues.

HISTORICAL.

In 1906 Dr. W. W. Crane suggested the value of cold air in the treatment of tetanus and yellow fever, and pointed out that the onset of tetanus was commoner during hot weather than during cold. Vincent of France noted (as Crane reports) that a case of idiopathic tetanus in a young man occurred several days after a "heat stroke." Experimenting with guinea-pigs inoculated with tetanus culture, he discovered that those kept in an incubator and subjected to a high temperature all developed the disease and died, while none of the controls were affected. As Crane points out, this shows that heat is an important factor in the development of tetanus. Dr. Charles C. Allison, of Omaha, has reported (Crane) on a desperate case of tetanus in a boy placed at the suggestion of Dr. W. J. McCrann, of South Omaha, in a cold storage room; he was much relieved immediately and finally recovered. Crane also points out that each temperature, high, medium, and low, has an influence of its own; that the summer incidence of such diseases as dysentery, enterocolitis, cholera morbus, etc., are well known; and that the winter incidence of bronchitis and pneumonia is also well known. He points out also that measles and typhoid are more severe and scarlet fever is less severe in warm climates.

Dr. Louis Perna, in 1909, severely criticized treatment of yellow fever by cold. Its advocate, Dr. Garcia, had said that the cold "increases the resistance of the organism" or favours the means of defence. Dr. Louis Perna says, however, that if the cold only "favours the means of defence," the statement should be accompanied by facts which sustain it. As a matter of fact, the figures of experiments given in this paper by Perna show that cold gave results which would condemn the use of the "polar chamber," or at least show that the treatment is futile. The experiments (in Havana) are reported as being made under the most favourable circumstances; but this seems almost to be incorrect when we learn that some of the patients suffered from chilblains, some from rheumatic pains, and some even had gangrene. It may be assumed that, if such complications as these did take place, the patients were not treated under favourable circumstances, but were exposed to too much cold. The first essential in cold-air treatment is proper comfort and protection for the patient. It is not suggested that patients should be scantily clothed, and that the vitality of any part of the body should be lowered. It must again be pointed out that cold air may either lower or raise the vitality of an animal; under favourable circumstances it unquestionably raises the vitality, but under unfavourable circumstances lowers it.

Raphaël Blanchard and Marc Blatin (1907) discussed the immunity of the marmot in hibernation to certain trypanosome infections. The marmot awake is fatally affected by inoculation with *T. brucei*, *T. gambiense*, *T. evansi*, and the trypanosome of El Dehab; but, on the other hand, the marmot in hibernation, that is, asleep, is immune to the four species of trypanosome enumerated above. This, he says, is not due to the action of antibodies, but to the fact that the animal during hibernation is subjected to a low temperature. C. C. Bass (1910) draws attention to the fact that pellagra is greatly benefited by the onset of cold weather, and that patients sent to Colorado were greatly relieved, and in fact became quite well, when subjected to the cold bracing climate. One patient was bedridden when she left, but was up in ten days and without recognizable symptoms of disease in two weeks. In view of this fact experimental cooling of wards was attempted, but was a mechanical failure, as expense evidently prevented proper experiments being carried out.

OBSERVATIONS.

I will now give as concisely as possible the results obtained in our experimental work here at the Liverpool School of Tropical Medicine.

A chamber was constructed 12 ft. long by 7 ft. wide by 6½ ft. high. It can be kept at any temperature between about 15° F. (= 9.4° C.) and 150° F. (65.5° C.). The temperature is reduced by an ammonia compressor worked by a 6-h.p. motor and a fan which drives in air through a chamber in which a saturated solution of

calcium chloride is kept constantly trickling over corrugated iron plates. The chamber receives light through a window, and is also fitted with an electric lamp. The motor is stopped during the night, and the temperature usually rises during that time to 36° or 38° F., or thereabouts, but this of course varies with the external temperature.

The animals treated were subjected to a temperature of 20° F. during the day, and in no way suffered discomfort. They were well fed and allowed plenty of straw. It is of great importance also to note that the atmosphere of this chamber was of low humidity (40 per cent. to 60 per cent.).

MAJOR WILLIAMS'S EXPERIMENTS.

Major C. L. Williams, I.M.S. (ret.) was in charge of the experimental work with this chamber from September, 1909, until April 13th, 1910, and I will first give a short account of the results of his experiments.

So far only one human case has been treated here by the cold. The patient, W. A., suffering from sleeping sickness contracted in North-Eastern Rhodesia, spent several days in the chamber and seemed to be greatly benefited by it. The patient himself said he felt much better after treatment, and several times he walked back to the hospital, a distance of fully 1½ miles, after his cold-chamber rest.

Table by Major Williams.

Animal Infected.	Number of Animals.	Average Incubation in Days.
<i>T. lewisi</i> (rat)	13 { Cold chamber—6 Controls—7	14
<i>T. brucei</i> (rat)	15 { Cold chamber—8 Controls—7	18 17.7

It will be noted that the incubation period was delayed in the cold in animals inoculated with *T. lewisi*, and slightly in those inoculated with *T. brucei*. The only animal which failed to show trypanosomes was one inoculated with *T. brucei* and placed in the cold chamber. Further, it was observed that the life of rats infected with *T. brucei* was prolonged in the cold; those of animals infected with *T. lewisi*, on the other hand, were shorter in the cold. It is difficult, however, to draw definite conclusions in this case, as animals tend to recover spontaneously from this infection. Major Williams also noted a slight prolongation in the life of animals infected with Caderas. Five guinea-pigs with tetanus were placed under observation; 1 died in nine days and a half when in the cold chamber, but it is doubtful whether this animal ever developed the disease. Two injected with 500 c.cm. of culture, and placed one in the cold chamber and one as control, died with similar symptoms in a similar time—fifty hours. As regards increase of or loss of weight in the animals, Major Williams says that in those animals on which accurate data can be founded, the results are as follows:

Table by Major Williams.

Animal.	Cold Chamber.		Controls.		Total.
	Gained Weight.	Lost Weight.	Gained Weight.	Lost Weight.	
<i>T. lewisi</i> (rats)	3	1	1	1	6
<i>T. equiperdum</i> (rats) ...	6	1	4	2	13
<i>T. brucei</i> (guinea-pig) ...	3	—	2	—	5
Tubercle	—	1	1	—	2
<i>T. evansi</i>	—	—	—	1	1
✓	12	3	8	4	27

It will be noted that all animals in the cold gained weight (with the exception of three, of which one was a case of tubercle), and this shows, on the whole, a favourable influence of the general nutrition. Major Williams also

inoculated 7 rats with pneumococcus culture, but these experiments were unsatisfactory as these animals evidently never developed the disease. Of 6 guinea-pigs inoculated with bovine tubercle, it was noted that the swelling at the site of inoculation burst a month later in 2 animals in the cold chamber.

Put shortly, the results brought out by experiments made by Major Williams in about 100 animals show:

1. The animals were comfortable in the cold chamber and their nutrition seemed to be favourably influenced.

2. The incubation period of *T. brucei* was delayed in the cold chamber and one after inoculation did not develop the disease.

3. The incubation period of *T. lewisi* was delayed in the cold.

4. Negative results were obtained in pneumonia, tetanus and cancer in mice.

5. The lives of Nagana and Caderas cases were prolonged slightly.

6. After inoculation of tubercle bacilli the abscess at the site of inoculation developed more slowly—that is, a month later in guinea-pigs treated in cold.

AUTHOR'S EXPERIMENTS.

In April, 1910, at the suggestion of Major R. Ross, a more accurate method for investigation of the number of parasites in the peripheral blood was begun. This was the thick film method elaborated by him and Mr. David Thomson in their study of a case of sleeping sickness (1910). By this means it is possible to detect parasites quickly when there are few in the blood, and it is possible also to count the parasites per cubic centimetre of peripheral blood.

Counts were made of the parasites at regular intervals of twenty-four hours; and as this was a laborious process and other parallel experiments were being carried out at the same time with drugs, etc., the number of animals was necessarily few. Hence the conclusions are drawn from few animals; but when we add these observations to those conducted by Major Williams we find that the results obtained by him are confirmed. I give as shortly as possible the results obtained since April 13th, 1910. In all these experiments regular counts were made every twenty-four hours.

Chart 1.—Graphs of the number of parasites per c.mm. of peripheral blood of guinea-pigs 1 and 2. Continuous line=guinea pig 1 (animal house). Dotted line=guinea-pig 2 (cold chamber).

Table of Guinea-pigs Inoculated with Trypanosomes.

Infection.	Number of Animals.	Treated in Animal House.	Treated in Cold Chamber.
<i>T. gambiense</i> ...	7	4	3
<i>T. rhodesiense</i> ...	2	1	1

Average incubation in animal house ...	4 days.
" " in cold chamber ...	13.5 "
Duration of life in animal house ...	64.2 "
" " in cold chamber ...	97.25 "

Table of Rats Inoculated with Trypanosomes.

Infection.	Number of Animals.	Animal House.	Cold Chamber.
<i>T. gambiense</i> ...	5	3	2
<i>T. rhodesiense</i> ...	3	2	1

Average incubation in animal house ...	4.8 days.
" " in cold chamber ...	6.3 "
" life in animal house ...	14.2 "
" " in cold chamber ...	16.3 "

The results obtained with *T. rhodesiense* and *T. gambiense* are, therefore, in favour of treatment in a cold dry atmosphere. The animals did not develop the disease so quickly and they lived longer. There is another point of interest brought out, and that is the influence of cold upon the numbers of parasites actually circulating in the peripheral blood. Here the general rule is that the parasites are fewer at the beginning of infection when an animal is treated in the cold—that is, if we examine the graphs of the numbers of parasites in blood of two guinea-pigs of practically the same weight inoculated with *T. rhodesiense*, and in both of which the numbers of trypanosomes injected were the same, we find the following (see charts):

Guinea-pig 1 (animal house), 364 grams in weight, had an average number of 7,976 trypanosomes per c.mm. of blood per day during the first four weeks of infection.

Guinea-pig 2 (cold chamber), 350 grams in weight, had an average number of 4,272 trypanosomes per c.mm. of blood per day during the first four weeks of infection.

Chart 2.—Graphs of numbers of parasites per c.mm. of peripheral blood of rats 1 and 2. Continuous line=rat 1 (animal house). Dotted line=rat 2 (cold chamber).

Again, the same point is illustrated by the graphs of two rats of the same weight—namely, 113 grams—both inoculated with *T. gambiense*.

Rat 1 (animal house), had an average number of 54,171 trypanosomes per c.mm. of blood per day during the first ten days of infection.

Rat 2 (cold chamber), had an average number of 14,728 trypanosomes per c.mm. per day during the first ten days of infection.

We must admit, however, the existence of cases which did not seem to react to the cold, and in which the parasites quickly developed, in spite of treatment; but the conclusion to be drawn from all our animals is that the parasites tend to be fewer in the cold if the animal is not subjected to exposure. This we would explain by the fact that the body resistance of the animal is raised.

I would also point out that the charts refer to two selected cases, chosen because the animals were much the same in weight. We must be guarded in drawing hasty conclusions till further work has been done and until the question of individual resistance of the animal hosts (apart from treatment) has been further considered. These charts show distinctly lower numbers of parasites in those treated in the cold chamber.

We found that in rats the incubation period of *T. brucei* was delayed in the cold, but the parasites develop very rapidly afterwards, and the animals are quickly killed (in about six days). In guinea-pigs we found that the incubation period was three days in both the cold and the animal house, but the animal kept in the cold developed the trypanosomes much more slowly. In four rats inoculated with *Sp. duttoni* we found that the parasites were less numerous in the peripheral blood of those in the cold chamber.

SUMMARY.

1. We must distinguish carefully between cold and exposure, only the former being likely to be beneficial.
2. Animals in the cold chamber were livelier than those in the animal house, and the fact that the majority of these gained weight shows a favourable influence on nutrition.
3. Experiments in rats and guinea-pigs inoculated with *T. gambiense* and *T. rhodesiense* show:
 - (a) Delayed incubation in the cold.
 - (b) Prolongation of life in the cold.
 - (c) Tendency for fewer parasites to occur in the peripheral blood of animals kept in the cold.
4. Incubation period of *T. lewisi* and *T. brucei* delayed in the cold.
5. Prolongation of life of animals infected with Caderas and Nagana.
6. It was noted in two guinea-pigs after inoculation with tubercle that the superficial abscess which formed at the site of inoculation developed much more slowly in the cold (a month later).
7. In rats infected with *Spirochaeta duttoni* the numbers of parasites circulating in the peripheral blood were fewer in the animals treated in the cold chamber, and this was also observed in guinea-pigs infected with *T. brucei*.
8. The patient, W. A., said he felt better after his sojourn in the cold chamber.

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UNDER the will of the late Mr. William Taylor of Eastbourne, the Consumption Hospital, the Cancer Hospital, the Royal Hospital for Incurables, Putney; the Royal Free Hospital, London; the Royal Infirmary, Liverpool, and the Home for Confirmed Invalids each receive (subject to the life interest of the testator's wife) a sum of £2,000, half that sum going to the Samaritan Free Hospital for Women.

AN ANALYSIS OF THREE HUNDRED AND TWENTY-SIX CASES OF ASIATIC CHOLERA.

By HENRY STEVENS, M.R.C.S., L.R.C.P.,

FUNCHAL, MADEIRA.

I AM indebted to my friend Dr. Lomelino for the following statistics. He was medical officer in charge of the Funchal Isolation Hospital during the recent cholera epidemic, and I had an opportunity of watching his devoted work during that period.

From the time that he took over the charge of the isolation hospital until the end of the epidemic he had under his care 326 cases of cholera, of which 120 ended fatally.

Deaths.

- 3 died of syncope during convalescence, but had previous history of morbus cordis.
 - 2 died of meningitis.
 - 1 died of bronchopneumonia.
 - 1 died of thrombosis and pulmonary embolism.
 - 2 died of uraemic coma following upon suppression of urine.
 - 2 arrived dead.
 - 5 arrived moribund and died within two hours.
- The remainder died of collapse while under treatment.

Of the 326 cases, in roughly 75 per cent. there was an acute onset; in many it was fulminating. In the remaining 25 per cent. the onset was gradual. The duration of symptoms in those who recovered was three to ten days. In only 5 per cent. of the cases were cramps in the legs and abdomen absent. After acute symptoms had passed off some 3 per cent. of the patients went into a condition resembling typhoid, with tympanites, slight secondary diarrhoea, headache, and temperature above 101° for more than a week. Some of these gave Widal's reaction in the stronger dilutions, but they all recovered within a fortnight.

About 10 per cent. of the patients were chronic alcoholics, and this class of the community seemed especially prone to take the disease.

Of the female patients fully 10 per cent. were lactating, which seems a high percentage. There were also 5 pregnant women among the patients. Of these, 4 aborted, 2 between the second and third month and 2 between the sixth and seventh month; 2 died, but without any perperal complications.

Among the 326 patients there were 30 babies under 3 years of age and 42 persons over 60.

Complications.

Among the 326 cases there were:

	Cases.
Anuria of more than three days	15 (only 2 died)
Urticaria	12
Intestinal haemorrhage	9
Parotitis	5
Thrombosis and embolism	1 (fatal)
Temperature of over 101° for more than first week of convalescence	8
Ophthalmic complications:	
Conjunctivitis	about 30
Keratitis	10 (some ulcerative)
Iritis	2

Carriers and Contacts.

The epidemic, comprising about 1,700 cases for the whole island, has been disseminated entirely by food and actual contact, and not by means of water supply. It has only been stamped out by rigid isolation or segregation of all "contacts."

Systematic examination of the faeces was carried out in the case of all convalescents, all inmates of the "contacts" segregation block, and all hospital employees. Of the 206 convalescents, 20 carried the vibrio in the faeces for more than a fortnight after the disappearance of all active symptoms. Out of about 350 inmates of the "contacts" block, only 6 actually developed the disease, but many who never showed symptoms were found to carry the vibrio in their faeces for more than three weeks after being in contact with a patient.