

nearly two degrees, or 7200 seconds, and that we have just seen by the illustration of the D lines that lines 3 inches apart can be thus divided, we may see for ourselves that, at any rate, over 2000 lines, if they exist, can be mapped. But these lines do exist, the whole of this new region being apparently as intimately filled by them as the visible spectrum by the Fraunhofer lines. In further evidence of this, here is a portion of the lower spectrum in the comparatively unknown part extending from $\lambda = 1.4\mu$ to $\lambda = 2.2\mu$ including the great band Ω shown as a single inflection in my first communication to this Association, but here resolved into thirty or more subordinate lines (Fig. 3). This illustration includes a part of the new region discovered on Mount Whitney in 1881; and in the small portion here exhibited, you may see that about 200 lines are discriminated.

I am now trying to bring what may be called the first stage of the long labour, a portion of which is here described, to a close, this first stage consisting

the expense of the invisible, nor even on such a logarithmic one as that proposed by Lord Rayleigh, but on a conventional scale, which I will ask you to tolerate, as it is simply meant to show the actual extent and importance of the region covered here as compared with that known to Newton. In this illustration, with which I close my remarks, the mean dispersion throughout the invisible rock-salt spectrum, as far as 4μ , is taken as the standard, and both spectra are laid out on that common scale. On the left is the visible spectrum known to Newton; next this, is the region known through photography, now extending a little beyond the band, $\rho\sigma\tau$, which marks what at the time these researches were commenced, was considered by the then most distinguished investigator, in the infra-red, the end of the heat spectrum. Beyond, and on the right, is a part of the new regions of the spectrum developed by the bolometer, and of which charts may be shortly expected on the scale of which a specimen in detail has just been shown.

I cannot close this statement without expressing the

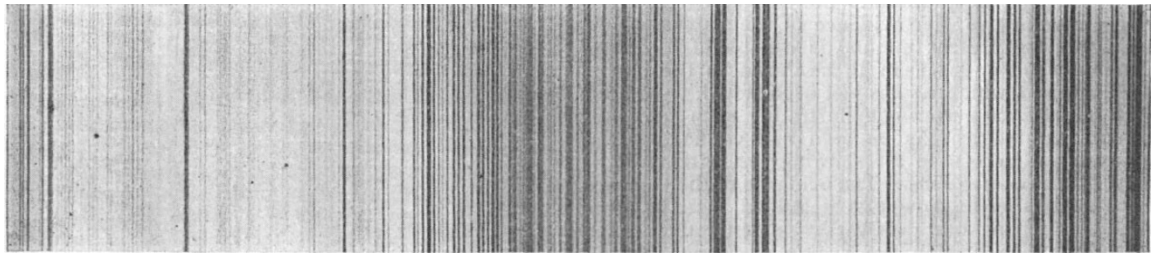
1.4 μ

FIG. 3.—Bolograph of the portion of the infra-red solar spectrum lying between wave-lengths 1.4μ and 2.2μ .

2.2 μ

chiefly in the discovery of, and mapping the relative positions of new spectral lines.

I will only refer to what it seems to me the second part of this work is likely to be, and to the different kind of interest which may not improbably belong to it, from that which belongs to this, the first.

We are thus far in the position of early students of the visible spectrum, who simply drew the lines they saw, without inquiring into their meaning. Nevertheless, to have discovered and mapped a great number of these lines is only a beginning, for their real value lies in their interpretation, and this is still chiefly to come. As to the possible importance of this interpretation, it is not enough to remind ourselves that three-quarters of the whole energy of the sun exists here, and not in the upper spectrum. We must remember also that while, as a rule, in the upper and visible spectrum a great proportion of the lines are caused by absorption in the solar atmosphere, and a perhaps smaller portion by telluric absorption, here, on the contrary, we are led, by everything we already know, to expect that the great telluric absorptions on which meteorological predictions and other immediately practical interests depend, may be expected to be found, and it is on the comparison of these energy curves taken at different periods of the year, and at different altitudes of the sun, that those who are engaged in the work see good cause to hope for important results in the future.

Before I conclude, let me present a collective view of the field in which work has been going on in these later years at the Smithsonian Observatory, on the same scale, with the visible spectrum. I say "on the same scale," meaning, not on a wave-length scale, which expands the invisible at the expense of the visible, and not on a prismatic scale alone, which expands the visible at

gratification with which I have laid it before the same body that listened to that made on the same subject twelve years ago, or my sense of my good fortune, in doing so before an audience in which I recognise many of the same eminent men who so kindly received that first presentation of these researches.

THE TREATMENT OF DIPHTHERIA BY ANTI-TOXIC SERUM.

FOUR years ago Prof. Behring published his remarkable paper "On the mechanism of immunity against experimental diphtheria in animals." In this memoir the author stated that it was possible to immunise animals against the diphtheria bacillus by the injection of culture attenuated by heat or the addition of 1 in 500 trichloride of iodine to the cultivating medium. The same result could be obtained by the inoculation of the pleura exudation of animals dead of experimental diphtheria or by the injection of chemical compounds, such a trichloride of iodine, after inoculation of virulent diphtheria-bacilli.

Behring's most important discovery, however, was that the serum of animals immune against the bacillus of diphtheria and its poisons had the power of "destroying" in vitro and in the animal body the chemical poison secreted by this bacillus; and that animals, after a mortal dose of diphtheria poison had been injected, could be not only immunised, but actually cured, by the introduction into their system of the serum of animals immunised against the specific bacillus and its poisons. In a further series of researches he found that the serum of such animals possessed this power to a most remarkable ar

almost incredible degree, and that the therapeutic value of this serum increased up to a certain extent with the amount of diphtheria-toxine which had been introduced into the system; whilst, on the other hand, the same toxine injected in too large quantities might cause the serum to lose its "anti-toxic" property.

Behring afterwards immunised large animals, such as sheep, horses, &c., against diphtheria by the repeated injection of diphtheria-toxine, and he observed that their serum was of great value when injected into human beings suffering from this disease. Before proceeding, however, it may be convenient to discuss these statements at somewhat greater length, and illustrate them by an account of a few experiments.

Let us draw some blood from a horse which has been thoroughly immunised against diphtheria, and decant the serum after its separation. We now take a filtered diphtheria culture, a given quantity of which we know to prove fatal to a guinea-pig of a certain weight in a certain number of hours. Let us divide, for instance, 5 c.c. of this filtered culture into five doses, and inject 1 c.c. into a guinea-pig (A) weighing 500 grammes without the addition of any serum. Four other guinea-pigs of the same weight as the first receive the same amount of toxine and 1 c.c., 0.1 c.c., 0.01 c.c., 0.001 c.c. of the horse's serum respectively. The first guinea-pig (A) will die in less than twenty-four hours, but of the others, the three first will recover without any symptom of illness; whilst the last, which has received 0.001 c.c. only, will probably die after some delay. We know, then, that the dose of serum which will protect a guinea-pig of a given weight against a known amount of toxine injected at the same time as the serum, lies somewhere between 0.01 c.c. and 0.001 c.c., and, by further experiments, the exact dose may be accurately determined. In this way we may form an idea of the strength of the serum, but we must always remember that the data thus obtained are but approximate ones.

The curative serum may be introduced into the animal the day before the toxine is injected, but, in that case, a much larger quantity of serum will be necessary to protect the animal. If the serum be inoculated at the same time as the toxine, and in a different part of the body, the quantity of serum must also be increased if the curative effects are to be apparent. If some time is allowed to elapse between the injection of the toxine and that of the curative serum, the quantity of serum—in order to be effective—must be proportionately greater; but I have seen animals recover when the injection of the curative serum had been delayed *eleven hours* after the introduction of the toxine, which proved fatal to the control animals in 28–48 hours. In this latter case the dose necessary to cure was 5000 times that sufficient to immunise when the serum was injected with the toxine.

Can any opinion be formed as to the mechanism in which this serum exerts its action? The first explanation which suggests itself is that when the curative serum and the toxine are mixed together in the syringe or in the animal's body, the toxine is either destroyed or simply neutralised, just as the acid in a given solution may be neutralised by an alkali.

Yet there are several facts which negative this opinion, or rather which tend to prove that this destruction and neutralisation of the toxine, if destruction or neutralisation there be, is effected through the agency of the cells of the body. In the first place, if the whole were simply a chemical process, we should expect it to take place with mathematical precision. Thus, if 0.001 c.c. of horse's serum did destroy or neutralise 1 c.c. of toxine, this neutralisation should be apparent whether the mixture be injected into a guinea pig, a rabbit, or a sparrow. But it is not so; on the contrary, it has been found that in certain animals a very small amount of curative serum is sufficient to render harmless a certain amount of toxine

when the same amount of serum utterly fails to do so in animals of another species. Even if the same species of animals be used the curative effect will differ in intensity, according to whether the mixture be injected directly into the blood, or into the subcutaneous tissue. Moreover, if a number of guinea-pigs be injected each with the same amount of toxine and varying doses of curative serum, it is of frequent occurrence that some animals will resist when they have received but a very small quantity of serum; while others, which have received equal or even larger quantities of serum, speedily perish. Had we to deal with a simple chemical neutralisation or destruction of poison, identical results should occur in all animals. The action of the curative serum may also be inhibited by weakening the cells of the animal body by the action of bacterial or other protoplasmic poisons. Hence I consider that the term "anti-toxic," which has been used up to the present to denote this property of the serum, is only approximately correct; and I would prefer to substitute the word "curative," until such time as the mode of action of the serum has been accurately determined.

Before speaking of the application of this method to the cure of diphtheria in the human subject, and to the results which have been obtained in the hands of such experimenters as Behring, Roux, Ehrlich, Kossel, Wassermann, Heubner and others, it must be pointed out how the disease in man differs from and resembles that produced experimentally in animals by the subcutaneous inoculation of the bacillus diphtheriæ, or of its poisons. In both man and animals the symptoms are, to some extent, produced (Roux, Behring, Sidney Martin) by the absorption of the poisons secreted by this specific bacillus. But in man the production of these poisons is facilitated by the fact that the bacillus lives on the surface of the membrane, where it is exposed continually to the action of the air entering and leaving the lungs. Now, it has been shown experimentally that the easiest way of obtaining a large amount of diphtheria toxine from the diphtheria bacillus growing in an artificial medium, is to expose the surface of this medium to a current of air. In the respiratory passages of man these conditions are exactly fulfilled, and the bacillus is able to produce large quantities of toxine. In the second place, the upper respiratory passages are crowded with all sorts of non-pathogenic and some pathogenic micro-organisms, the chief among the latter being the staphylococcus albus and aureus, and the various kinds of streptococci. These multiply on the soil prepared by the bacillus diphtheriæ, and secrete their toxine, which being absorbed, add their poisoning action to the deleterious action of the specific bacillus. In the preceding paragraph, I have drawn attention to the fact that the toxines of another micro-organism will inhibit the action of the curative serum; and there can be little doubt that the toxines secreted by these micro-organisms in man will have the same effects. The formation of the membrane also, and the mechanical obstruction so produced, may in themselves be the cause of death. It must be added, also, that diphtheria is chiefly a disease of the poor, and that in many cases the diagnosis is delayed, and the treatment is not begun until the patient is almost moribund. It is plain, therefore, that in the diphtheria of man we have all the conditions which are favourable to the production of the poison, and the inhibition of the action of the therapeutic serum. Hence we cannot be astonished that the death-rate at the Hôpital Trousseau in Paris amounted during the last six months to 62 per cent. of all cases admitted for this disease, and not treated with curative serum.

An examination of the statistics lately published by Dr. Roux, the eminent director of the Institut Pasteur, will allow us to form some idea of the value of the curative serum when applied to man. The reason for choosing these statistics is that they contain all the

elements necessary to enable us to form an accurate opinion. The mortality among 3971 children admitted during 1890-1894, and who were treated on ordinary lines, *i.e.* without curative serum, amounted to 51 per cent., the highest mortality being in 1890, when it reached 59 per cent., and the lowest in 1892, when it fell to 47 per cent. On February 1, 1894, Dr. Roux began the inoculations. As soon as a child suffering from diphtheria was admitted into the Hôpital des Enfants Malades, it received 20 c.c. of serum subcutaneously, and if no improvement took place, 10 c.c. or more were again injected next day. 448 children were thus treated from February 1 to July 24, 1894, and 109 died, the mortality being 24.5 per cent. At the Hôpital Trousseau, on the other hand, 520 children were admitted during that period, and treated without the injection of curative serum. Of these 316 died, giving a mortality of 60 per cent. This difference is striking enough; but it is even more marked when we come to analyse the results. In the first place, we must eliminate from Dr. Roux's statistics 128 cases which were shown by bacteriological examination not to be diphtheria. This mistake is perfectly legitimate, as it has been shown that without a bacteriological examination, it is impossible to make an accurate diagnosis. The injection of the serum in a doubtful case is followed by no harm, and as the result of the bacteriological examination cannot be known for twenty-four hours, the injection of the serum will, at any rate, prevent the child catching the disease from his neighbour. The mortality among such cases we know to be very slight, and in the statistics of previous years, as well as in those of the Hôpital Trousseau, these cases are included among the cures, so that the proportion of cures appears to be much higher than it really is. These cases being excluded from Dr. Roux's statistics, there remain 320 children in which the bacteriological examination revealed the presence of the diphtheria-bacillus. Of these 20 died on admission, before any therapeutic measures whatever could be employed. Of the 300 other children 78 died, giving a mortality of 26 per cent. We may further divide these into uncomplicated cases, and those in which tracheotomy had to be performed for laryngeal obstruction. Of the uncomplicated cases, the mortality in Dr. Roux's wards amounted to 12 per cent.; whilst at the Hôpital Trousseau, where no serum was used, the mortality during the same period reached 32 per cent. In the preceding years it was 33 per cent. in the wards in which Dr. Roux carried out his experiments.

Turning now to the cases in which tracheotomy had to be performed, we find that 49 per cent. of Dr. Roux's cases died. At the Hôpital Trousseau in the same period 86 per cent. of the tracheotomised children perished. Similar results have been obtained in Germany, the mortality in some wards falling as low as 14 per cent. Prof. Ehrlich has shown that the question of time is a most important element, and that the chances of obtaining a cure are infinitely greater when the remedy is applied at an early stage of the disease. The following table, reprinted from the *Deutsche Medicinische Wochenschrift*, will explain this:

Time elapsed from onset of disease to injection of serum.	Number of cases.	Number of cures.	Number of deaths.	Cures, per cent.
1	6	6	0	100
2	66	64	2	97
3	29	25	4	86
4	39	30	9	77
5	23	13	10	56.5

It will be noticed that the number of cures diminishes according to the length of time which has elapsed since the onset of the disease.

It appears to me to be difficult to explain away the results obtained in France and Germany by simply saying that the epidemic has been a mild one; for in other hospitals and institutions in which the curative serum has not been used, the mortality has remained the same, or even increased. In fact, it is plain that the serum treatment of diphtheria is now established on a firm basis, and that it is only right that we should at once give the children in this country the benefit of the results of experimental investigation which has been principally carried on abroad. The British Institute of Preventive Medicine is now taking steps to provide the serum at cost price.

Finally, it is right to draw attention to the fact that although the knowledge of the biology of the diphtheria bacillus, and of the effects of its poison, has been based on the investigations of different observers—French, German, and English—yet the discovery of the curative effect of the serum of immunised animals is the merit of one man only—Prof. Behring, of Berlin.

M. A. RUFFER.

NOTES.

THE Paris Academy of Moral and Political Sciences has bestowed the Audiffret prize of twelve thousand francs upon Dr. Roux for his treatment of diphtheria.

A STATUE of Claude Bernard, the eminent physiologist, was unveiled at Lyons on Sunday last, in the presence of a distinguished company.

THE *National Zeitung* states that news has reached Berlin from the Kilima-Njaro district that the German botanist, Dr. Lent, and the zoologist, Dr. Kretzschmar, have been killed, with several of their black followers.

DALZIEL'S correspondent at New York says that a dispatch received from Buenos Ayres gives particulars of a severe earthquake, attended by great loss of life, which occurred on Saturday, October 27, at the town of San Juan de la Frontera, the capital of the Province of San Juan, in the Argentine Republic. Many of the principal buildings are said to have been destroyed. The shock extended to the towns of La Paz, Cordova, and Rosario. The *New York Herald* of Monday published a telegram from Buenos Ayres stating that two thousand persons have perished in the earthquake at La Rioja, and that twenty thousand are homeless. This alarming report has not, however, been confirmed.

NUMEROUS memoirs have already been based upon the rich collection of Dutch birds brought together by the late Mr. J. P. van Vickevoort Crommelin, of Harlem, and presented, after his death, by his daughter to the Leyden Museum. Ornithologists will therefore welcome the appearance of a complete catalogue of the collection, which has been compiled by Dr. Jentink, the director of the museum, and forms the fourteenth volume of the catalogues of the Muséum d'histoire naturelle des Pays-bas. Nearly three hundred species are in all enumerated, and the majority of these are represented each by a considerable number of specimens. A separate record is given of every individual, notifying the sex and age, the place and date of capture. An explanation which Dr. Jentink furnishes of the exact locality of all the places mentioned should be of material service to the student of the geographical distribution of these birds.