I.K. THERAPY in PULMONARY TUBERCULOSIS

by

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PREFACE.

Among the more recent substances used in the treatment of pulmonary tuberculosis and which are especially antagonistic to the tubercle bacillus and its products, is the preparation of Spengler, Immunkërper, Immune Substances, or shortly I.K.

The literature regarding this product is extremely scanty, and to this dearth seems to be due much of the apathy regarding I.X. manifested by medical men who are called on to treat pulmonary tuberculosis.

There seems to be a fear of the preparation and a strong unscientific bias against it. All discussion centres round tuberculin and many are inclined to sneer at I.K. and relegate it to the therapeutic rubbishheap without giving it a trial fair or unfair.

Considering the value I have found I.K. to yield, I have made it the purport of this work to may open whatever good results have been obtained and incidently to show mistakes, in the hope that through error further good may be realised. It must not be inferred that I place absolute reliance on I.K. In my work I use tuberculin almost as extensively as I.K. and in the treatment of pulmonary tuberculosis I am confident tuberculin will keep its fair share of credit. Tuberculin however has italimitations, and as I.K., properly and scientifically used, has achieved results not unworthy of note, it merits a genuine consideration and a just criticism.

It seems fitting here to call attention to two books on I.K. therapy, and to urge the importance of their perusal, in order to comprehend the theoretical and laboratory sides of the subject. These books are The Treatment of Tuberculosis by means of Immune Substances (I.K.) Therapy, by Walter H. Fearis, (London, John Murray, 1912) and I.K. Therapy with special reference to Tuberculosis, by W. E. M. Armstrong, M.A., M.D., (London, H. K. Lewis, 1914.) To these authors I am greatly inaebted for many valuable hints, and in my preliminary remarks on the preparation of I.K. and on certain nonclinical points, I have drawn extensively from both books, for the obvious reason that the practical consideration of such an aspect of I.K. has been entirely with-held from me. In this book I have tried to approach the study of I.K. purely on clinical grounds with a result which I must leave the reader to estimate.

In conclusion, my best thanks are due to Dr Edward E. Prest, who first of all directed me to this particular method of treatment and under whose supervision my initial attemps at I.K. Therapy were made.

I.K. THERAPY IN PULMONARY TUBERCULOSIS.

WHAT IS I.K?

In 1907, Dr. Carl Spengler of Davos discovered that tuberculosis immune substances were manufactured and stored in the erythrocytes and that relative to the serum they contained as much as me 1,000,000 to 1 of these substances. This discovery has been confirmed by Fuch_-Wolfring's investigations on more than 3,000 bloods, and similar results have been obtained by Fearis and others. Following on this observation, Spengler injects rabbits intramuscularly with living bacteria, inducing a very high degree of bacteriolytic anti-toxic immunity against tubercle bacilli and bacteria frequently associated with them, and which are said to be responsible for the condition called secondary infection. The blood of these rabbits is collected aseptically, diluted, acidified with lactic acid, and the bactericidal and antitoxic qualities adjusted. This product is termed I K. Original Immune-körper or Immune Substances.

ACTION OF I.K.

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One c.c. of I.K. Original contains 1,000,000 lytic-antitoxic units which act in the following The lysins destroy the bacteria causing manner. tuberculosis, and the toxins liberated as a result of this lysis, become neutralised by the antitoxins. In this way a passive immunity is obtained by the introduction of immune substances prepared cutside the individual. Resulting from such a passive immunization, the cells of the patient are protected from poisoning by bacterial toxins. Accordingly they are able, in response to autoinoculation of the neutralized toxins, to generate further immune substances, and thus an active immunity is obtained without any toxic effect. In addition, there is the possibility of a further active immunity being generated by the lysinized bacteria and tubercle bacilli acting as vaccines. It will be observed that I.K. itself contains no active immunising agents, but that such agents are formed autogenously. The primary action of I.K. is therefore to produce passive immunity whilst its secondary action is the production of active immunity.

METHOD OF DILUTION OF I.K.

In order to use I.K. in the treatment of pulmonary tuberculosis, it is essential to dilute the original preparation to proper standards of strength. The diluting fluid may be either a solution of sodium chloride or of carbol sodium chloride as follows.

R/

Sod. Chloride pur 0'5 Aqua Destill ad 100'0

or

Ŗ

Sod. Chloride pur 0'5 Acia Carbol pur 0'5 Aqua Destill ad 100'0

In both instances the resulting fluid must be filtered and sterilized. The latter preparation is by far the more satisfactory. Spengler urges the following precaution. The solution must not be alkalized, for the I.K. being a preparation from the slightly acid blood of immune animals might, if alkalized, have too strong a lytic effect and decompose if kept in stock. To make the dilutions in small quantities, a 1 cc record syringe graduated in 1/10ths may be used, or when larger quantities are required a 5 cc or 10 cc syringe. The procedure is the same as in making tuberculin ailutions. To begin with 0'1 cc of <u>I.K. Original</u> is mixed with 0'9 cc of the diluting fluid. This makes a solution of strength 1 in 10. Of this solution 0'1 cc is added to 0'9 cc of the diluting fluid, resulting in a solution of 1 in 100. And so on with the other strengths. In this manner **a** series of ailutions results as follows:-

| Dilution | I. | 1 in 10 |
|----------|-----------|-----------------------|
| 11 | II. | l in 100 |
| Ħ | III. | l in 1000 |
| 11 | IV. | l in 10,000 |
| Ħ , | v. | l in 100,000 |
| n | VI. | 1 in 1,000,000 |
| 1 | VII. | l in 10,000,000 |

The solutions should be kept in sterile glass stoppered bottles with fairly wide mouths - each bottle being labelled with the strength of solution it contains. It is wise to date each preparation, so that no error need arise through the use of an antiquated solution. Dilutions made up with all care and kept properly in a dark place when not in service, should last from 14 days to a month. It is with regard to the question of keeping the dilutions that the employment of the second-mentioned diluting fluid is recommended; there is no doubt that the carbolic acid prevents the appearance of a whitish flocculant fungus which is apt to grow when only saline solution is used and which must find its entrance while a dose is being extracted from the bottle.

METHOD OF ADMINISTRATION OF I.K.

There are two serviceable methods which cover all cases - injection subcutaneously and per os. Another method, that of inunction, is redundant and never need be used; and it is mentioned here only because of its possibility. There is no necessity to asscribe the technique of giving a hypodermic injection. The most convenient syringe is the 1 cc "record"divided into 1/10ths and 1/50ths; and as I.K. is acid in reaction, it is necessary to use platinumiriaium needles and not steel ones. These needles do not spoil by boiling, and it is possible to get them of such fineness, that the process of giving an injection will occasion the patient no pain whatever. Furthermore, by using fine needles the dirty necessity of covering the puncture is obviated a practice not uncommon among those who use large needles for handiness. The most convenient site for injection is the extensor surface of the upper arm. The usual precautions as to sterlizing the skin must be taken by using lysol or spirit scap followed by methylated spirit or, where the arms are clean, spirit alone. The injection must be made subcutaneously a fold of skin being raised up and the needle inserted in an oblique direction. In giving I.K. per os a larger needle through which to suck up the required

amount into the syringe is used, as the wider the bore of the needle, the less time is spent in the process. Once the desired quantity has been obtained and freed from air bubbles, a further amount of ailuting fluid is added sufficient to fill the syringe, and the total contents expelled into an ordinary teaspoon. The dose is then conveniently given to the patient and nothing is lost, as must happen if given from a glass vessel by drinking.

ABSORPTION OF I.K.

The rapidity with which I.K. is absorbed may be measured clinically by studying the time it takes to manifest its action for good or ill subjectively or objectively. Whereas it is not possible to record subjective evidence graphically, the same cannot be said regarding temperature data when a reaction takes place with untoward feelings as subjective evidence, or where there is a fall in a febrile temperature following an administration of I.K. Generally speaking the absorption of I.K. is extremely rapid - its effect being noticeable in about an hour. Variations in the rapidity of absorption are, however, met with in both the subcutaneous and oral routes of administration.

In the case of subcutaneous medication the time taken depends on the vascularity of the tissue into which the injection lands, whereas when given orally, factors depending on the stomach and its contents come into play. In the majority of cases however, there is no clinical distinction as regards rate of absorption to be found between the two routes of administration.

Judging from this and from the efficacy of I.K. administered in either way, it must be taken that I.K. is not dissociated in the stomach. Furthermore no irregular absorption of I.K. can be noted when given by the oral route.

GENERAL PRINCIPLES OF DOSAGE.

There are two methods of treatment by Spengler's I.K. the gradual, and the rapid method, each of which will require a separate description as to the principles concerned. The same principles of dosage apply to both the subcutaneous and oral routes of administration.

The Gradual Method.

This method of treatment aims at the somewhat gradual destruction of the bacteria and also the gradual attainment of an increasingly high degree of immunity. It consists in beginning with minimum doses in extreme ailution and slowly passing on to the higher concentrations. Treatment can be commenced in practically all cases with a dose of 0'15 cc, or 0'3 cc of ailution VI. In passing from one dose to a subsequent one, the method of doubling will be found to be the least troublesome and at the same time to be the optimum method as far as results go, pre-supposing a suitable straightgoing case. Starting with 0'15 cc, the scale of dosage would thus run as follows:- 0'15, 0'3, 0'6 of ailution VI. and continuing 0'12, 0'24 and so on of ailution V.

In practice however, in order to preserve a uniform scale, and as in no way does it mitigate treatment, one should proceed with 0'15 cc. instead of 0'12 cc of Dilution V. By doing so the scale now assumes a uniform character of 0'15, 0'3, 0'6, 0'15, 0'3, 0'6. Following such a scale, treatment may be continued until 0.6 cc of I.K. Original is reached, although in many cases it is not necessary to go so far.

As regards the interval between the consecutive doses, one week will be found the most satisfactory in the majority of instances. In some cases, however, doses may be given twice weekly with advantage, but the circumstances calling for such a departure will be considered elsewhere. The final cose (0'3 cc or 0'6 cc of I.K. Original) in the scale advised above should be repeated at ever increasing intervals if thoroughly tolerated, until the condition of the patient warrants one in believing that recovery has taken place, or if such a result has been obtained at the end of the scale, it may not be necessary to so repeat the dose.

The patient can then be left alone for a month's trial, or treatment may be broken off by giving a cose of a weak dilution such as 1 in 1000, and then left. This latter method of succeenly breaking the scale will be found very effective. In some cases where it is considered unwise to leave off treatment suddenly, the dosage may be tapered off by a descending series. Suppose 0'6 cc of I.K. Original has been given, the subsequent dose of 0'6 cc of Dilution I. can be administered followed by 0'6 cc of Dilution II., and so on at weekly or twice-weekly intervals until Dilution \forall I. or Dilution \forall II. is reached, when treatment can be stopped, or if necessary an ascending series commenced again. Such a procedure however is rarely required.

As regards the duration of treatment this must be continued as long as there is necessity, but generally in a case that has responded satisfactorily to weekly administrations of I.K., treatment lasts under six months. Mention has been made that at the end of the scale dosage the patient may be given a month's trial without any treatment whatever. At the completion of that time the condition of the patient should be noted and, if satisfactory, the probationary period can be further extended to two months; and so on. In the event of any untoward symptoms reasserting themselves treatment should be again undertaken by the same method or by the rapid method about to be described.

The Rapid Method.

This method aims at a more rapid attainment of immunization, and is carried out in the following manner: Commencing with a dose of Dilution VI. and allowing an interval of a week to elapse, a similar dose of Dilution V. is given. Thereafter follow access at weekly intervals, each of which is 10 times stronger than the one preceding.

Treatment by this method may be continued until I.K.

Original is reached. Generally however it is better, when one has reached the stronger dilutions such as III. or II. to adopt the gradual method owing to the tendency in most cases, for lytic reactions to occur. The significance of these reactions will be discussed later. It is sufficient at present to indicate the scales of dosage to be pursued in suitable cases and under the best of circumstances. The same methods for concluding treatment apply here as in the gradual method.

LYTIC REACTIONS.

This is a reaction characterized by an increase in the temperature, pulse, sputum, and cough, and is accompanied subjectively by symptoms of malaise, lassitude, sleeplessness, pain in the chest, etc., and objectively by a loss in weight. It is due to the too great destruction of oacteria by the bacteriolytic component of the I.K. used, giving rise to toxins far in excess of the antitoxins available in a given dose. The reaction comes on early, and is usually felt by the patient within twelve hours. Just as with the tuberculin reaction, it will be best described by considering it as a triple entity and paying attention to its manifestations: (1.) G<u>eneral;</u> (2.) Focal; (3.) Local.

The General Reaction.

The most characteristic element ig the rise of temperature. Just as in the tuberculin reaction, there are several varieties of the lytic reaction. In Charts I. and II. are shown prolonged reactions of a severe type characterized, in addition to the rise in temperature, by an increase in sputum and pulse, and a considerable loss in weight. Chart III. shows a sudden sharp reaction taking place rapidly, and, reaching its maximum, quickly passing off. In Chart IV. is an example of a wery severe continuous lytic reaction. Such reactions tend to be exceedingly prolonged, and if left untreated may extend over several weeks. Corresponding to these severer forms are lytic reactions of a milder nature which follow the same type of curve; and combining the qualities of the short and the prolonged reactions are all kinds of intermediate varieties.

Occasionally the lytic effect does not take place until the third or fourth day after the administration of the I.K. This is the delayed lytic reaction (Charts V. and VI.) and when of a mild nature it closely resembles a recrudescence of the disease (Chart XX.) owing to the effects of the dose having worked off. The differential diagnosis between such a delayed reaction and recrudescence will be considered in detail later, as it is of great importance in treatment.

In very rare instances the lytic effect is characterized by one or two secondary oscillations due in all likelihood to slight focal reactions echoing the primary reaction. Chart VII. shows such a condition.

Another lytic reaction demanding earnest attention owing to its particularly intractable nature, is the cumulative lytic reaction. This is due to giving the patient a dose the same, or about the same as one already given within or about a week. Chart VIII. shows a typical cumulative lysis of a very severe nature. It is an interesting point that cumulative lytic effects are mostly associated with access of the weaker dilutions such as 1 in 1,000,000 or 1 in 100,000. As one progresses with treatment, reaching stronger dilutions, it is found that cumulative lysis does not take place where ordinary precautions are observed. (Chart XII) although its occurrence has been noted. (Chart XIII.)

The Focal Reaction.

This takes place in the seat of or near the tuberculous lesion, and is manifested both subjectively and objectively. The subjective signs have already been enumerated, malaise, pains in the chest, etc. Objectively, the important manifestation is the increase in sputum with, it may be, the occurrence of blood in it. On examination of the chest an increase in physical signs is evident, just as in a tuberculin focal reaction. Owing to this attribute of I.K., that it is able to cause a focal reaction, it might be found of use in the diagnosis of latent tuberculous lesions although it does not appear wise to stir up activity intentionally by such a method.

The Local Reaction.

This reaction or swelling of the arm at the site of or surrounding the point of injection is not a very common event with I.K., and when it does take place it is often associated with other lytic phenomena.

SIGNIFICANCE OF LYTIC REACTIONS IN TREATMENT.

The occurrence of the severe forms of lytic reactions must be viewed with alarm. If the symptoms at not pass off within three or four days, a relieving dose should be given, that is a dose of a weak dilution such as VII. or VI.; or if the lysis has been due to a medium dilution, or has taken place with the 1 in 10 dilution or with the original I.K., by giving a dose of Dilution IV. or III. Following on the relieving dose the temperature usually falls, with noticeable improvement in the general condition. This is shown in Charts IV. and VI.

It is interesting to note here that it has been shown that the weak dilutions are to the higher relatively more potent in antitoxic qualities, so accounting for the antitoxic value of the relieving dose.

Following on the disappearance of all lytic symptoms, treatment should be again resumed on the gradually increasing system, commencing from the relieving dose as the initial one in the series. It is unwise to proceed by the rapid method after a lytic reaction of a severe nature, as by this system of dosage there is a great chance of having further reactions.

While no difficulty as to what to do presents

itself with the severe lytic reactions, there is always consideration required when a mild lysis occurs. Where a mild lytic reaction has had for result an increase in weight, improved appetite, and an amelioration of other symptoms, it is wise to go on by acubling the dose, careful regard being paid to the temperature, so that the following dose be given when the lytic effect has fully passed off. In this way no lysis in the cumulative sense can occur. Charts IX and X. are illustrative of the beneficial effects following a slight lytic reaction. Where, on the other hand, a slight lysis has obtained with no material benefit to the patient, it is better not to proceed in the usual manner by doubling the dose, as by this procedure a more severe lysis may take place. This error in treatment is shown in Chart XI. However satisfactory the results of a dose have been, it is unwise to give exactly the same dose at the usual interval in the expectation of similar results. This holds particularly with regard to the weaker dilutions in as much as cumulative lytic reactions of a very pronounced intractable type are apt to occur. When the stronger dilutions such as 1 in 100, 1 in 10, or Original I.K. have been reached, it may be beneficial to repeat the dose where a slight lytic effect has been produced; but this course should never be acopted where good results have been obtained without

lysis. (Chart XII.) Even where a slight lytic reaction has taken place with the stronger dilutions there is always some of a cumulative lysis setting in, on repeating the same dose. (Chart XIII.) In cases where treatment has been interrupted for a period of two or three weeks, there is no danger in giving the same dose as that last given.

In the foregoing, attention has been devoted entirely to the significance of the general and focal reactions in treatment, to the exclusion of the local reaction. The latter, however, although not so important, has a value of its own. This reaction is usually accompanied by other lytic phenomena under which circumstances it loses its individual significance. It happens however, that the local reaction may be the only sign of a lysis having taken place - and when this is so, the presence or absence of the local reaction becomes of moment. Its extent must be judged as in the general reaction, and treatment pursued accordingly. If the reaction is slight and of value like the mild lysis already described, it is best to go on increasing the dose in the usual way. If, on the other hand, the local reaction is severe, and even - as may happen - accompanied by general lytic phenomena, it is better to give a diminished dose or a relieving administration, or if considered safe, the same dose that called forth the reaction. Either of these measures should be adopted unless in well-known cases which have a tendency to react locally, as the occurrence of a local reaction in one not subject to such, very often heralds the approach of a general lysis. (Chart XIV.)

PSEUDO LYTIC REACTIONS.

AL:

In addition to the pure lytic reactions described above, there are certain temperature elevations, which although not due to I.K. administration, are apt to be mistaken for such. Such rises in the temperature curve are divisable into two kinds:

(1.) Those due to physiological causes.

(2.) Those due to pathological causes. Those due to physiological Causes.

It is very often observed that the premenstrual rise in temperature coincides with a dose of I.K. having been given. This is shown clearly in Charts XV. and XVI. Unless such a condition of matters is looked for it may be supposed, when next the patient comes for treatment, that a slight lytic reaction has taken place. Of much less frequency are two other menstrual temperature elevations, the one occurring during the menstrual period and the other immediately following. As these menstrual disturbances of temperature are often accompanied by tiredness and a slight loss in weight, it is very important, where one is dealing with female patients to be thoroughly conversant with the menstrual history of each, in order to avoid error.

Those Due To Pathological Causes.

Of pathological causes it is necessary to distinguish two kinds.

- (a) Those associated with the tubercular condition.
- (b) Those associated with other conditions.

Those Associated With The Tuberculous Condition.

The occurrence of autotoxic symptoms during I.K. administration must be carefully watched for, in order that one may not be led into the error of regarding the temperature elevation as being due to lysis. Such autotoxic conditions arise where the patient has indulged in too violent exercise, and even from such slight causes in many cases, as having had a bath, or a restless night. In dispensary practice where the patient may have some distance to travel in order to procure treatment, an autotoxic rise of temperature on the day following his visit may be very misleading, and it becomes necessary in gome cases to differentiate between rest and exercise pulse-temperature data in order to fully eliminate the possibility of a slight lysis. Charts XVII. and XVIII. show autotoxic rises of temperature taking place during the currency. of I.K. treatment.

Another pseudo lytic elevation of temperature

associated with the tuberculous condition is that due to recrudescence of the disease. When the temperature rises towards the third or fourth day after an administration of I.K., and is accompanied by a feeling of malaise, etc., the point arises as to whether this is a delayed lytic reaction (Chart VI.) or is due to toxic symptoms of the disease reasserting themselves owing to the effects of the dose having worked off. Clinical considerations alone are usually sufficient to establish an opinion one way or the other. The weight of the patient, pulse rate, history of the onset of subjective symptoms with reference to feelings of well-being, appetite, etc., give one a fairly good idea of the cause, and moreover if these attacks are of common occurrence, taking place regularly after each injection or administration per os, it is conclusive evidence that a further dose of I.K. is necessary, and that the untoward condition is aue to recrudescence of the disease. Chart XIX shows such a recrudescence temperature. The same condition is shown in Chart XX. In this instance after the tendency to recrudescence had been noted, doses were given twice weakly with the result that the temperature steadied.

For purposes of treatment the different diagnosis between the two conditions of delayed lysis and recrudescence is all important. In the case of delayed iysis a relieving dose is required, whereas in the event of recrudescence an increased dose is indicated.

Dr W. E. M. Armstrong points out that where tubercle bacdilli are present in the sputum a bacterioscopic test may be applied to differentiate between the two conditions. Stained by the Structural Method described in his book, <u>I.K. Therapy with special reference to</u> <u>Tuberculosis</u>, degenerated and mutilated bacilli will be found in the sputum if the temperature-rise, etc., is due to lysis, whereas if due to recrudescence, clearly stained and healthy young bacilli will be found.

Those Associated With Other Conditions.

Pseudo-lytic reactions due to other pathological conditions take place; but apart from being liable to give one a wrong idea of the tuberculous disease and its treatment, they are of little importance. Chart XXI. shows a rise of temperature following a dose of I.K. but which was due to an alveolar abcess. Similar rises are met with associated with sore throat, neuralgia, common colds, etc. Chart XXII. In order to differentiate these temperature rises from lytic reactions it is only necessary to interrogate the patient, when the condition will be recognised.

LOCAL REACTION.

The following causes may produce a swelling of the arm at the site of the injection. They are all due to faulty methods and need not occur:

- 1. The needle is blunt or too large.
- 2. The dose is too bulky.
- 3. Injection into skin.
- 4. Sepsis.



This is a rare condition, occurring most commonly in early female cases. The condition manifests itself following the first administration, usually subcutaneous, of a uose of an extreme gilution. The patient feels ill, the temperature rising very rapidly just as in the short severe lytic reaction which it resembles in every way. (Chart XXIII.) No treatment apart from rest is required. In cases showing hypersensitiveness, it is unwise to continue it on the same lines that called forth the reaction. For example, if the reaction follows an injection, the exhibition of I.K. should be stopped for about fourteen days, when treatment may be resumed by the oral route. This procedure overcomes all hypersentiveness, and should the condition of the patient demand it later, treatment can be continued subcutaneously. To neglect a hypersentiveness temperature elevation and go on treating by gradually increasing the dosage is disastrous. Typical lytic reactions follow, manifested locally by swelling of the arm, generally by malaise and increased temperature. and often focally by haemoptysis, etc. (Chart XXIV.) It would thus appear that the hypersensitive reaction is essentially a lytic reaction taking place at the very inception of treatment by I.K.

OBSERVATION OF CASES FOR I.K. TREATMENT.

Priot to underatking treatment of any kind, it is essential to have a complete mental view of the condition of the patient, and for this reason it becomes necessary to make a thorough examination.

In dealing especially with a disease like pulmonary tuberculosis, where significant factors may be found scattered through a series of preceding years, the examinamust tion not only referre to the present illness, but should embrace data regarding previous health, family history, and all that comes under the heading environment, Little need be said concerning this aspect of the examination, as in no wise does it particularly affect treatment by means of I.K. as opposed to any other method. The importance however of an exhaustive study of the previous health should always be borne in mind.

Attention to such an aspect of the examination will be well repaid by the knowledge derived concerning the duration of the tuberculous process, juaged from the history of significant illnesses such as pleurisy or influenza - the latter often being, if recurrent, a tuberculous autoinfoculation. Of more immediate importance, however, are the symptoms of the present illness.

This aspect of the routine examination is belittled

too much, considering the amount of valuable information it yields as to the activity of the disease. After all, it is the presence of symptoms that makes the patient seek advice; it is not simply because he has or has not some particular kind of pathological specimen in his chest. The following symptoms are those to which attention must be given :- Cough; Sputum; Haemoptysis; Night sweats; Pain in the chest; Shortness of breath; Alteration in weight; Loss of appetite; Indigestion and debility. In order to fully appreciate the meaning of these symptoms it is essential to know the date of the onset of each. These symptoms, or a combination of a number of them, form the actual disease from the standpoint of the patient, and as the first signs of success in I.K. therapy are subjective, it is wise for the physician to make particular note of them.

The next part of the routine examination is objective, and comprises the recording of any important data connected with the various systems of the body:-Respiratory; Alimentary; Circulatory; Genito-Urinary; etc. The data of greatest importance for treatment purposes under this section of the examination are the Temperature (rectal); Pulse rate; Body weight; Amount of sputum; and of course the facts elicited by a thorough and exhaustive examination of the chest. More need not be said concerning these data, as they are of importance in all forms of well-regulated specific treatment, and anything of particular interest connected with treatment by I.K. will be mentioned under a more appropriate heading.

SUITABILITY OR UNSUITABILITY OF CASES FOR I.K. TREATMENT.

Judging by physical signs, symptoms, and all the other data one employs for the summation of any particular patient, it is impossible to say definitely regarding any that patient whether or no I.K. treatment will prove of benefit. This may be said also regarding tuberculin, although with both tuberculin and I.K. there is in the mind of the experienced worker some instinct that leads him to the selection of a particular method of treatment. It is not instinct in the ordinary acceptation of the word. It is primarily the outcome of an indefinite observation of events in the past - a sub-conscious observation - which leads ultimately to observation of a definitely conscious nature.

Putting aside this means, which can only be obtained by a sincerity in work occupying some time, there is a method which is scientifically accurate and which gives one a definite knowledge as to the suitability or winsuitability of the particular patient for I.K. treatment. This is the method of experiment. A dose of I.K. can be given to the patient, not as a test in the diagnostic sense in which tuberculin is used, but as a preliminary trial or test in the therapeutic aspect.

Such a test may reveal several things. It may show

that the patient is eminently unsuited for treatment owing to the condition of hypersensitiveness to I.K. For it is a reasonable attitude to take up that if the temperature rises to a febrile point and continues high for several days auring which the patient is definitely ill, then I.K. treatment should not be continued. (See Hypersensitiveness.) The initial trial dose on the other hand may show that the patient is eminently suited for treatment by I.K. Such a suitability would be shown for instance by a fall or a steadying in temperature accompanied by an amelioration in the subjective condition of the patient.

In other cases, as far as physician or patient can judge, the trial dose may have had no effect whatever. In such cases it is well to go on with the treatment until I.K. is found under the usual conditions of administration to be: (1) Beneficial; (2) Harmful; or (3) Inert. Before concluding that I.K. is inert Fearis(<u>The Treatment of Tuberculosis by means of Immune</u> <u>Substances (I.K.) Therapy.</u>) urges that the following methods of increasing the lytic effect should be tried.

1. Increasing the lytic effect of I.K. by diminution of the acidity of I.K.

2. Repetition of doses of the same strength, especially very weak doses of I.K.

3. The method of increasing lytic action mentioned by Benchr and Hoffman in which, after increasing the dose by ten-fold increases until the original is arrived at, one returns back in one step to a dose of the strength the same as that with which the treatment was commenced, after which the dose is increased a hundred to a thousandfold. (Chart XXX.)

Fortunately the cases requiring such measures are extremely rare. In the great majority of instances in which I.K. appears at first to be inert, it will be found that if administered on the rapid method by increasing coses ten-fold each time, some result will obtain. Should it be found essential, however, to try any of the methods given of increasing the lytic effect, these methods should be (2) or (3) as above. To decrease the acidity of I.K. involves one in difficulties with succeeding doses and therefore method (1) should be discarded. Repetition of doses method (2) has already been mentioned when dealing with the lytic reaction as being dangerous, especially where small doses are concerned, in that such a procedure is apt to provoke a cumulative lysis. For this reason the method of repeating doses of the same strength should be used as seldom as possible. Method (3) is by far the best. Moreover, the ease with which it is applicable to the rapid method of dosage advised enhances its value. Having increased the doses rapidly to I.K. original, the administration of a small dose of Dilution VI.

after the manner of a relieving dose, will be found of the greatest value especially subjectively (Chart XXX). This action is also very marked where a good result has obtained all along the ascending series, as has already been observed under general principles of dosage.

I.K. however, is not an absolute specific. It fails, as all measures must do through faulty administration, and in our present state of knowledge of I.K. there is much still unknown regarding it in both its theoretical and practical aspects. Putting aside such reasons for failure there still remain many others reasons to be found in the peculiarities of the patient's general condition. Patients with severe complicating illnesses such as extreme anaemia, profound debility, or who are suffering from bad cardiac disease, are better left untreated. Cases hopeless from anatomical considerations must be judged as individuals, owing to the fact that in many cases subjective amelioration may be obtained through skiltul administration of I.K. The same individual standards must also be employed when dealing with secondarily infected cases. Many hitherto regarded as beyond any help will be found to derive the greatest benefit. Indeed it is in this class of case that a practitioner experienced in I.K. therapy often locks for his most wonderful results.

CONTRA-INDICATIONS TO THE USE OF I.K.

Theoretically the use of I.K. is not contraindicated in any case. In practice however, patients are found in whom, as far as can be judged, I.K. produces no benefit, and even in some cases harm. In discussing the question of suitability or unsuitability of cases for I.K. treatment it was explained how selection could be made by experiment. In some cases however, such a procedure seems scarcely warrantable, cwing to the hopelessness of the disease ever being improved. Such cases are those manifesting cachexia of a marked nature accompanied by great rapidity of the pulse, and fever. Cases with accidental concomitants such as diabetes, cardiac disease, nervous disease, etc., must be judged individually, although the treatment of such cases is usually disappointing. Owing to the enormous importance of the erythrocyte system of the patient, cases showing proffound disease of this system such as leukaemia or pernicious anaemia, should be left alone. In the less severe anaemias, additional treatment directed to the blood condition should always be adopted. The incidence of pregnancy is not a contraindication, and treatment under such a condition will be discussed later. In addition to the contra-indications mentioned there are other circumstances of an external

nature which justify the with-holding, or the cessation, of treatment. Such circumstances arise when the patient wilfully interferes with the recording of his temperature, a crime against himself which is often committed when the physician is a keen advocate of Rest in bed.

CLASSIFICATION OF CASES IN I.K. TREATMENT.

For the purpose of I.K. therapy the arbitrary division of pulmonary tuberculosis cases into stages is of little value. This can be said especially of division on anatomical principles, although such a division has a meaning in conveying a mental impression of the type of the case. The same applies also to methods of division according to the evening temperature. When these two methods however are joined, and made even more widely embracing by taking cognisance of pulse cata, one arrives at a method of division whicn, while still defective as all arbitrary methods of division are, reaches as near as possible to the ideal.

There are several methods of division on anatomical lines which, despite slight variations in their stage definitions, result in the ultimate classification of cases into Stages I. II. III. It is presumable that taken on the whole such classification approximates a uniformity, for so much in physical diagnosis depends on the observer and his scheme of interpretation. Arbitrary divisions according to temperature are also inaccurate, but when classified by this means some idea of the toxic process and of the severity of the disease is obtained. Even by this method discrepancies arise, as for instance when an advanced dying case has no temperature elevation, or where the acute early case has. The following scheme adopted by Spengler is however a working scheme.

Afebrile temperatures; not exceeding 37 °C. or 98'6 °F.

Sub-febrile temperatures; over 37 °C. or 98'6 °F. and not above 38 °C. or 100'4 °F.

Febrile temperatures; over 38 °C. or 100'4 °F. While such methods of classification, or similar methods should always be employed for statistical reasons, it must be borne in mind that for treatment by I.K. the question in no way depends on the amount of pathological change present, or on the severity of the aisease, but on the suitability of the patient for I.K. treatment. This has already been indicated, and the method for determining such suitability or unsuitability of given.

ADMINISTRATION OF I.K. IN SPECIAL CASES.

Under General Principles of Dosage methods of administration of I.K. have been given, suitable for the great majority of cases of pulmonary tuberculosis. Generally speaking such cases are those with afebrile and sub-febrile temperatures.

The safer method to pursue is the gradual method of treatment. It is applicable to all manner of cases, and at any rate until sufficient experience in I.K. therapy is gained, should be the only method used. The interval between the doses and the slower or more rapid passing on to stronger concentrations are points which depend on how the patient responds to the treatment, and which have already been described in actail. (Charts XXV and XXVI.) The rapid immunization method being more dangerous on account of the tendency to provoke lytic reactions, should only be used in the afebrile and sub-febrile types manifesting no severe clinical symptoms. (Chart XXVII.) In cases where any doubt is entertained as to a lytic reaction setting in, the case should be transferred to the gradual method.

Under the same heading (General Principles of Dosage) different methods of giving the final doses have been dealt with. As examples of these methods, XX IX Charts XXVIII, XXX, XXXI, are added. Chart XXVIII shows the cessation of treatment in reaching I.K. Original. Charts XXIX and XXX indicate the sudden breaking of the ascending series by the administration of a dose of a weak ailution. Chart XXXI is an instance of tapering off treatment by giving a descending series. The lytic effect which is very often beneficial and to which attention was drawn by Benöhr and hoffman is shown in Chart XXX.

While the two foregoing methods cover the greater number of cases one meets with, exceptional cases arise which demand further study. Such special cases are the following:-

- 1. Early febrile cases.
- 2. More advanced febrile cases.
- 3. Cases with hectic fever.
- 4. Bronchitic cases.

5. Cases with inverted temperature.

It is in such cases that the administration of I.K. must be tempered in a special sense to the requirements of the individual. This regulated adaptation of dose and interval to each patient is difficult to describe; but with a general knowledge of the action of I.K. and a critical survey of the case under treatment, it is fairly easy in practice. The following remarks on such types will be found instructive as regards their treatment, always bearing in mind the

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applicability of any scheme to the individual concerned.

I.K. In Early Febrile Cases, (Stage I.)

The early febrile case is best treated by enforcing absolute rest in bed to limit autoinfoculation. With such treatment the temperature usually subsides to normal limits with marked improvement in the condition of the patient. The time required for such a result to take place is extremely variable, depending on the severity of the process and the manner in which the patient reacts to his own poison; and in some cases the temperature may remain elevated over a period of weeks, and show no signs of coming uown. In such cases the daily variation tends to approach nil - the temperature assuming a flat look. It is in such protracted cases that I.K. is of benefit. Treatment may be given on a slow or rapid method of immunization, twice weekly in the former and once weekly in the latter, and pushed, if found beneficial to the patient as shown by an improvement in subjective signs. By watching the effect carefully, and paying strict attention in case of a lytic reaction supervening, the temperature will be found to fall, often quite dramatically. This treatment may be carried out by putting the patient to bed, and also in cases where rest cannot be enforced as in dispensary practice. Chart XXXII. illustrates the condition in an ambulant case while Chart XXXIII. is that of a patient on absolute rest. It will be noticed that less time is taken when rest is enforced. When the dose required to cause the fall in temperature is reached a severe local reaction evidenced by swelling of the arm often takes place.

I.K. In More Advanced Febrile Cases. (Stages II. and III.)

Just as in early febrile cases, the ideal treatment for this class is absolute rest in bed. In dispensary work however, one meets cases where owing to conditions of housing, poverty, or necessity to work, it is impossible to get the patient to go to bed even where the urgency for such a proceeding is explained. Such cases are often oread-winners, men who are ardent workers and who have no wish to go on benefit. To try to enforce rest in bed by refusing to give dispensary treatment to such cases simply means that no treatment of any kind will be obtained. The patient will go on his own way.

Without deprecating rest, I.K. will be found of marked utility in cases of this nature. Administration should be subcutaneously, as hypersensitiveness is uncommon in this class of case, and if found beneficial, dosage should be pushed twice weekly by the gradual method until the requirements of the patient become known. In the treatment of this type of case I.K. must be regarded primarily as an antitoxic agent, its action in this capacity being often very pronounced. Accordingly, if the temperature shows a tendency to rise after a fall due to the antitoxic propertizies in a given dose of I.K. a further dose should be administered. In this way, by the continued exhibition of antitoxins the temperature will be found to subside, and then the case can be treated as an ordinary afebrile or sub-febrile case. (Charts XXXIV. and XXXV.

I.K. In Hectic Cases.

Cases showing Septic Fever with a great daily swing of about 4 °F. require very careful treatment. Such cases are often hypersensitive to I.K. administered subcutaneously, although it is better to commence treatment by this route in order to learn if such hypersentiveness exists. If the patient is found to react too strongly to subcutaneous treatment, administration of I.K. per cs should be resorted to. Treatment commenced with Dilution VII. on the gradual method, with intervals of a week or more, will usually be found satisfactory; the prolonged interval allowing the poisoned organism to utilize any advantage derived from the given dose. Particular attention must be paid however, to the temperature and the subjective symptoms of the patient, If the temperature is found to rise after a fall que to the administration of I.K., a further dose is indicated. By thus watching the effect of each dose, it will be aiscovered whether the administration should be made once or twice weekly, and also whether the gradual or the rapid method of immunization should be adopted. Theoretically it is desirable to push the dosage; but from considerations of the severity of the disease one has to be careful lest lytic reactions occur. It will be

seen from the above that it is particularly in this class of case that treatment must be adapted to the requirements of the individual. With careful administration it is in this type of case that the physician often meets with his most wonderfully dramatic results. Following on the inception of treatment in a case which is responding, there is usually a marked improvein both subjective and objective signs. The anticatarrhal effect of I.K. is particularly noticeable a reduction in sputum even to fifty per cent sometimes taking place. (Chart <u>XXXVI</u>.)

I.K. In Bronchitic Cases.

Cases are met with having certain characteristics which are indicative of other organisms being at work than the tubercle bacillus. These cases are definitely catarrhal, and clinically one would be justified in a diagnosis of bronchitis or bronchiectasis. The sputum is often abundant, and may average up to 8 ounces. per diem, and when examined microscopically in the ordinary way, selecting a piece and staining by the Ziehl-Neelson method - is usually negative. Symptomatically however, there are alarming symptoms such as night sweats or haemoptysis, in addition to a long history extending over years in which is recorded the absolute failure of all former methods of treatment. Moreover, in many cases where the patient is an adult with children an examination of these as contacts will often reveal the tuberculous nature of the parental disease typically exemplified in them. Temperature data in bronchitic types yield little information from a diagnostic standpoint, as such data are extremely variable. In some the daily curve follows a normal type, whereas in others the morning temperature is elevated one day and low another, the continuous temperature record being decidedly irregular.

I.K. can be administered on either the gradual or rapid method in such cases, regard being paid more particularly to subjective signs and sputum measurements than to the temperature, which in this class is not a good indicator of the success or otherwise of treatment. In the treatment of this type of case the anticatarrhal action of I.K. is very evident, showing the polyvalency of the preparation for organisms frequently associated with the tubercle bacillus.

Chart XXXVII. is illustrative.

I.K. In Cases With Inverted Temperature.

In rare instances cases are met with displaying a morning temperature making the highest daily register. Such cases are usually difficult to treat, and are very often disappointing from the prognostic point of view. This inverted temperature due to the disease process must not be confounded with the inverted temperature occurring in persons working during the night and sleeping during the day. In such cases the temperature assumes a normal characteristic on a return being made to opposite conditions of work and rest (Chart <u>XXXVIII</u>.)

In cases with pathologically-inverted temperature the administration of I.K. is of benefit. Treatment should be pushed rapidly; due regard being paid to the response evinced by the patient. In slight cases the rapid method of immunization should be used, whereas in severer types, the gradual method twice weekly will be found more advantageous. Strange as it may seem, the temperature usually begins to show ordinary characteristics after the occurrence of a slight lytic reaction. Accordingly, in treating cases with inverted temperature the production of a slight lysis should be aimed at. Subsequent treatment should be carried out on the principles already laid down. (Chart <u>XXXIX</u>.)

ADMINISTRATION OF I.K. IN CHILDREN.

For the administration of I.K. in children, little requires to be added to what has already been said concerning administration in adults. Even with the very youngest child found suitable, no difficulty need be experienced, as in such cases I.K. can be given per os. In older children the subcutaneous route may be employed. Generally it is better to proceed by the gradual method of immunization, giving the doses once weekly until a maxium is reached of from 0'3 of Dilution I. to 0'3 of I.K. Original, depending on the result obtained, and the age and condition of the child.

In children showing continuously high fever, but who are otherwise in good general condition, it is aavisable to push the administration as described under early febrile cases. In this way the toxaemia is reduced and finally entirely counteracted. In severe febrile cases where the child is very ill, slow procedure is required initially, access being limited to the lower dilutions V. VI. and VII. Following on a beneficial result, treatment can then be undertaken on the usual lines.

In the conditions of ill-health following on whoopingcough, broncho-pneumonia, etc., where catarrhal processes are left in the lungs as sequelas, marked results may be obtained by the careful administration of I.K. Oral administration by the gradual method is indicated in the acute forms, whereas in the more chronic varieties the subcutaneous route can usually be adopted and the dosage pushed by the gradual method twice weekly. As in the case of adult patients however, the response must be closely watched, and the treatment be suited to the requirements of the individual.

ADMINISTRATICN OF I.K. IN PREGNANCY.

The incidence of a normal pregnancy in no way interferes with the exhibition of I.K. as a therapeutic measure in pulmonary tuberculosis.

Treatment in such cases is usually highly appreciated, and in dispensary work it is much against a patient's will to desist from attending in spite of gradually increasing difficulties. Even in advanced Stage III cases, with abundant, positive sputum, marked results may be obtained. Chart <u>XL</u>. shows such a result.

As pregnant cases often manifest a monthly rise in the temperature curve corresponding to the menstrual rise of the non-pregnant condition, the physician must be careful not to confuse such elevations of temperature with the elevations due to a slight lytic reaction.

EVIDENCES OF SUCCESS OR FAILURE OF TREATMENT.

The first signs of improvement by treatment with I.K. are subjective, and it is a fairly common occurrence for a patient to say how much better he feels even after the first administration. These subjective signs of improvement vary in different patients. In one, a feeling of well-being may be experienced - not the well-being of vigorous health. but the well-being relative to a former state of depression in some form or another. And being a relative state, its intensity is measurable only by reference to the preceaing state. In others an improvement such as an increased appetite for food is felt, or a lessening in the "tightness in the chest." Generally speaking, there is no analytical power in the majority of patients one has to deal with, and in answer to a leading question "How are you to-day?" the reply, "I am much better," is indicative of an improvement in the chief symptom without reference to any other symptom which may or may not be more alarming from the medical standpoint.

The feelings of the patient however, form a substantial groundwork for a complete idea of the pathological condition as regards its activity, and any view exclusive of subjective signs must be erroneous and misleading, and in the treatment of a disease like pulmonary tuberculosis - a disease protracted and wearisome to the sufferer - it is the patient who is first able to discern the horizon of hope even although it be sometimes illusory.

Apart from these indefinite signs of improvement, signs which are not readily recorded accurately by the physician, there are other signs of a more material nature. Foremost among these are the temperature data which have already been considered with the routine administration of I.K. The next important observation is the amount of sputum. Liable as the expectoration is to large variations depending on external conditions of atmosphere, it does not, taken alone, form a very accurate method of estimating the efficacy of treatment; but considered along with other data, it is of very great value. For instance, taken in conjunction with an elevated temperature, headache, etc., it might inaicate a Lytic reaction which calls for care although one must be careful to differentiate between a sputum to a lypic reaction and a simple in encase due increase due to a passing catarrh which affects phthisical patients just as well as ordinary healthy individuals. One is apt to become alarmed at a sputum increase from \$ oz. to 3 ozs, when dealing with tuberculous patients,

especially when one is in areaa of lytic reactions; but general reflection on one's own condition during the passage of a common cold should make the phenomenon less distressing. Under a later heading the special effect of I.K. on the sputum will be discussed; at present it is sufficient to indicate the importance of sputum measurements as a guide to treatment.

The body-weight may or may not increase simultanecusly with the initial doses. While an increase is desired, a diminution in weight unaccompanied by other untoward signs should not be viewed with alarm, as under these circumstances at the commencement of treatment, it is indicative of no bad effect.

The pulse-rate should be carefully recorded. This should show a diminution in rapidity in cases where it was heretofore accelerated.

The foregoing observations have referred to streatment evidence of success or failure in the commencing stages, The same data fired good in the color stages A but here other data are observable and of utility. Of additional subjective signs may be noticed the absence of mental depression, nervousness, and the vague feelings of losing all hold on life. The diminution in night sweats, headaches, dyspepsia, anorexia, etc., all point in the same direction towards amelioration, whilst objectively, body-weight and sputum observations give evidence of improvement. In a case responding satisfactorily to treatment the temperature ultimately assumes a flat appearance with a daily variation of from 0'2 to 1'0 °F. Such temperatures of complete immunization are shown in Charts <u>XLI</u>. and <u>XLII</u>.

I.K. IN PROPHYLACTIC TREATMENT.

The protective immunizing property of I.K. has been shown by experiments on rabbits. These experiments described by Fearis (The Treatment of Tuberculosis by means of Immune Substances (I.K) Therapy) and quoted from Carl Spengler: Tuberkulose - und -Syphilis - Arbeiten, sufficiently indicate from a laboratory point of view the complete lytic-antitoxic immunity conferred by even such a minute dose as 0'1 cc of Dilution VI. As the main element in any Anti-Tuberculosis scheme lies in preventive measures, such experiments are of great value from the Public Health standpoint. Physicians see daily cases which cannot be definitely labelled as suffering from pulmonary tuberculosis - cases marked by debility or a tendency to recurring colds or some other complaint usually regarded as trifling, but which in the light of personal histories of other cases must be looked upon with alarm as very often prodromal evidence of severe disease. Many such cases are "contacts" of definitely tubercular patients or even of such probably mis-named cases as Asthma or Chronic Bronchitis. Very often the routine examination of these suspects reveals nothing of an objective nature on which to base a diagnosis, which

must accordingly rest entirely on subjective or even probable evidence. In these circumstances it is wrong to wait for definite symptoms and signs to develope. The very fact that the patient is not right is the necessity for treatment and moreover, in such cases treatment is usually simple in application and short in duration as the rapid method of immunigation will be found suitable in the majority of instances.

GENERAL REMARKS ON THE VALUE OF I.K. IN VARIOUS FORMS OF TREATMENT.

Treatment on an extensive scale may be divided into four forms.

- 1. Dispensary.
- 2. Sanatorium.
- 3. Hospital.
- 4. Domiciliary.

Subdivisions such as the Open-air School and Farm Colony exist, but it will be sufficient to inuicate in a general way the value of I.K. in the four large groups.

Value of I.K. In Dispensary Treatment.

Sufficient has been said in the foregoing to show the value of I.K. in Dispensary Practice where all varieties of patients are met with. Its applicability to the early as well as to the advanced case, afebrile or feorile, gives it a range particularly suitable for use in such dispensary work - a range which is denied to tuberculin. Moreover the rapidity with which its effectiveness is displayed, raises a hopefulness in the patient, who being unable to appreciate readily the protracted nature of ambulant treatment is apt to regard any treatment with suspicion if good results are not quickly forthcoming. Again being non-toxic and free, when given properly, from any of the sequelae which threaten to follow the administration of tuberculin, I.K. becomes of marked value in the treatment of patients who are met with to whom the administration of tuberculin is contra-indicated for some reason or another, and who, if tuberculin is the only therapeutic agent used, must be denied any treatment of a specific nature. In such cases I.K. has been shown to be of service. The use of I.K. therefore enlarges the scope of ambulant treatment and makes the dispensary a unit of increased value in any anti-tuberculosis scheme.

Value Of I.K. In Sanatorium Treatment.

The value of I.K. is not so readily appreciated in Sanatorium practice as it is in dispensary work. Under hygienic-dietetic treatment as carried out at a Sanatorium, the patient is removed from the harmful surroundings which contributed to the development of his diseased condition and placed in the best possible environment, where rest and exercise are carefully watched, where proper food is given, where the importance of fresh air is recognised, and where there is constant medical supervision. Treatment on such Sanatorium

lines alone is in many cases sufficient to improve the condition of the phthisical patient, so that when any supplemental treatment such as I.K. is given there is difficulty in separating for statistical purposes the good accruing from one method of treatment from that derived from the other. Τt would appear from the above observation that the relative merits or demerits of any given specific treatment must be ultimately proved in Dispensary work. No matter how one may arrage <u>controls</u> in Sanatorium treatment, there is still the overlapping factor at work, and control cases and specifically treated cases are not absolutely alike. It is in Dispensary practice that specific treatment is seen in operation alone or virtually alone. The patient remains in his natural environment and, although this is somewhat altered for the better by following advice regarding rest, ventilation, food, etc., the change is of much less marked nature than that obtained by transferring a patient to a Sanatorium environment. The question at issue however in no way effects the position of I.K., for if it is found of utility in dispensary practice, one must assume its value when combined with what in reality one aims at obtaining in ambulant treatment. The all important

point which distinguished proper Sanatorium treatment is the constant medical supervision exercised in the former. It is this supervision which constitutes a Sanatorium what it is, and places it beyond the conlines of a convalescent home. Owing to this factor Sanatorium observations should far out-weigh many of those obtained at a dispensary where necessarily much that is required for statistical and scientific purposes is observed and recorded by the patients themselves. In the matter of sputum measurements, for instance, it is exceedingly difficult in dispensary work to obtain records of a sufficient accuracy from which to tabulate results. Certainly the patient observes but it is an observation which finds expression in such statements as "Spitting more," "Spitting less," or "No spit, " Again in dispensary work observations concerned with the blood, the pulse, the diseased focus, etc., following an administration of I.K. must for obvious reasons be omitted. In these respects the dispensary physician is at a loss in estimating the complete value of I.K. and must look to his Sanatorium colleague for the complementary evidence required.

Value of I.K. In Hospital Treatment.

Although Hospital treatment is meant primarily for

the hopeless and dying, cases are met with who, under the hygienic-dietetic life begin to regain ground considered at first as absolutely lost, and who are ultimately able to be transferred to Sanatorium treatment. While in the treatment of such advanced cases, general measures must be predominant, there is no doubt but what the careful exhibition of I.K. is productive of great good. Its antitoxic quality makes I.K. eminently suitable for administration to an already toxin-saturated body, and as has already been indicated, it is often from among his advanced and generally considered hopeless cases that the physician experienced in I.K. therapy obtains his most striking results. As has already been pointed out, I.K. often produces a rapid subjective improvement and even although nothing else than this were achieved in the treatment of the advanced case, the production of a feeling of well-being would not be little.

Value Of I.K. In Domiciliary Treatment.

Under the Sanatorium Benefit Schemes which are in operation under the Insurance Act, the Domiciliary treatment of Phtnisical patients has become of much importance and there is an ever-growing responsibility thrown on the general practitioner regarding his

methods of treatment of such domiciliary cases. Hitnerto with few exceptions, specific treatment has been confined to specialists in that particular department, and practitioners have aided this restriction by quite a legitimate fear of specific therapy. The advent of I.K. however opens up a further field in Domiciliary treatment, whether that treatment is being given to early febrile or to very advanced cases. Relative to Tuberculin, I.K. is simple in its application, and moreover there is no reason to think that I.K. treatment will ever assume the polymorphous characteristics of Tuberculin treatment, which in a great many instances is now carried out in the most heart-rendingly haphazard manner and with a peculiar absence of imagination. Under such circumstances it is much better for those who are concerned with the ultimate value of specific treatment that tuberculin be left in the hands of a few, although on the other side there seems no reason why I.K. cannot be productive of good when used in general practice if a careful consideration of the first principles of I.K. therapy be made. It is the general practitioner who is the outpost in the campaign against tuberculosis in all its forms. It is he who is first brought into contact with the case as an individual requiring treatment, and on his diagnostic skill depends in great measure the chances of the patient. Leaving aside cases of certain tuberculosis, he is in daily touch with <u>contacts</u> and able to observe any showing signs of ill health, malnutrition, or a tendency to <u>colds</u>, and many other symptoms which from a consideration of afterhistories are important prodromal manifestations of a tuberculous process. Consequently for the practitioner to use I.K. in such a pre-tubercular class, would be an all important aspect in any anti-tuberculosis scheme and would relieve the specialist of much time which could be devoted to cases of a more difficult nature.

EFFECT OF I.K. TREATMENT ON BODY WEIGHT.

Of objective data indicative of success in the treatment of pulmonary tuperculosis, the weight of the body claims a prominent position, especially when treatment is being carried out while the patient remains at home in his ordinary surroungings. In the following table (Table I.) an effort has been made to guage the effect of I.K. in this capacity. Fortyfive cases were taken, 15 in Stage I., 15 in Stage II., and 15 in Stage III. The cases were of both sexes, and of all ages, and treatment was carried out while they remained in their ordinary surroundings, and under the worst of hygienic circumstances to be found in a densely_populated mining area. Moreover the patients were either Insured persons or the dependants of Insured persons and accordingly in many instances unable to procure sufficient and proper nourishment owing to their relative poverty. For each stage group there are two columns, one giving the increase or decrease in weight at the end of the first week of treatment, and the other similar data at the end of the first four weeks. These two

periods have been selected for the following reasons:-

- (1.) They cover a preliminary or experimental period of 4 weeks.
- (2.) No other treatment such as Cod Liver Oil or Extra Nourishment is given during this preliminary period.
- (3.) Being a preliminary period there is no selection of cases as to suitability or otherwise, although of course if the case is found eminently unsuitable after the first dose(severe Lysis or Hypersensitiveness). treatment is stopped.

TABLE I.

Differences of weight in pounds, of patients undergoings

I.K. Treatment.

| | Stage 1. | | Stage 11. | | Stage 111. | |
|-----|----------------------|-----------------------|----------------------|-----------------------|----------------------|-----------------------|
| | At end of 7 days. | At end of 28 days. | At end of 7 days. | At end of 28 days. | At end of 7 days. | At end of 28 days. |
| 1. | 4 | 4호 | 3 1 | 5 | 2 3 | 3] |
| 2. | - 1 | $=\frac{3}{4}$ | 3호 | 7 = | - 2 | 1 |
| 3. | 8 <u>1</u> | - 21 | 0 | 11 | ଛ | 2] |
| 4. | 1 4 | 11 | - 34 | 1 1 1 | 1 | 11 |
| 5. | . 34 | | 1 | l | 1 | - 34 |
| 6. | - 14 | $-\frac{1}{4}$ | 3 4 | - 2 | - 1 | - 34 |
| 7. | 14 | l | $-1\frac{1}{4}$ | - 34 | 1 | 11 |
| 8. | - 1/2 | 3 | 1 | - 14 | 11 | l |
| 9. | 2 | 11 | 11 | l | 8 3 | 3 3 |
| 10. | $-1\frac{1}{4}$ | - 1 | - 11 | - 34 | - 1 | 2 |
| 11. | 1 | 13 | 1 | l | - 1/2 | - 1 |
| 12. | 0 | 1 | ł | 41 | 4 | 1 |
| 13. | 1 | 134 | 34 | 2 | 3 } | 5 <u>3</u> |
| 14. | 34 | l | 1 | 14 | - 1/4 | 34 |
| 15. | 1 4 | r. 1 | - = | 11 | ł | · 41 |
| als | 73 | 18 | 111 | 26 | 14 ¹ /2 | 28 |
| | - 3 | - 5 | - 4 | - 5 1 | - 43 | - 2 |

Taking the cases as a whole, it will be observed that at the end of the 1st week there is a nett gain of

 $4\frac{3}{4}$ lbs for Stage 1. cases

 $7\frac{1}{4}$ lbs for Stage 11. cases

 $9\frac{3}{4}$ lbs for Stage 111. cases

or $2l\frac{3}{4}$ lbs for the 45 cases comprising the three groups. This gives an average gain in weight at the end of the lst week of 7'7 ounces. In a similar manner it can be found that the average gain in weight at the end of the first 4 weeks is $2l^{2}$ ounces.

These increases may be further analysed as follows according to the stage of the desease.

| Average | e gain : | in weight | Average gain in weight | | | |
|---------|----------|-----------|--------------------------|----------|------|--|
| at end | of lst | week. | at end of first 4 weeks. | | | |
| 1. | 11. | 111. | 1. | <u> </u> | 111. | |
| 5'0 | 8'2 | 10'4 | 13'8 | 22'1 | 2717 | |
| Ozs. | Ozs. | Ozs. | Ozs. | Ozs. | Ozs. | |

TABLE 11.

Although the series in the table has all the faults of a short series, there is a marked tendency for the data towards one direction which is significant. Of especial importance is the average gain in weight for the 45 cases taken as a whole, for the two periods of 1 week and 4 weeks, without any reference to age, sex, or stage distribution. Considering the adverse conditions of the patients and the entire impossibility of attributing the increase in weight to hygienic-diatetic measures, one can only conclude that the I.K. procured the improvement. From Table II. it would appear that I.K. exerted a more marked benefit in III. stage than in I. or II. stage cases, and that II. stage cases did better than those in I. stage. The reason is that the more advanced the disease the greater is the relativity established with the condition approximating health, so making the improvement which sets in all the more appreciable. In other words as far as weight is concerned, the III. stage case has the greatest range in which to manifest improvement.

THE EFFECT OF I.K. TREATMENT ON SPUTUM.

The importance of measuring the daily amount of sputum has already been mentioned as having a significance in indicating success or failure of treatment. In Dispensary practice however the difficulty of getting patients to be accurate with their expectoration is very greatly due to the long period in which many of them have exercised no control over its disposition or to having become accustomed to spitting in a paper and then burning it. Consequently the statistics which follow regarding this aspect of I.K. Therapy are extremely scanty when only the cases which showed any degree of accuracy in sputum observation are selected. In cases of very advancea disease however, where the patient is staking all in getting better, more care is taken, and for the purpose of the following table (Table III.) only such cases have been chosen. All were III. Stage cases (Turban- Gerhardt) with Tubercle Bacilli present in the sputum. The treatment was carried out ambulantly at a Dispensary. The period of 28 days has been selected in order to show the rapidity with which I.K. exerts its anticatarrhal effect, as in the majority of cases the greatest reduction in sputum takes place at the

commencement of treatment. It is the residue of sputum - often a small amount such as one $\frac{1}{2}$ or a morning spit which is aifficult to remove-and indeed in many cases one is led to the conclusion that such a residue sputum is in no way connected with the tuberculous process but is dependent on other causes such as the vitiated atmosphere of an industrial area. Although no observations have been made on the disintegrative effect of I.K. on Tubercle Bacilli, a total disappearance has been noted. Even where such good result cannot be obtained, it is fair to assume that by reducing the amount of sputum, the number of bacilli expectorated will be also reduced - especially where a total disappearance of sputum has been effected.

TABLE 111.

| Amount of in Ozs. at commenceme Treatment. | the in Ozs nt of days T | . after 28 reatment. | Differences in Ozs. due Diminution. | |
|---|----------------------------|-------------------------|--|--|
| 1. 5 2. 3. 3. $5\frac{1}{2}$ 3. $5\frac{1}{2}$ 4. $1\frac{1}{2}$ 5. 4 6. 6 7. 8. 9. $1\frac{1}{2}$ 10. $3\frac{1}{2}$ 10. $3\frac{1}{2}$ 11. $2\frac{1}{2}$ 13. $2\frac{1}{2}$ 14. 3 15. 2 16. 5 17. $1\frac{1}{2}$ 20. $1\frac{1}{2}$ 23. 6 24. $1\frac{1}{2}$ 25. 4 | | | 34 34 34 15 15 11 12 14 13 34 13 1 1 1 1 1 1 1 12 14 13 13 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | |

These results may be analysed as follows:-

six In fifty per cent the sputum was diminished on an average of 1'96 ozs.

In eight per cent the sputum was increased on an average of 1'5 ozs.

In thirty-six per cent the sputum remained stationary.

By a continuation of treatment, the percentage of cases in which the sputum remains the same after 28 days treatment, will be greatly lessened as in some instances it is only by using the higher doses that the anti-catarrhal effect of I.K. becomes evident. The cases manifesting an increase however are usually found disappointing.

THE EFFECT OF I.K. TREATMENT ON FEVER.

The antifebrile action of I.K. has already been remarked on under different headings in the foregoing. An endeavour will now be made to show this action in tabular form. In the following table (Table IV.) data containing a series of 20 cases are given. The cases were all advanced III Stage cases with tubercle bacilli present in the sputum and manifesting some degree of fever. Treatment was carried out ambulantly at a dispensary. It is hoped that the restriction to such a type of case undergoing the least suitable treatment will enhance the value of the results obtained despite the shortness of the series observed. Furthermore it should be noticed that the results are those derived from 28 days of treatment. This period has been chosen mainly because of the freedom from other concomitant treatment, and also because the shorter the time taken the more readily demonstrable must the antifebrile action of I.K. be. The temperatures are Fahrenheit - taken orally. Owing to the daily variations in temperature, some difficulty was experienced in estimating the degree of fever present. Accordingly for tabular purposes the highest record was taken (1.), of the week preceeding treatment

and (2.) of the week after 28 days Treatment.

| - | Highest Temperature during week precede- | Highest Temperature during week after 28 | Difference due to I.K. | |
|--|---|--|--|--------------------------------------|
| | ing Treatment. | days Treatment. | Reduction. | Elevation. |
| 1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11. 12. 13. 14. 15. 16. 17. | 100'0 99'8 100'0 99'6 100'6 99'8 100'4 100'4 | 100'0 100'4 98'6 99'2 100'6 99'0 100'0 99'4 101'4 99'8 99'0 100'8 99'0 102'4 98'4 101'2 99'0 | Reduction. 1'4 0'4 0'4 1'0 2'2 2'0 2'0 2'2 1'4 1'5 | Elevation. 0'6 - 0'3 1'8 |
| 18. 19. 20. | 100'0 101'0 99'8 | 99'6 101'0 99'8 | 014 - - | - |

TABLE 1V.

These results may be analysed as follows:

In 60% the fever was reduced on an average of 1'3 ^oF.

In 15% the fever was elevated on an average of 0'8 $^{\circ}$ F.

In 25% the fever remained stationary.

It should be noted that these results are not final results. In many of the cases where the temperature remained stationary or became elevated - improvement set in on further treatment being pursued.

ECONOMIC ASPECT OF I.K. THERAPY.

The expensiveness of present day tuberculosis treatment on a National scale is a point very often raised in criticism and especially so with regard to Sanatorium treatment. Towards Dispensary treatment a greater leniency has been shown but there is ample reason to believe that with the increasing demand for treatment which will result from a growing public and medical consciousness of the gravity of the situation, the economic aspect of all forms of treatment will ultimately be brought into greater prominence. The question will then obtrude itself "Which kind of treatment is the most rapid and at the same time the most effective, for if rapidity and effectiveness can be combined, then this treatment must in the long run be the cheapest." Attention has already been called to the rapidity with which I.K. exerts a beneficial effect in suitable cases, and with increasing knowledge of the administration of the treatment one may lock for an ever widening field of application. Some authors have shown that I.K. treatment is more rapid and more effective than either Sanatorium treatment or Sanatorium and Tuberculin treatment combined, but at present it is too early to be dogmatic, especially when neither Sanatorium treatment nor Tuberculin treatment are definitely stable quantities. It seems

absolutely essential that Sanatoriums should exist, for the Le are cases and many such cases suitable for no other kind of treatment, needing as they do strict discipline in every department of their lives to effect a good result. Again, Tuberculin applied either in Sanatorium or Dispensary treatment will continue to hold its own as a therapeutic measure of the utmost value in special cases, when its indiscriminate use has gone. carrying with it all the untoward results derived from such a practice. With the more extensive use of I.K. however, the time taken for either Dispensary or Sanatorium treatment will in the majority of cases be diminished and in this way there will be a financial saving. Not only with regard to Dispensary and Sanatorium treatment will this diminished expenditure be apparent. Considering the applicability of I.K. to the very earliest suspicious cases and also to the fairly advanced III. stage case, a saving will result in the former category by an increased prevention of the disease, and in the latter by a more thorough and satisfactory domiciliary treatment. As it is from such domiciliary cases that Hospital cases are recruited, it may be hoped that with improved treatment carried out at home a reduction in Hospital expenditure will be obtained.

RESULTS OF I.K. TREATMENT.

It is an extremely difficult task to give statistics of results in the treatment of a disease like Pulmonary Tuberculosis. While no doubt need be felt that a patient has become worse or has died. there must necessary be some chariness in saving a person has been cured. Indeed to say such a thing or to use the word cure in connection with Pulmonary Tuberculosis, is in the light of our present knowledge unwarrantable; and in gauging the efficacy of a line. of any treatment such as I.K. one must recollect the great tendency of the disease to arrest itself spontaneously. Apart however from statistical data, there are several points one may mention which are of interest. The treatment is appreciated by the patients. They feel the benefit of the treatment and are ready to acclaim its efficacy in no uncertain way. Should any contra-indication arise and it is decided not to give a dose, there is always the look of disappointment; and there is great difficulty in convincing the patient that it is all for the best. Attendance for treatment is usually regular and prompt, and in view of the fact that many of the patients persist in coming for treatment in spite of great financial embarrassment is surely an indication that I.K. has for them some intrinsic value. And after all, it is the patient

who is the final judge. As however, it is on clinical evidence that any treatment must stand or fall, the following summary of cases treated is given. (Table V.) It should be observed that in its compilation no selecttion has been made, all cases receiving more than 6 doses being recorded. The list includes patients treated ambulantly from October, 1913, with the general result brought up to date October, 1915. While this does not allow a sufficiently long interval of time to have elapsed, following the cessation of action ve treatment, in order to guage the full value of I.K. it is hoped that the consideration of the results as a whole will prove helpful in the just appraisment of the treatment carried out. Other cases belonging to the same time group but who received Sanatorium or Hospital Treatment in addition to Dispensary Treatment have been left out. A further group treated in a previous pericd of 6 months has also been omitted, as the treatment was carried out at a Sanatorium, which introduces an obvious difficulty in estimating the utility of I.K.

TABLE V.

SUMMARY OF CASES.

Explanatory Note:-

Stage Distribution (Turban-Gerhardt.)

Fever Distribution (Spengler.)

| | | l L | | · · · · · · · · · · · · · · · · · · · |
|---------------------------|---|--|---|---|
| General Result. | Well 14 Wonths after and at school | Fairly well and doing light work 7 months after treat- ment. | Well End Working 18 months Efter treat- ment. | Hell and working 18 months efter treatment. |
| Fever | Α. | AB • | AB | A |
| Symptoms on Discharge. | None. | Spit, reduc- tion from 3 ozs to 12 ozs | Mone. | None. |
| Dose | 20 Der 08. | ы С | 15 | 18 |
| Symptoms on Ádmíssion. | Cough, night sweats, loss in weight. | Cough, spit, pain, shortness of breath. Tubercle Bacilli present. | Cough, shortness of breath, spit 4 ozs. haemopty- sis. | Cough, spit, haemoptysis, night sweats. |
| Mode of Onset. | Cough 9 months | Pleurisy one year. | Pleurisy 6 months. Bronchitis 2 years. | Haemoptysis 5 months. |
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| Tedmun | • | N | з. | 4 |

| e. Result. | reduc- C Died in from to $\frac{1}{2}$ oz after treatment stopped. | reduc- B Well and rom to nil. B Working 3 months after treatment. course | I A Well and working 15 months efter treatment. | B Well and working 12 months after treatment. |
|---------------------------|--|---|--|--|
| Symptoms on Discharge. | Spit, redu tion from 6 ozs to $\frac{1}{2}$ | Spit, reduc- tion from 2 ozs to nil. Patient worked during whole course of treatment. | Occesional cough and spit. | None |
| ÐSOŒ | <u>б</u> | 6 S | 82 | 7 |
| Symptoms on Admission. | Cough, spit, night sweats, loss in weight. Tubercle Bacilli present. | Cough, spit, heemoptysis, night sweets, pain. Tubercle Bacilli present. | Cough, spit, shortness of breath, loss in weight. Pain in chest. | Cough, spit, haemoptysis, night sweats, debility. |
| Mode of Onset. | Tiredness, cough 6 months | Haemoptysis, pleurisy 12 yeers. | Cough 3 years. | Cough, spit pleurisy, 3 years. |
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| on & Symptoms on & General Discharge. A Result. | pit, 15 None. A. Well and eats, per working 14 months after treatment. | 1t,35.Cough, spit.A.Fairly wellats,Tubercleand workingBacilli pre-and workingBacilli pre-afterworked duringafterwhole courseof treatment. | it, 9. Cough and C. If any- is. 9. Cough and C. If any- is further spit, No further Balightly heemoptysis. preset after 13 months after treatment. | it, 30 . None. A. Well and ats. 12 None. A. Well and working 13 months after treatment. |
|--|--|---|---|---|
| Dol | | • | | |
| Symptoms on Discharge. | | pit. bre- hring hent. | ysis. | None. |
| Dose | 15 per os• | 35. | 5 | # = |
| Symptoms on Admission. | Cough, spit, night sweats, debility. | Cough, spit, night sweats, Tubercle Bacilli present. | Cough, spit, haemoptysis. Tubrucee Saelee present | Cough, spit, night sweats. |
| Mode of Onset. | Pleurisy ? years, cough 3 months. | Pleurisy 4 Vears, cough 3 months. | Pleurisy 2 years, haemoptysis 2 years. | Cough, Sister advanced phthisis. |
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| Stage | TTT | TIT | 111 | ц |
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| ləquinN | • თ | 10. | 11. | 1S I |

| General Result. | Well and at school 10 months after treatment. | Slight spit. Otherwise well and working 15 months after treatment. | Patient died 8 months after treatment. | Well End Working 10 months after treatment. |
|---------------------------|---|---|---|---|
| Fever. | а . | ব | | щ |
| Symptoms on Discharge. | None | Slight spit. | Slight im- provement generully. | None |
| Dose | 13. | 19. | 20. Der os. | 21. 21. |
| Symptoms on Ádmission. | Pleurisy. | Cough, spit 2 ozs Night sweats, pain. | Cough, spit, haemoptysis, night sweats, debility, hoarseness. Tubercle Eacilli present. | Cough, spit, pain, shortness of breath. |
| Mode of Onset. | Pleurisy on £dmission l week. | Haemoptysis, cough 2 yeers. | Pneumoñic phthisis 4 years. | Cough 10 years. |
| rever | | Ч | | щ |
| Stage | • TT | .111. | .111. | • L |
| XəS | • E | • E4 | • च्यि | म्प |
| V Ee | -2L | 12. | 14. | 14. |
| Number | 13. | 14. | 12 | 16. |

| General Result. | Well and working 1° months after treatment. | Well and Working 11 months after treatment. | Well and working ll months after treatment. | werking working 6 months Efter treatment. |
|---------------------------|--|---|--|---|
| Fever. | 4 | A | 4 | щ |
| Symptoms on Discharge. | None. | Shortness of breath, spit 2 oz. | None. | Spit, 2 oz. |
| Dose | <u>ں</u> | 17 | 71 | 24 |
| Symptoms on Ádmission. | Cough, sputum, night sweats, pain. Tubercle Bacilli present in sputum. | Cough, spit, night sweats, pain, loss in weight, debility. | Cough, spit, loss is weight, debility. | Cough, 1 ¹ / ₂ oz. spit, night sweats, loss in weight, Tubercle Bacilli present. |
| Mode of Onset. | Infleunza 3 months. | Cough 6 months | Cough, spit, 2 months. Sister advanced Phthisis. | Pleurisy 6 weeks. |
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| 93&t2 | Ч | .11. | г. | 1 |
| xəg | M | fq | दि | M |
| 9 3 A | LS. | 35 | 71 | С, X |
| redairN | 17. | 18. | 19. | 0 0 |

| | · | | | |
|---------------------------|---|---|--|---|
| General Result. | No change 12 months after treatment. Not work- ing. | kell and working lo months after treatment. | Well and Working 8 months after treatment. Died of tonsilitis. | Well and at school 15 months after treatment. |
| Fever. | ব | र | . t | 4 |
| Symptoms on Discharge. | Much improved Cough and spit the same. | ione. | None. | Slight cough pain in left side. |
| Dose | 17 | 16 | LS LS | 31 |
| Symptoms on Àdmission. | Cough, spit, haemoptysis, night sweats, Laryngeal, Tubercle.Bacilli present. | Cough, spit, night sweats. | Cough, spit, shortness of breath, debility, unable to work. | Couch, night sweets, shortness of breath. |
| Mode of Onset. | Pleurisy 2 <u>2</u> years. | Pleurisy 7 years. | Preumonia 3 times. | Pleurisy 4 Vézrs, also 6 weeks. |
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| egst2 | LLL | F-1 | LLL | r. |
| Xes | 17 | म्प | M | F4 |
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| | t | an a | · | |
|---------------------------|--|--|--|---|
| General Result. | well and at school ll months wftor treetment. | werking working 11 months aftor treatment. | Well End Vorking 6 months efter treetment. | Patient died 21 months efter treament. |
| Jevel. | а н - | ſϤ | ۲ | Ċ |
| Symptoms on Discharge. | . Mone | None. | L'one. | No 1mprove- ment in syntoms. |
| Dose | 15 03 | 71 | 61 | JO |
| Symptoms on Admission. | Cough, night sweats, short- ness of breath, debility. | Cough, debility. Haemor ty sis. | Jough, debility, pleurisy. | Cough, spit, heemoptysis, night sweats, loss in veight, extreme debility. Tubercle Eucilli present. |
| Mode of Onset. | Might sweets C 3 years, cough 2 years n Sister advance Phthisis. | Tfredness 3 Vetrs, cough. | Cough, debili- ty, Father advenced phthisis. | Pleurisy 3 Vetrs. Tubercular pneumonia 3 Vears. |
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| Stage | 11. | | H | TTI |
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| 98V | б | 00 22 | 13 | # + |
| Number | 25 | ເວ ເນ | 27 | 38 |
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| General Result. | dell and at school 15 months after treatment. | well and working 9 months after treatment. | Fairly well but not working 4 months after discherge. | Patient graduclly turning vorse ll months efter treatment. |
|---------------------------|---|--|---|--|
| Fever. | മ | 4 | ~ 1 | μ |
| Symptoms on Discharge. | None. | None. | Cough, spit, Only slight shortness of breath. | No improve- ment in symp- toms. |
| ÐsoT | 0 0: | 16 Der Os. | 34 | 15 |
| Symptoms on Ádmission. | Cough, spit, night Sweats, Shortness of breath. | Cough, spit, night sweats, loss in weight. Pain in Chest Debility. | Cough, spit, night sweats, shortmess of breath. Tubercle Bacilli present. | Cough, night sweats, pain in chest. Tubercle Bacilli present. |
| Mode of Onset. | Cough 18 months, influ- enza 3 years. | Tiredness 1 year, cough 3 weeks. | Pleurisy, cough. | Pain in chest pleurisy 3 months. |
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| Stage | TIT | TTT | TTT | .111. |
| XəS | • स्थि | F4 | M | м. |
| 9\$¥ | C | 13 | 35 | 40 |
| төбшиИ | -62 | 0 8 | 81. | 33 33 |

| General Result. | werking working Z months after treatment. | Well and working 3 months after treatment | Well and working 17 months after treatment | Well and working 19 months after treatment. |
|---------------------------|--|---|--|---|
| Fever. | m | Д | . ۲ | .₩ |
| Symptoms on Discharge. | None. | Slight pain in chest. | None. | None. |
| Dose | 19. | 18. | 20. | 26. |
| Symptoms on Admission. | Cough, spit, hcemoptysis, night svects, shortness of breeth. | Cough, pain in chest, shortness of breath, loss in weight. | Cough Debility, Shortness of Breath. | Pain in chest. |
| Mode of Onset. | Pleurisy 3 weeks. Eaemoptysis 3 weeks. | Pleurisy. Eusband died of Phthisis. | Recurring Influenza, Bronchitis. | Pleurisy 2 months. |
| төтөй | ش | Å | . A | <mark>ب</mark> |
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| xəs | E | E4 | • F4 | ĸ |
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| TedmuN | 33. | 34. | 35. | 36. |

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|----------------------------|--|---|--|--|
| General Result. | Well and working 6 months after treatment. | Well and at school 4 months after treatment. | Well and working 3 months after treatment. No spit. | Well and working with no cough 5 months after treatment. |
| .TOVOT. | . | ۳. ۳ | ش | Ř |
| Symptoms on Discharge. | None. | None. | None, T. B. disappeared in 4 months. No spit whatever at end of treatment. | Slight Cough. |
| Dose | °0. | 16. | 22 23 | 18. |
| Symptoms .on Ádmission. | Cough, Spit, night sweats. | Cough, spit, night sweats, Pain in chest, Loss in Weight, Debility. | Cough, spit, night sweats, Tubercle Bacilli present. | Cough. Haemoptysis. |
| Mode of Onset. | Bronchitis 3 months. Pleurisy 1 month. | Cough, Pleufisy 3 Vears. | Cough, Spit 1 month. Brother died of Phthisis. | Cough. Haemoptysis 3 months. |
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| Knmber | 37. | 38. | 39. | 40. |
| | - | | | T I I I I I I I I I I I I I I I I I I I |

| Ø 1 | | | | | |
|-----------------------------------|--|---|---|--|--|
| General Result. | Well and at school 5 months after treatment. | Well and at school 5 months after treatment. | Well and working 4 months after treatment. | Fairly well and work- ing 4 months after treat- ment. Bron- chiectosis. | |
| Ĩever. | A. | | 4 | m | |
| Sympto ms on Discharge. | None. | None. | Nome. | | |
| €soŒ | 17. | 4 0 | 18. | 24. | |
| Symptoms on Admission. | Cough, Hæemop htysis Shortness of breath. Loss in weight. | Cough, Spit, Night sweats, Pain in chest. | Cough, Spit, Haemoptysis, Night sweats. Pain in chest. | Cough, Spit, Haemoptysis. Pain in chest. Loss in weight. | |
| Mode of Onset. | Tiredness 8 weeks, 7 weeks. Haemoptysis, 3 weeks. | Pain in chest 10 weeks. Mother advanced Phthisis. | Pleurisy ? months. Haemoptysis & months. S | Cough, Spit ⁸ years. | |
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| rodmbW | 4 1 | 42. | 43. | 44. | |

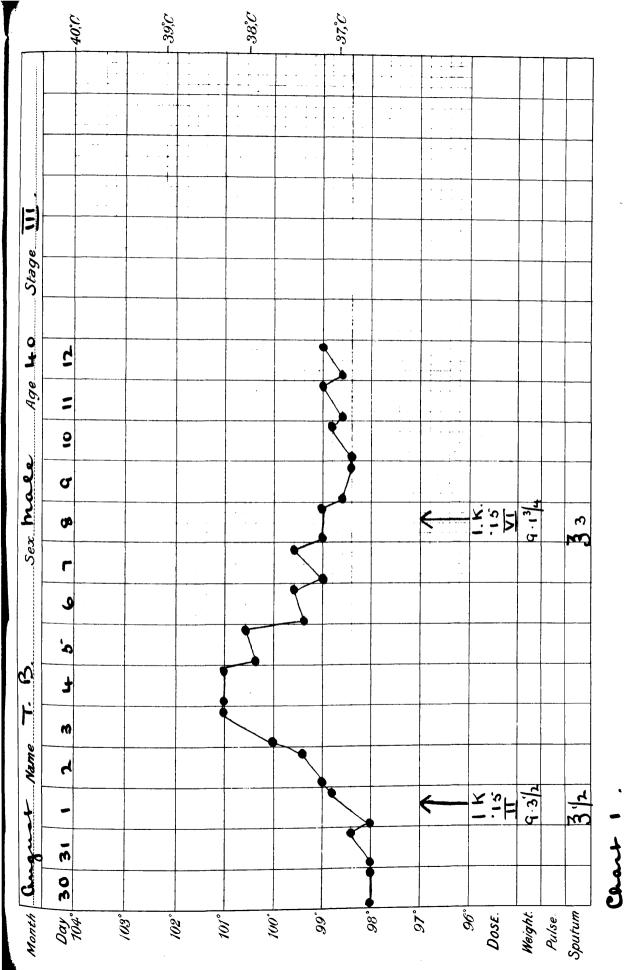
| | | | | and a second second second second |
|---------------------------|--|--|--|---------------------------------------|
| General Result. | Well and working 3 months after treatment. | Well and Working 4 months after treatment. | Well and working 4 months after treatment. | |
| .1979मे | A. | • | 4 | |
| Symptoms on Discharge. | None. Sputum re- duced from 12 ozs to nil. | None. | None. | |
| esoT | 16. | • თ | - 12 | |
| Symptoms on Admission. | Cough, Spit, Might Sweats, Pain in chest. | Cough, Fain in chest, Shortness of breath. | Cougn, Spit, Night sweats. | |
| Mode of Onset. | Recurring colds with much spit. | Influenza, Pleurisy l2 weeks. | Bronchial Symptoms 2 years. | |
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| 88 6 | 15. | 23. | 16. | |
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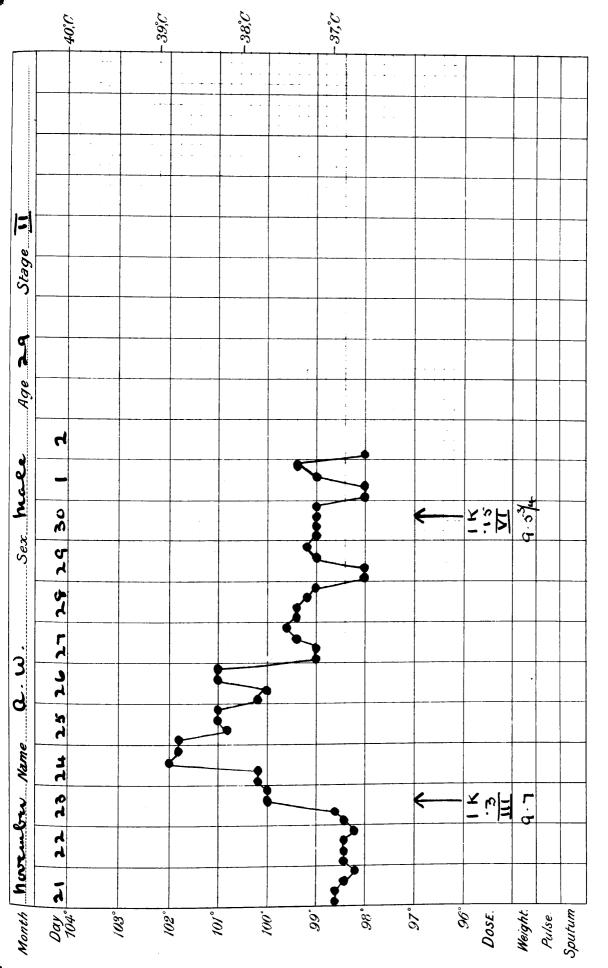
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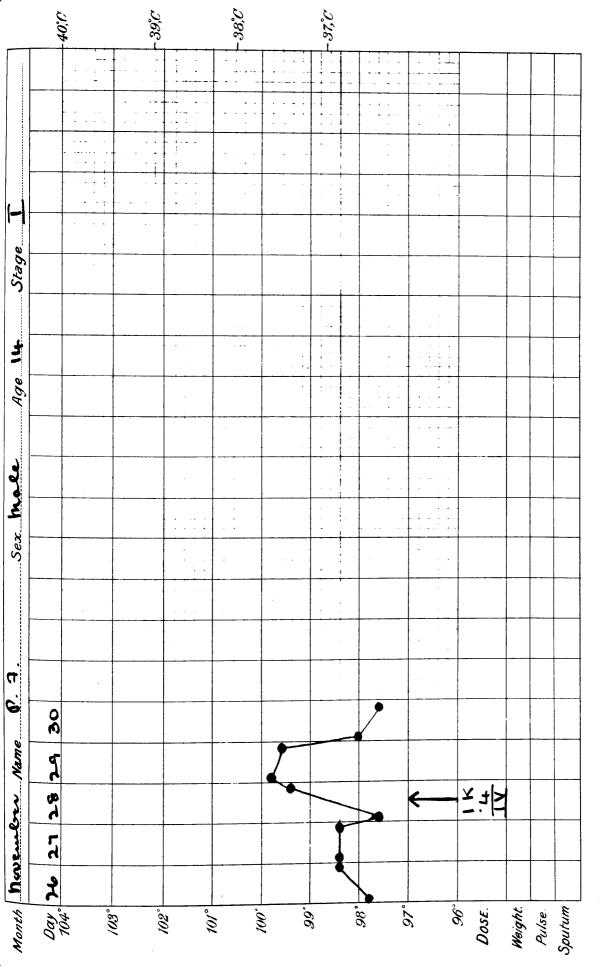
Explanatory Note: The method of administration of dose is indicated as follows:-Subcutaneously:

Orally





Ceart 11.



Ceart III.

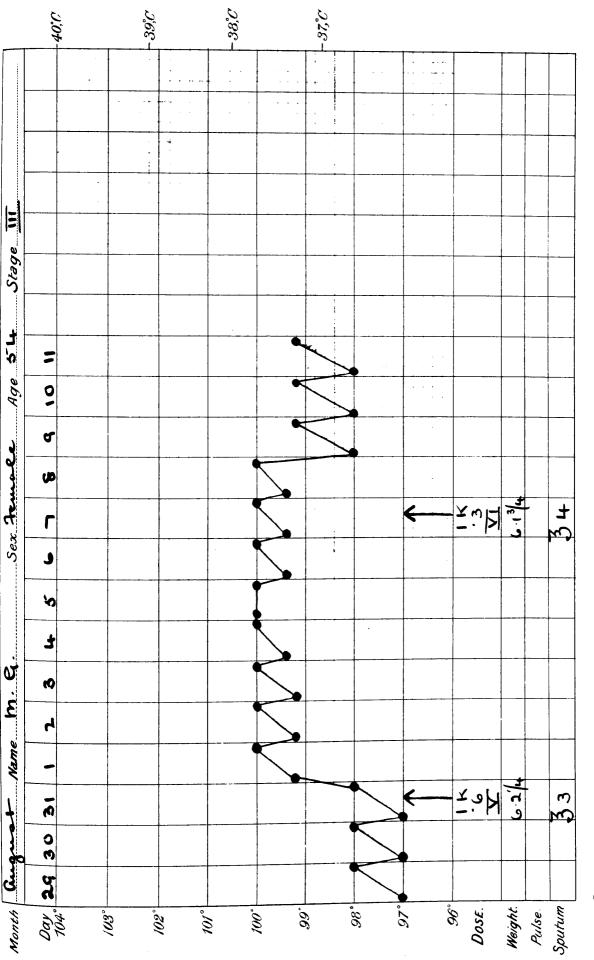


Chart 1V.

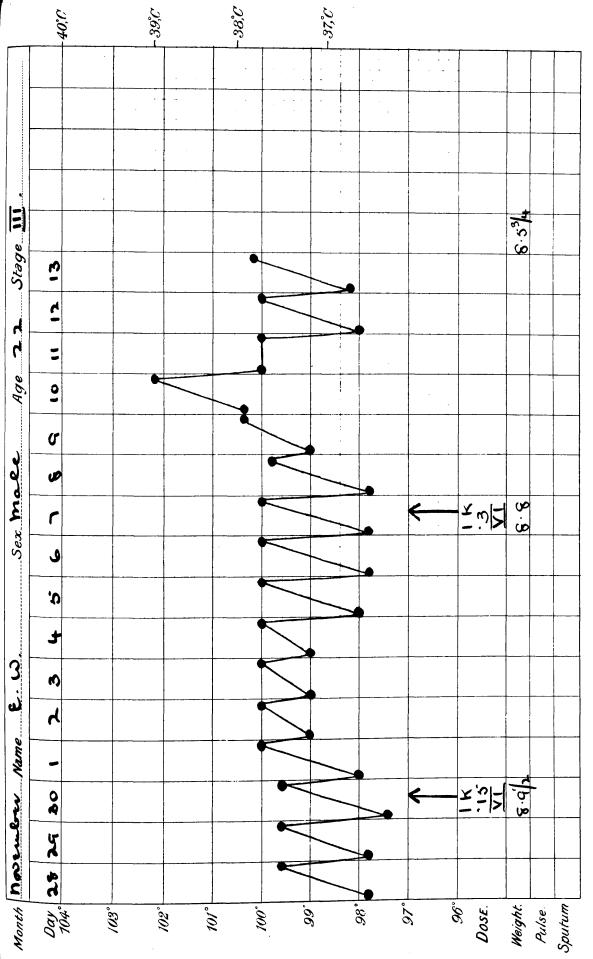
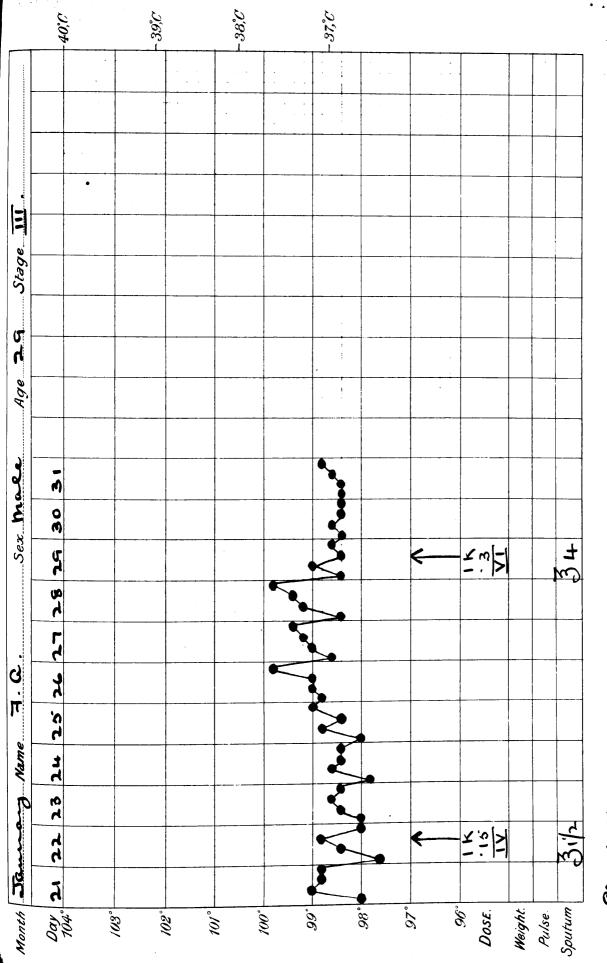
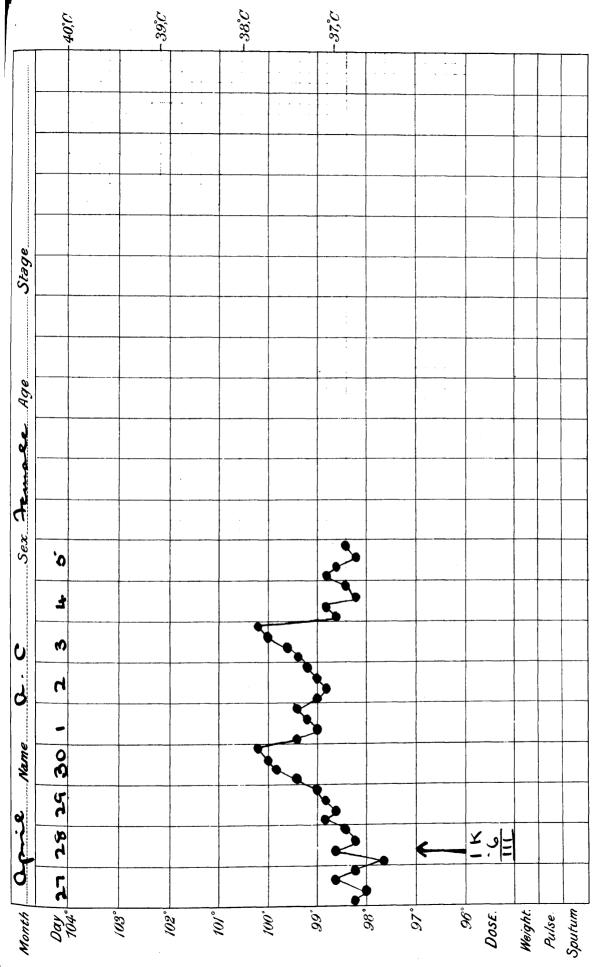


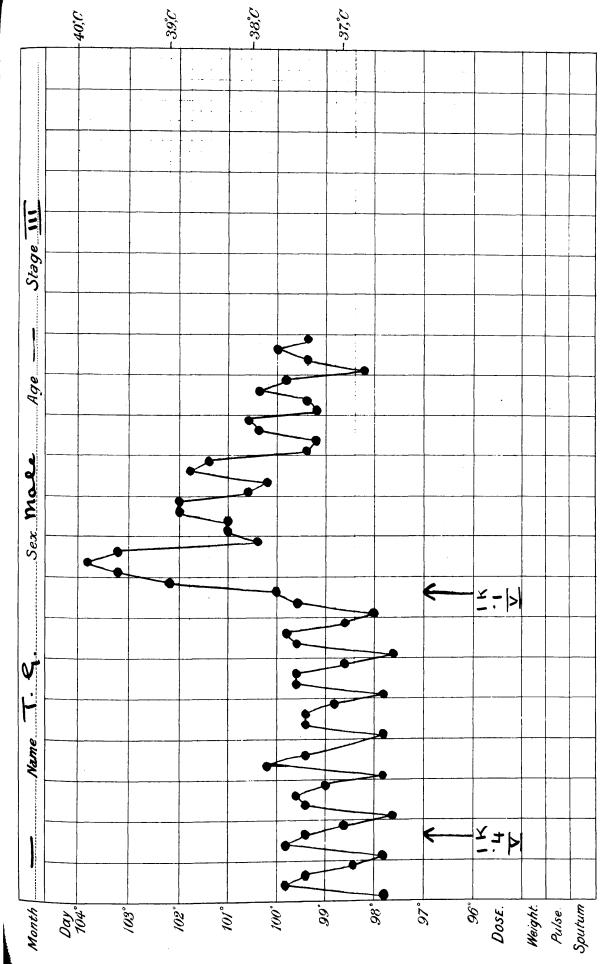
Chart V.



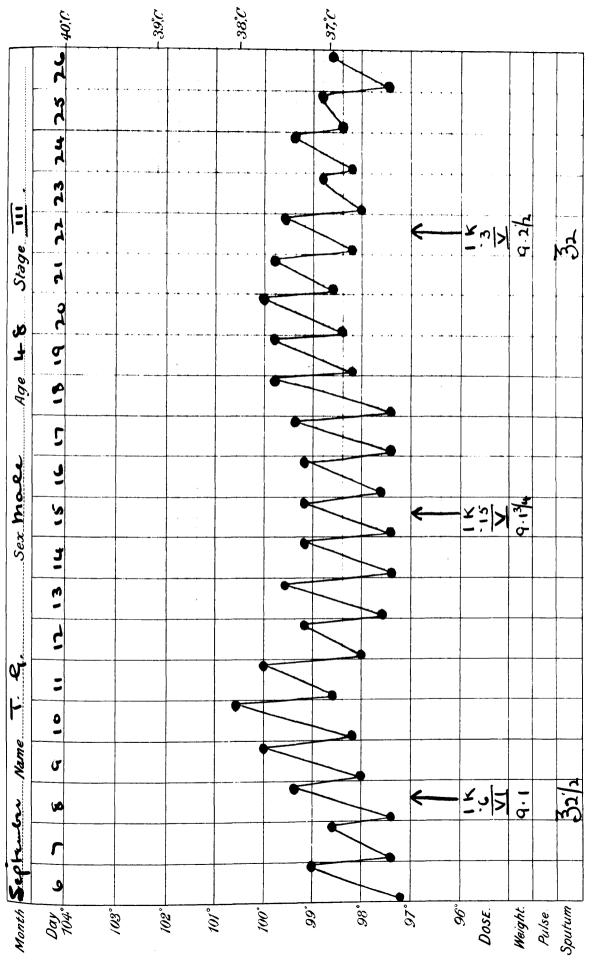
Cleart VI.



Clart VII.



Gent VIII



Clart 1X.

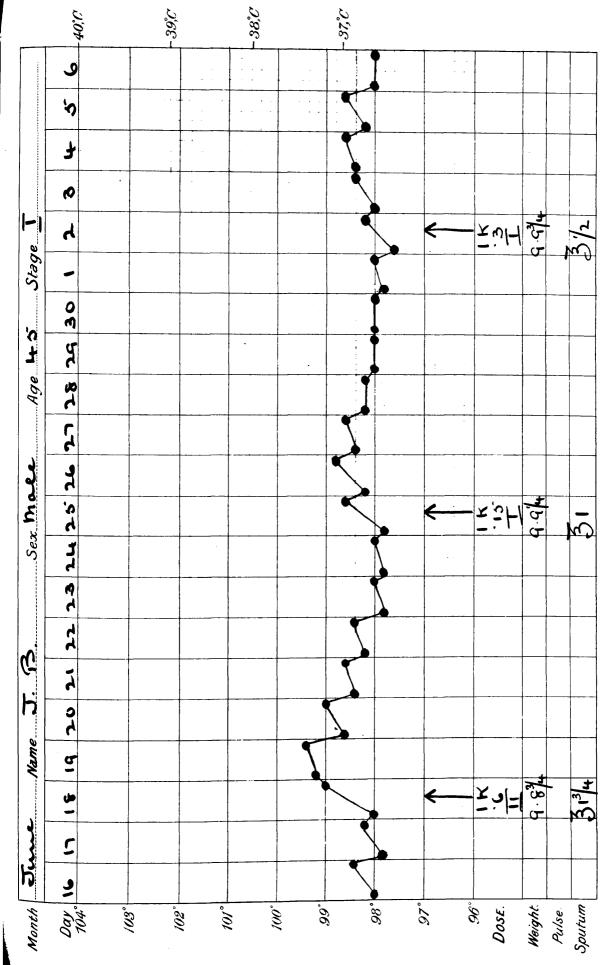


Chart X.

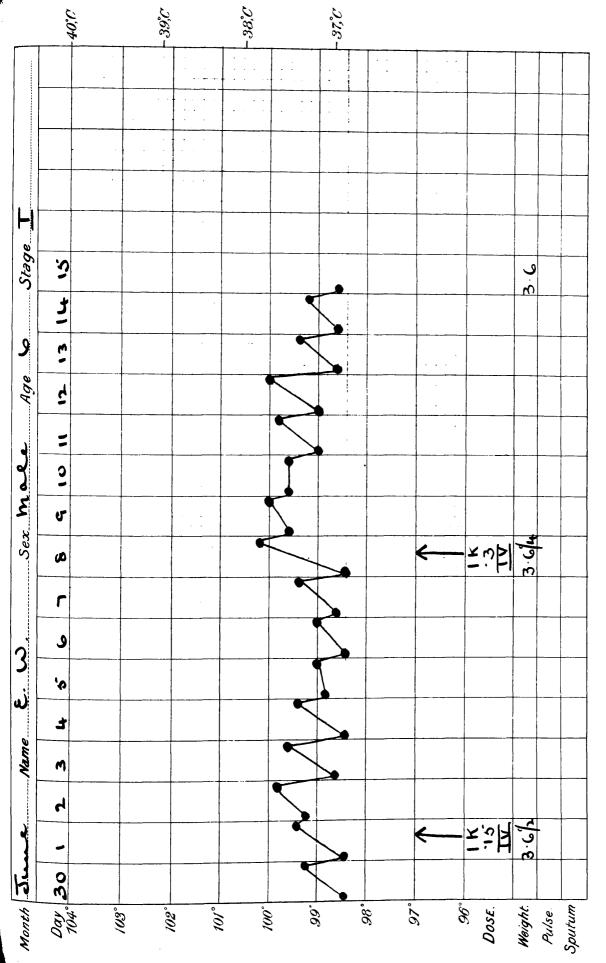
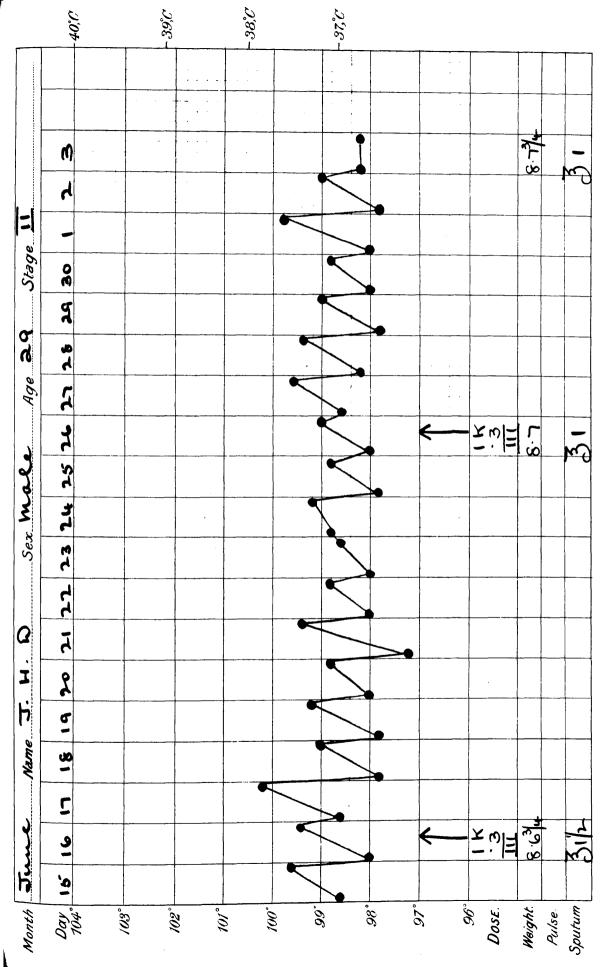


Chart XI



Ceart XII

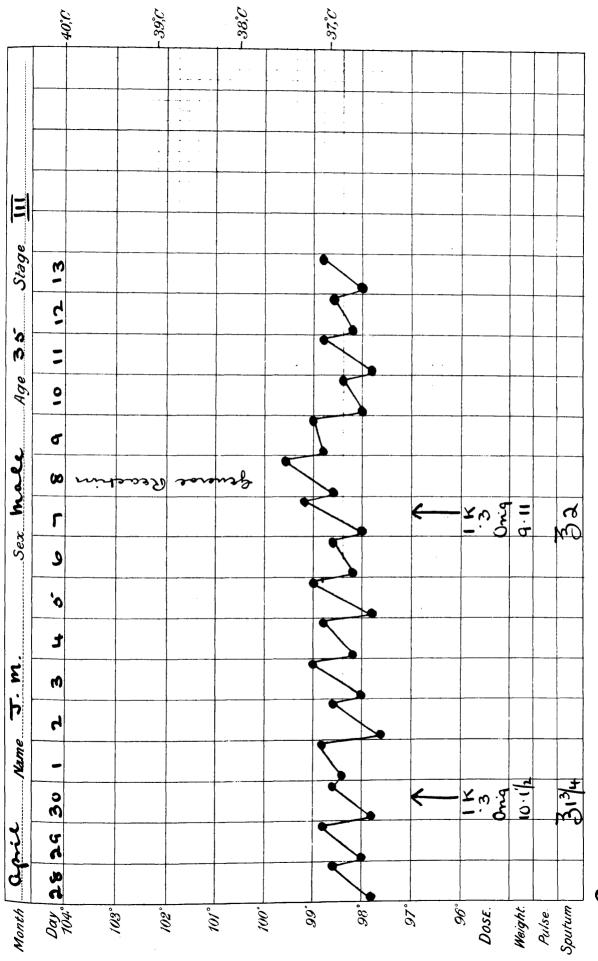


Chart XIII.

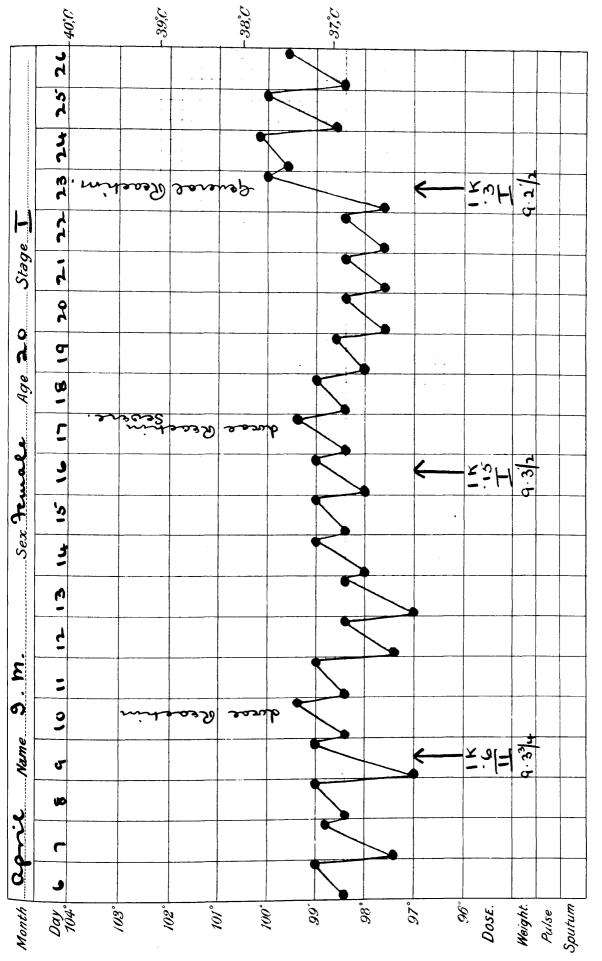


Chart XIV.

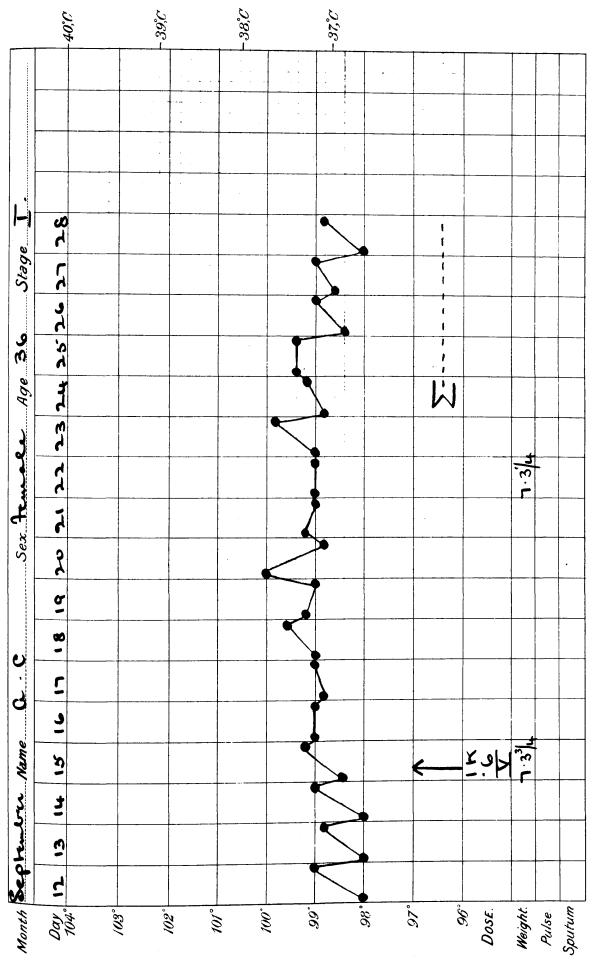


Chart XV.

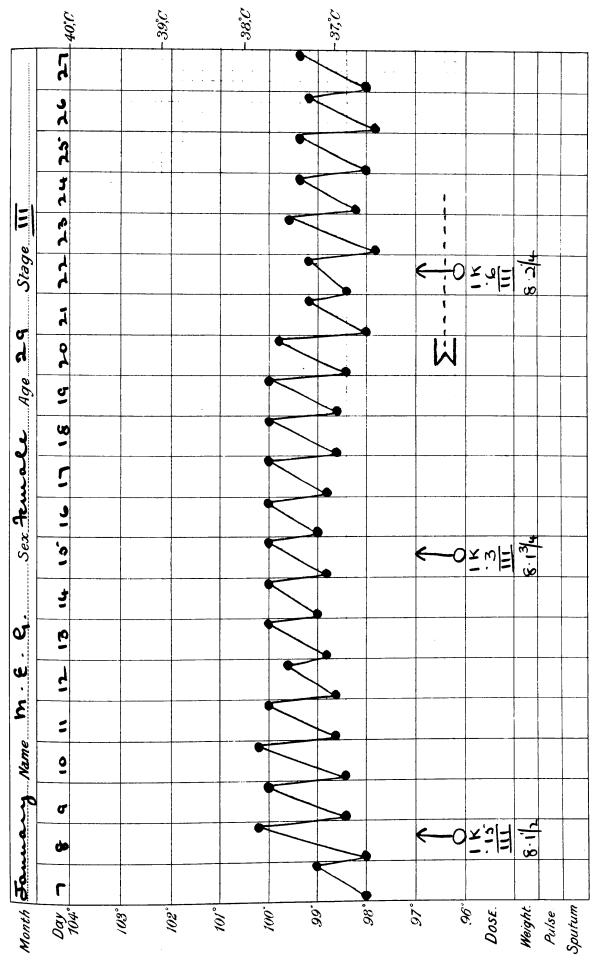


Chart XVI

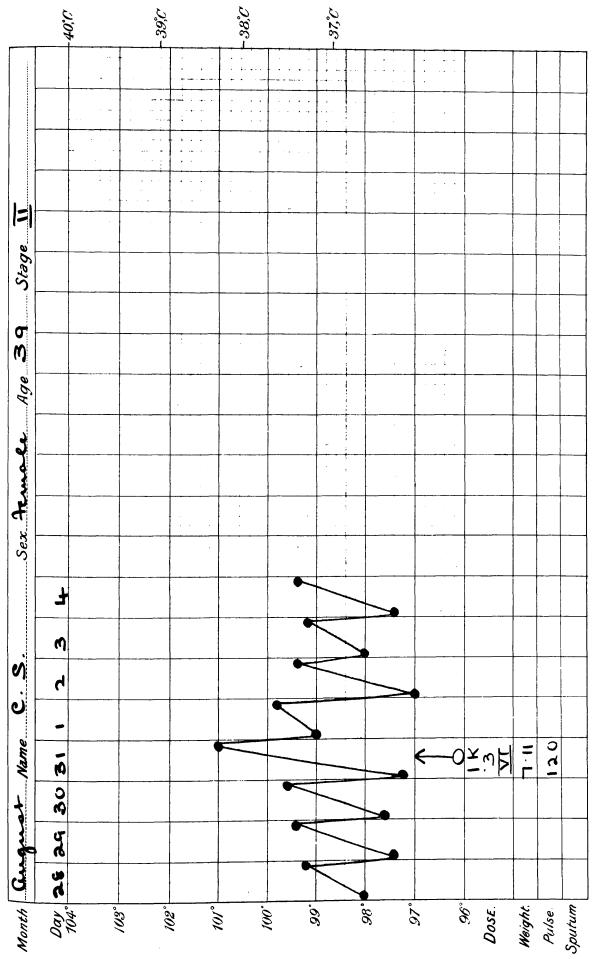


Chart XVII

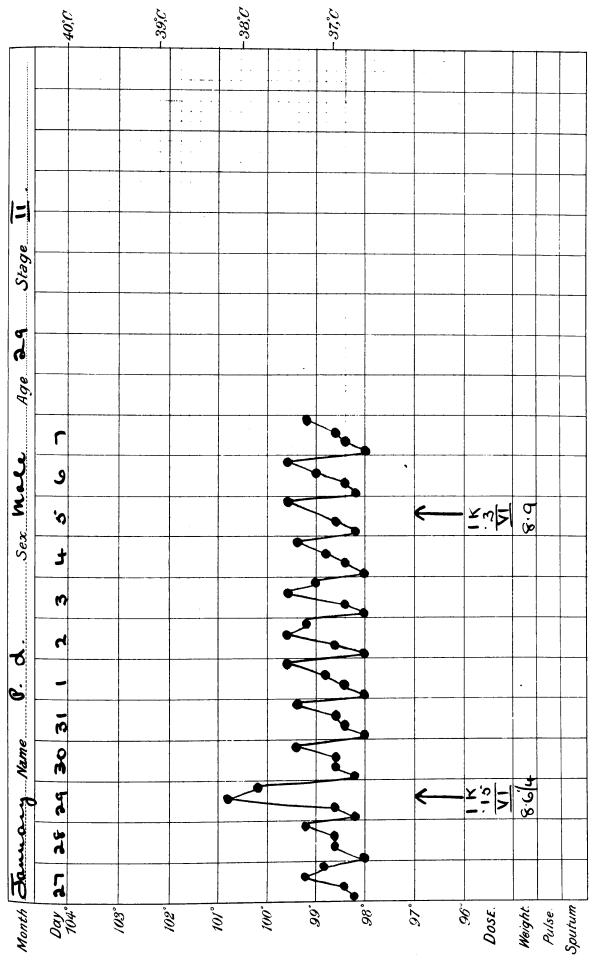


Chart XVIII.

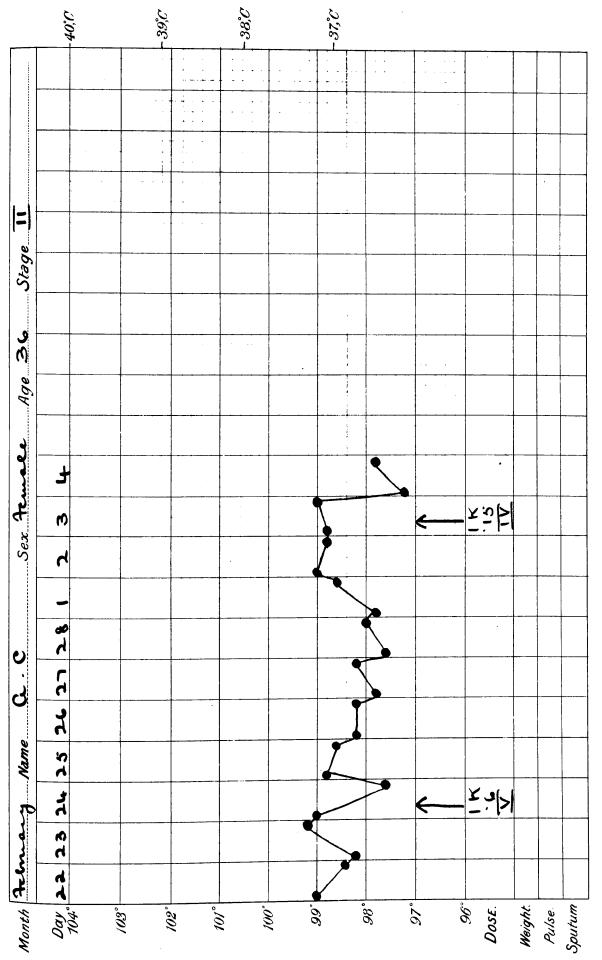


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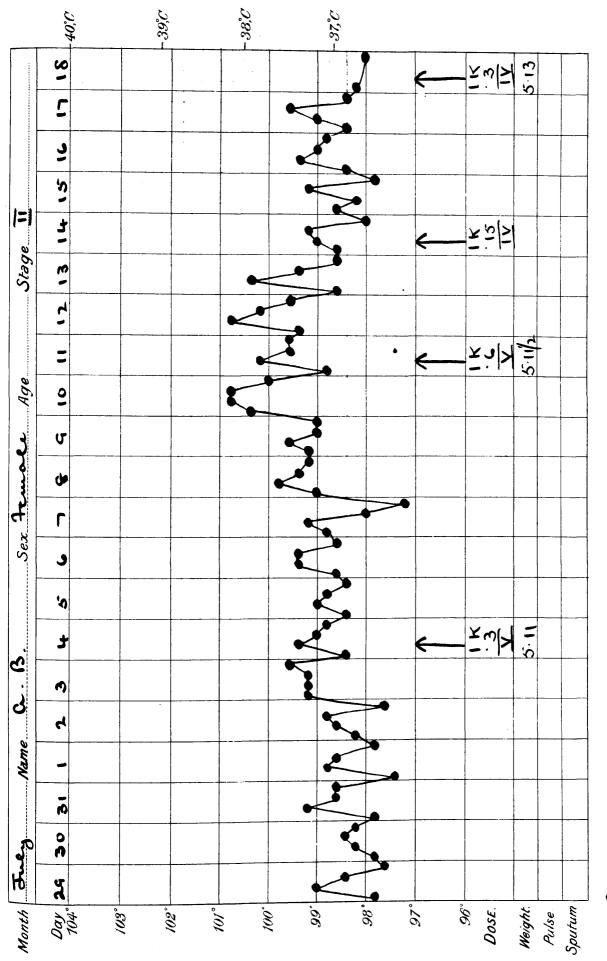
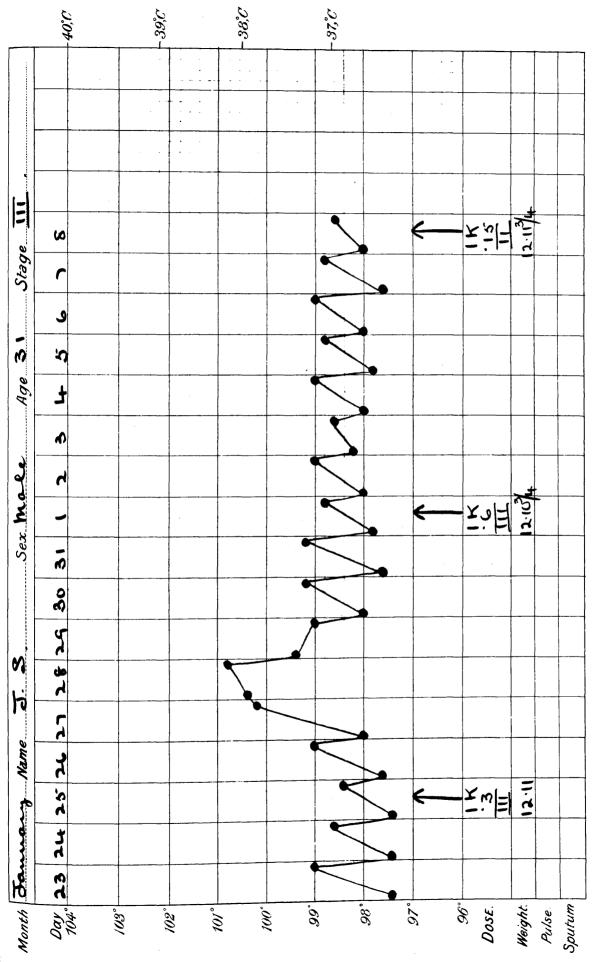


Chart XX.



CLANT XX1.

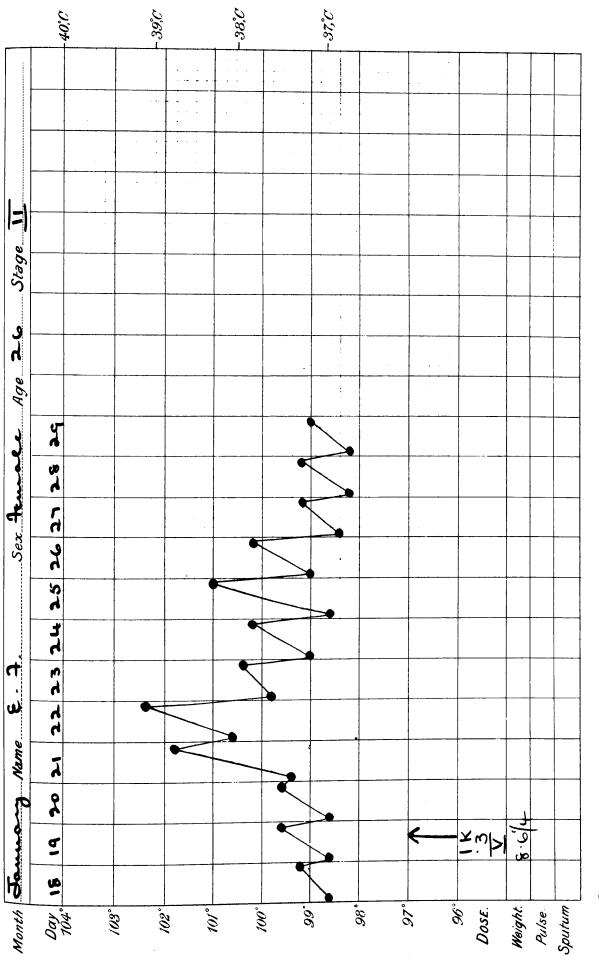


Chart XXII.

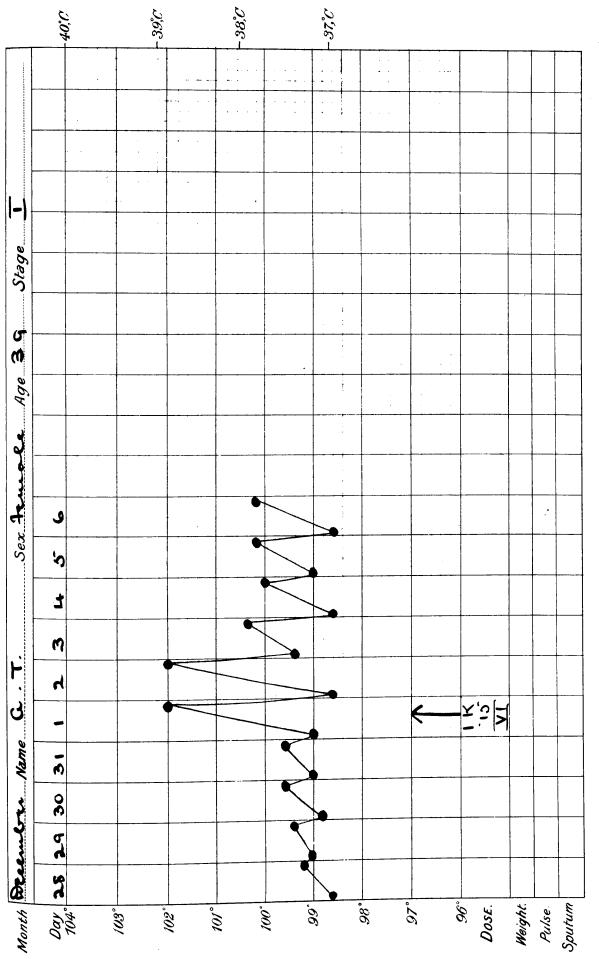


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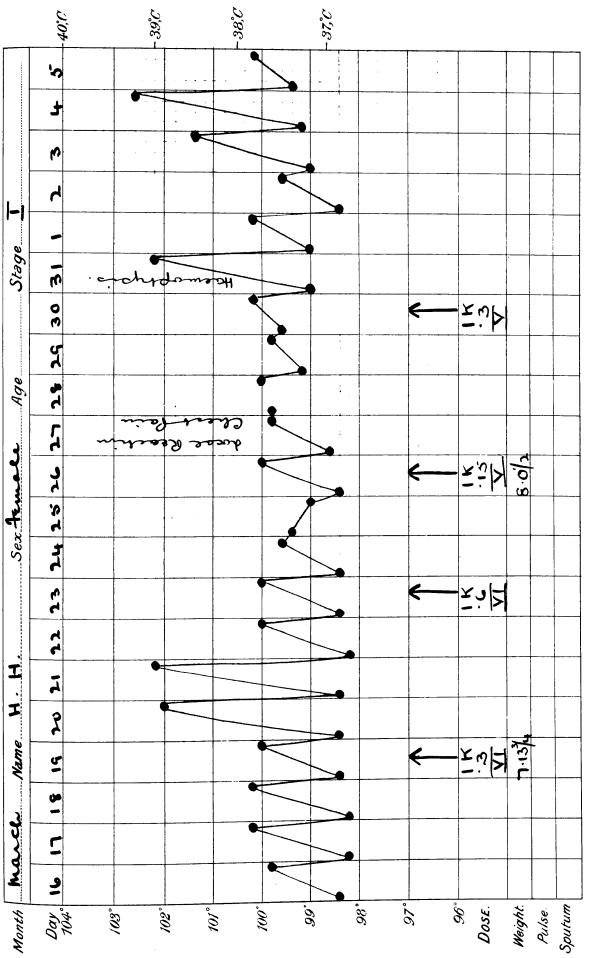


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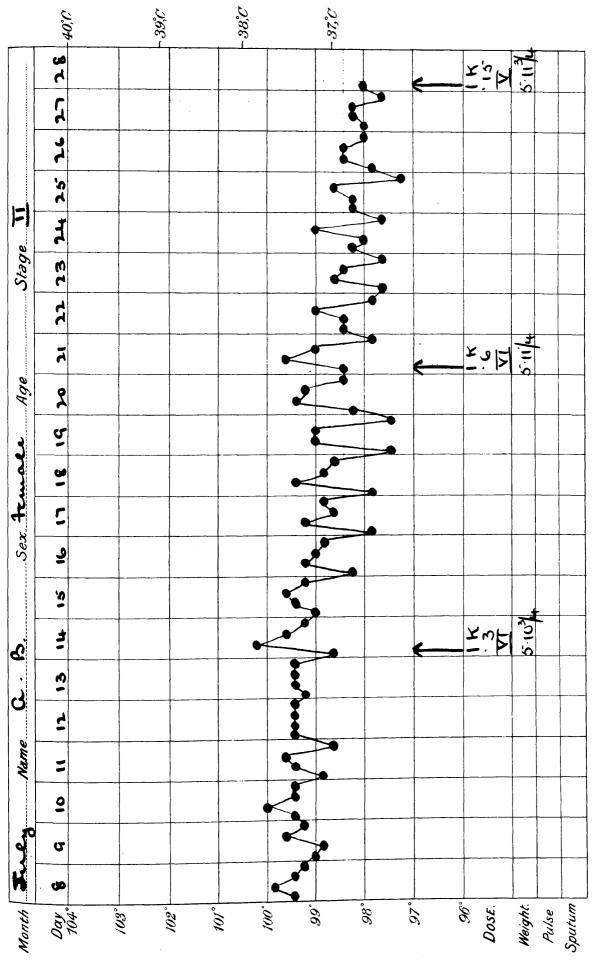
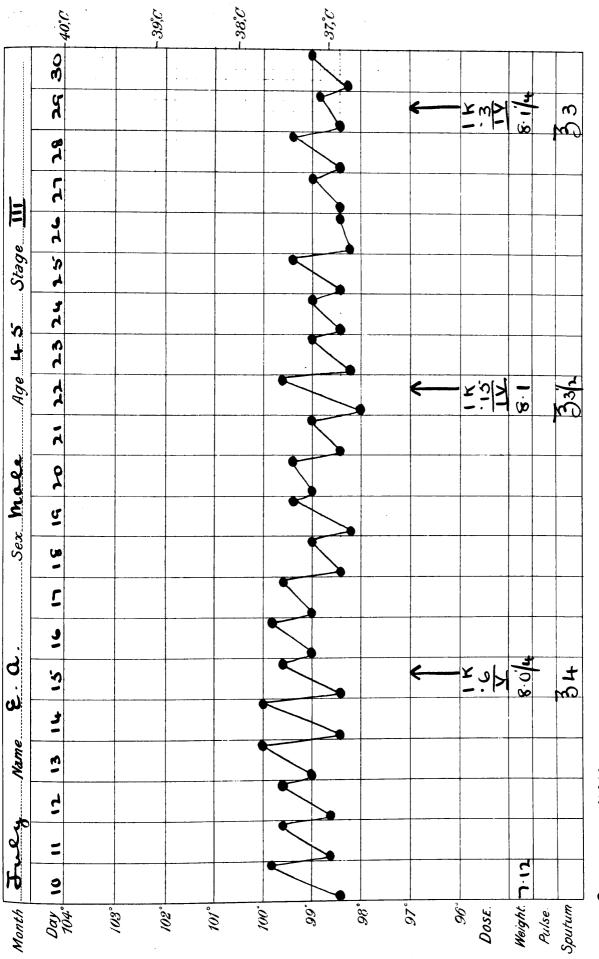
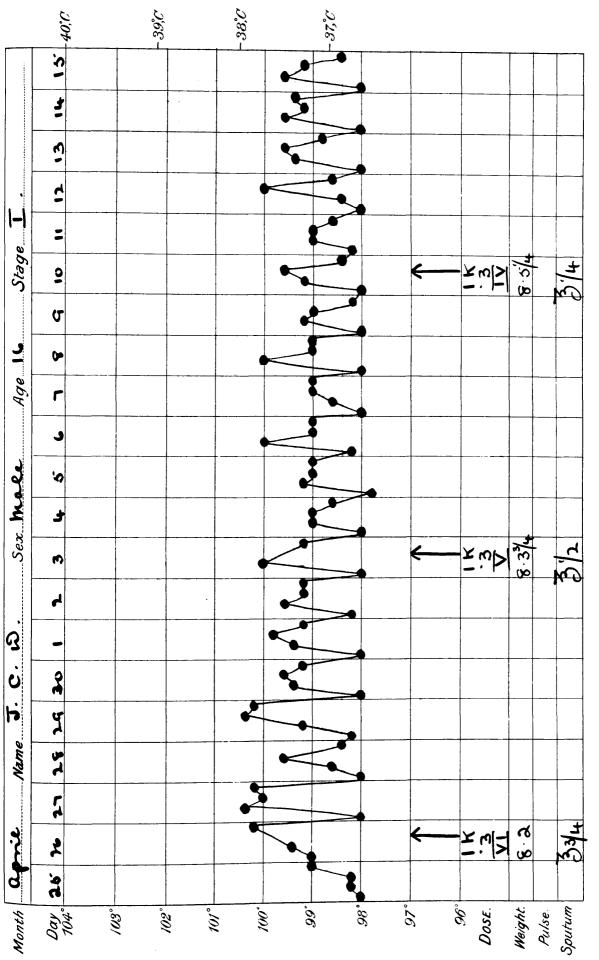


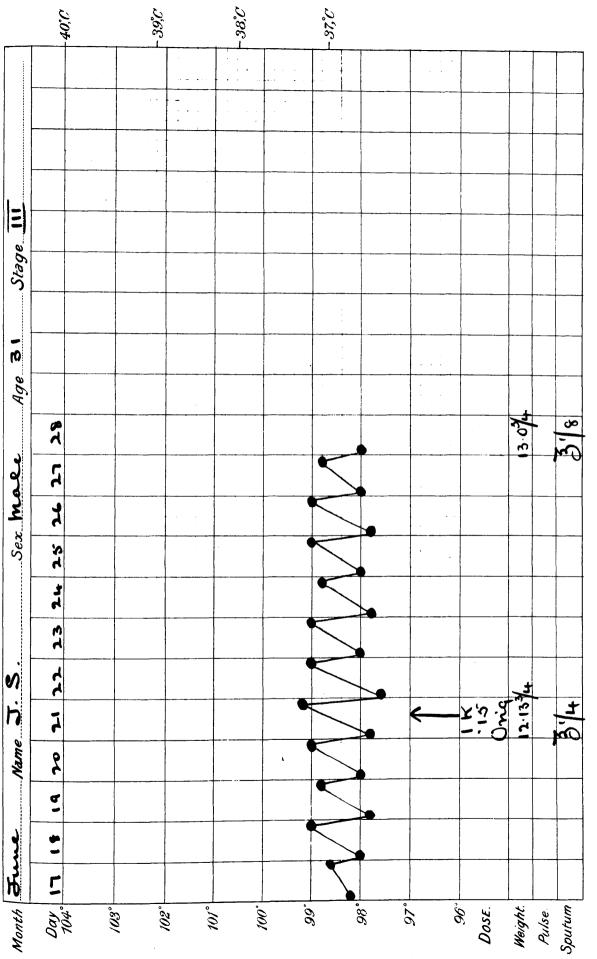
Chart XXV.



CLANT XXVI.



Cherry XXVII.



CLUL XXVIII.

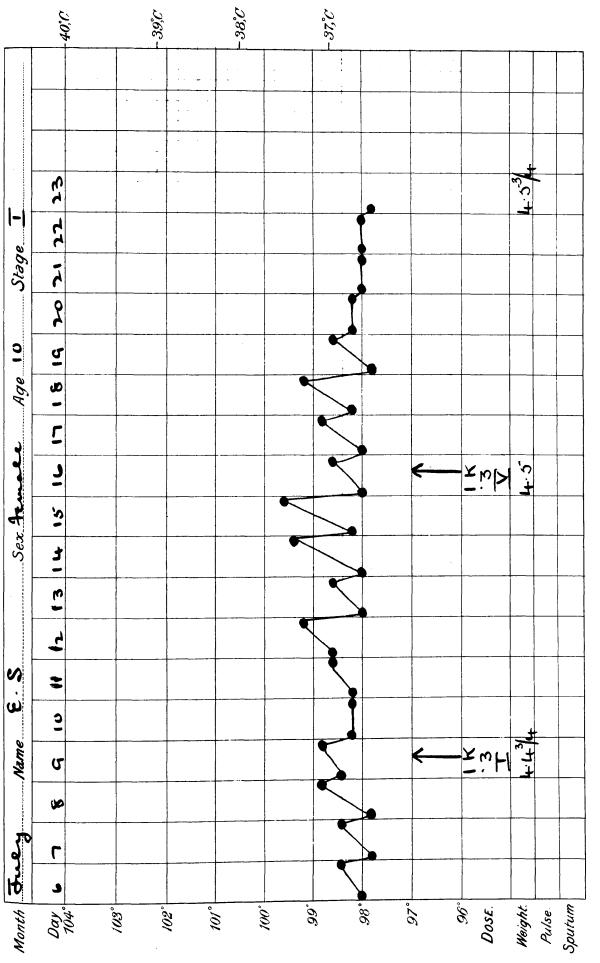


Chart XXIX.

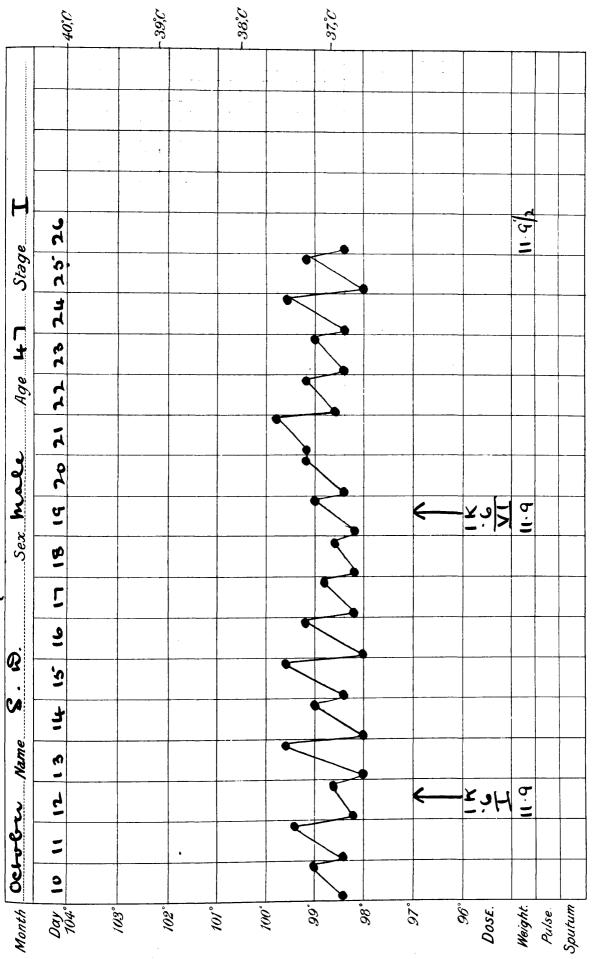
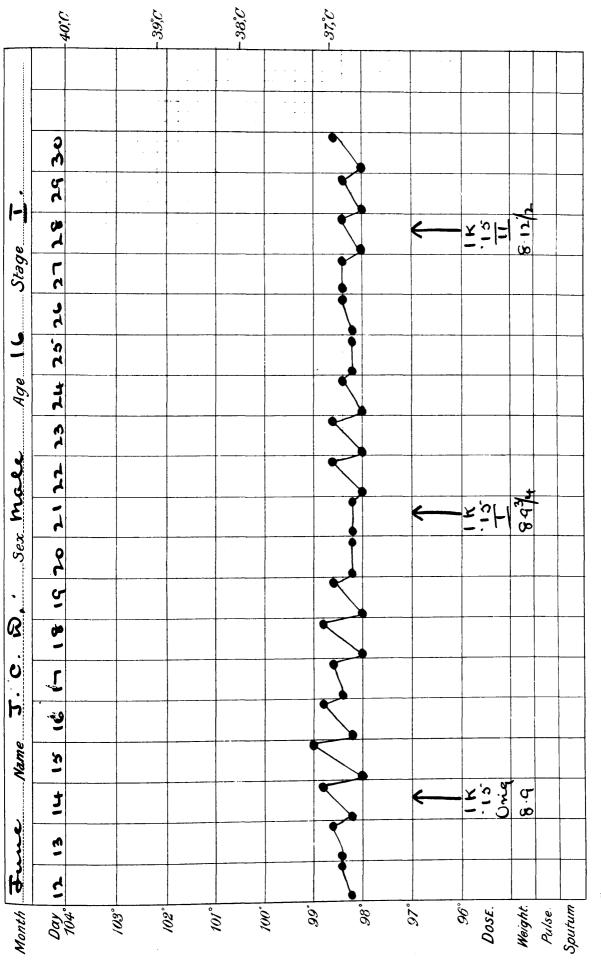


Chart XXX.



Ceart XXXI.

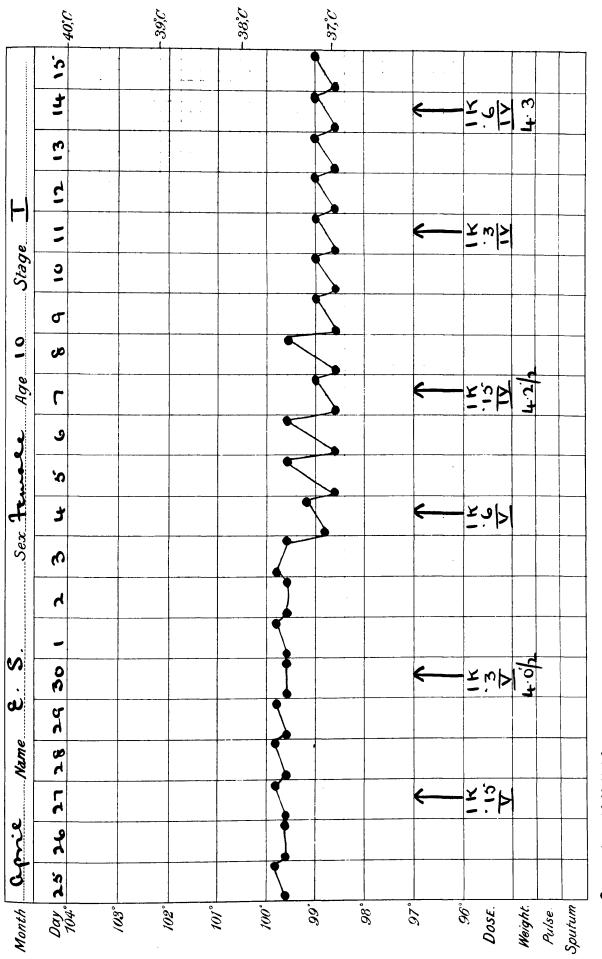


Chart XXXII.

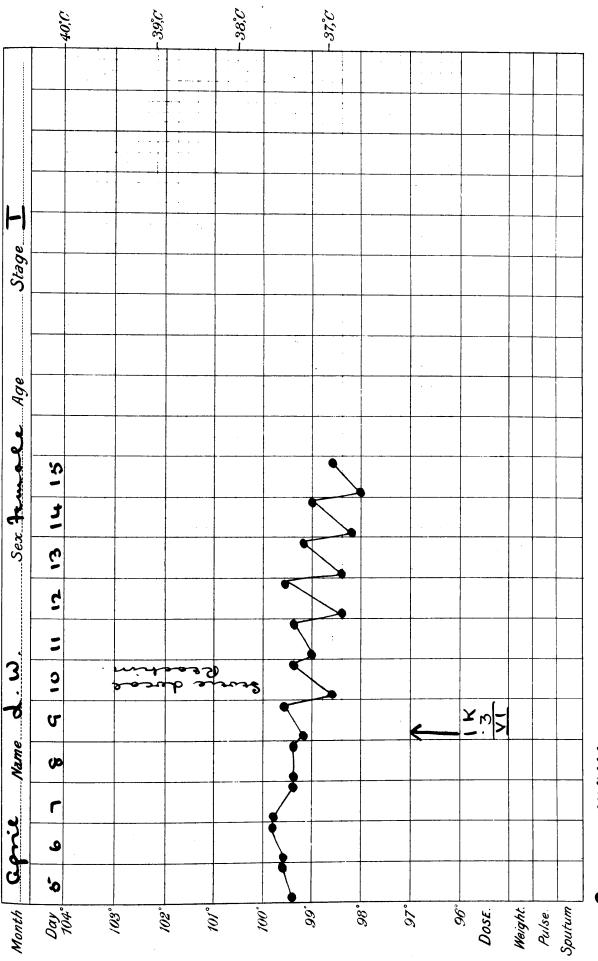
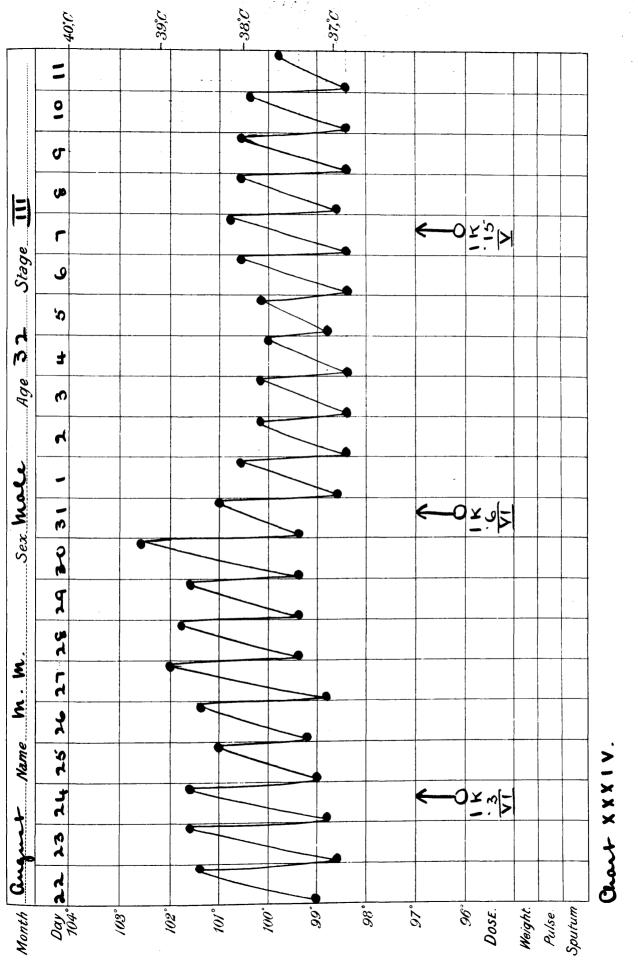
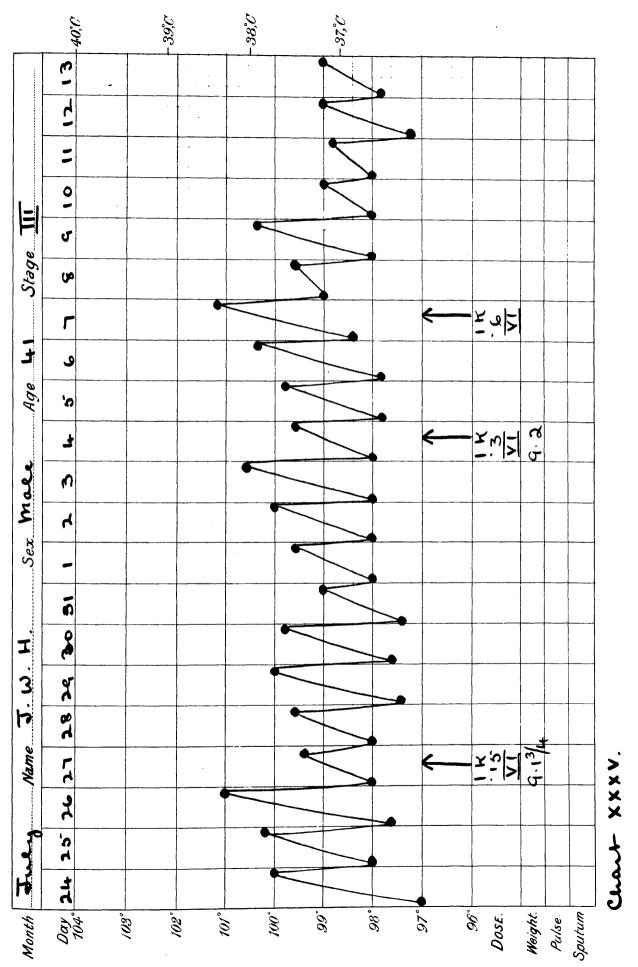


Chart XXIII.





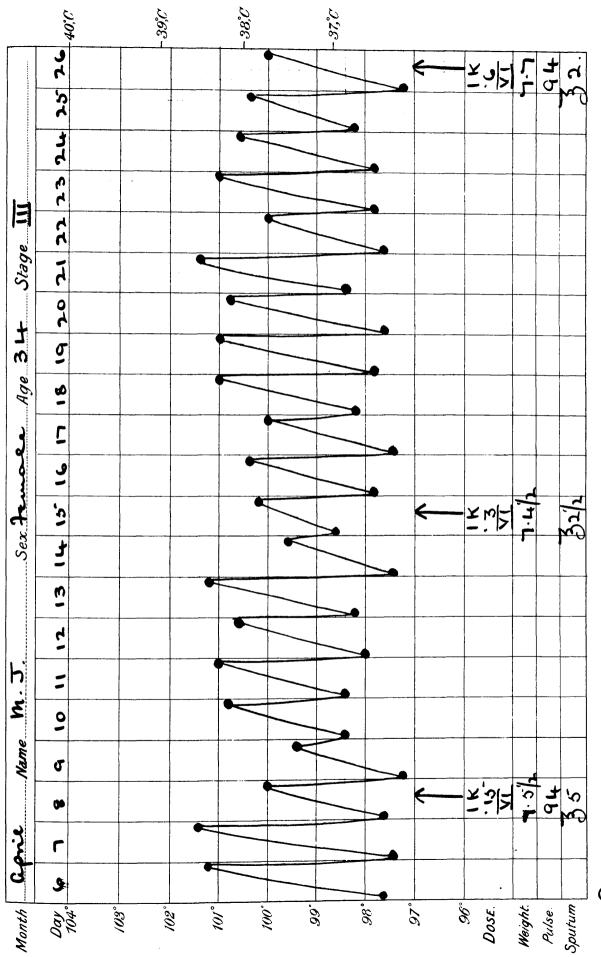
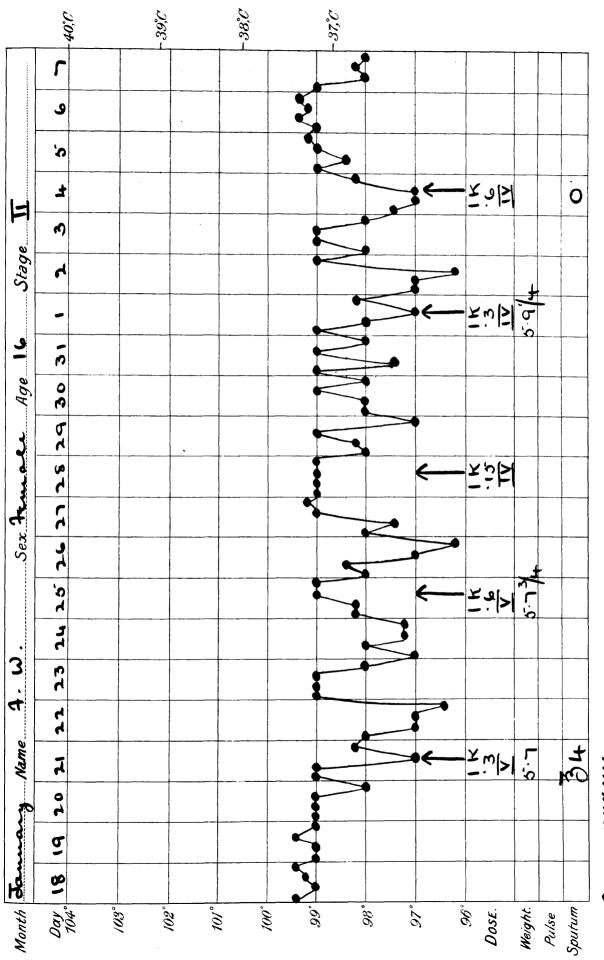


Chart XXXVI.



CALL XXX VII.

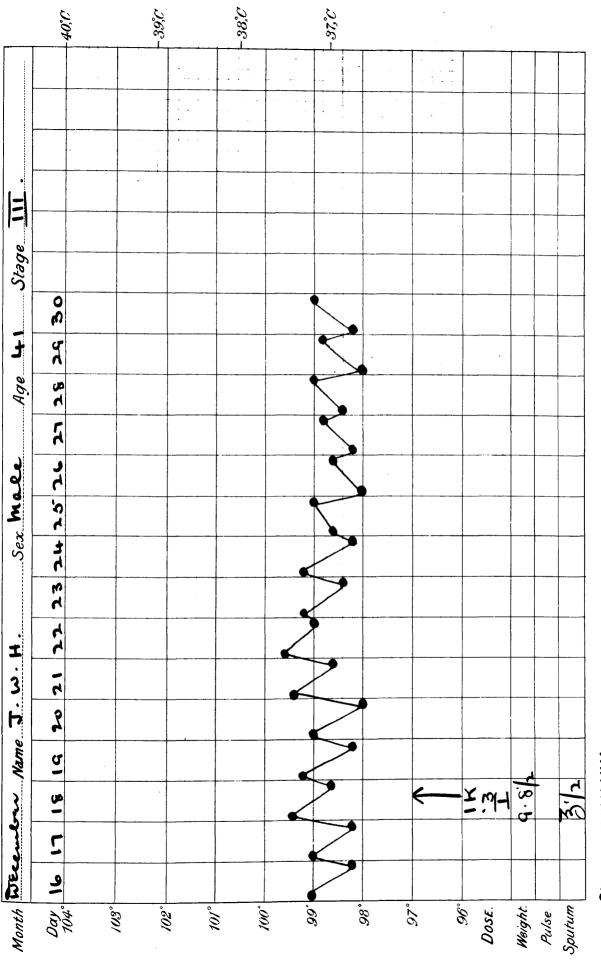
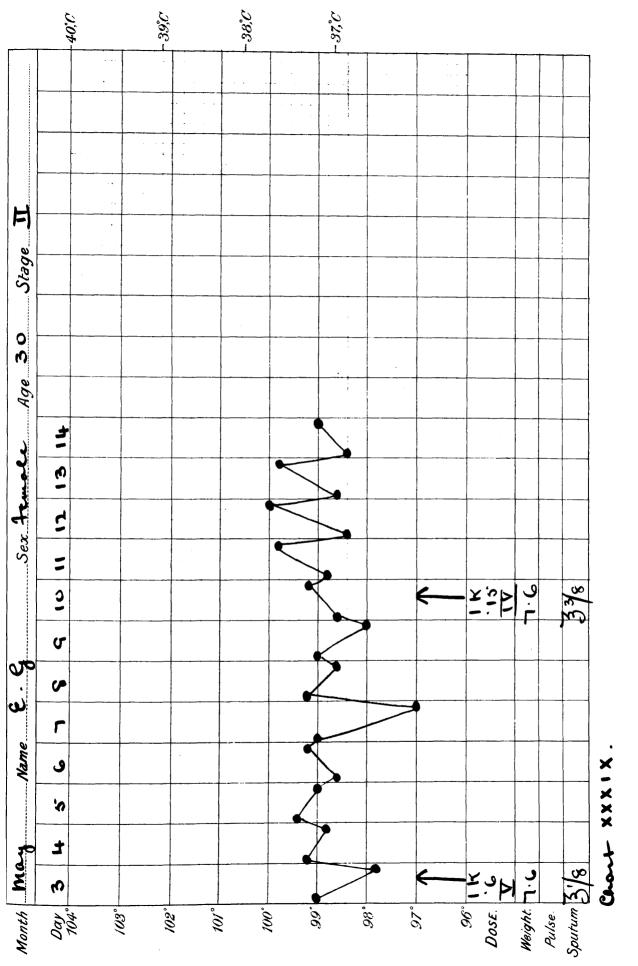
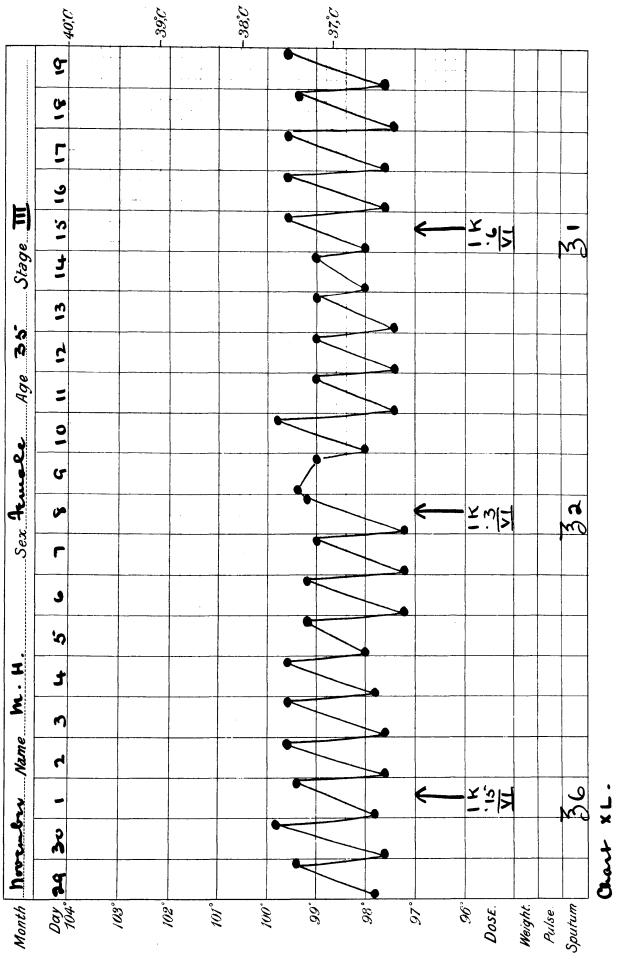


Chart XXX VIII.





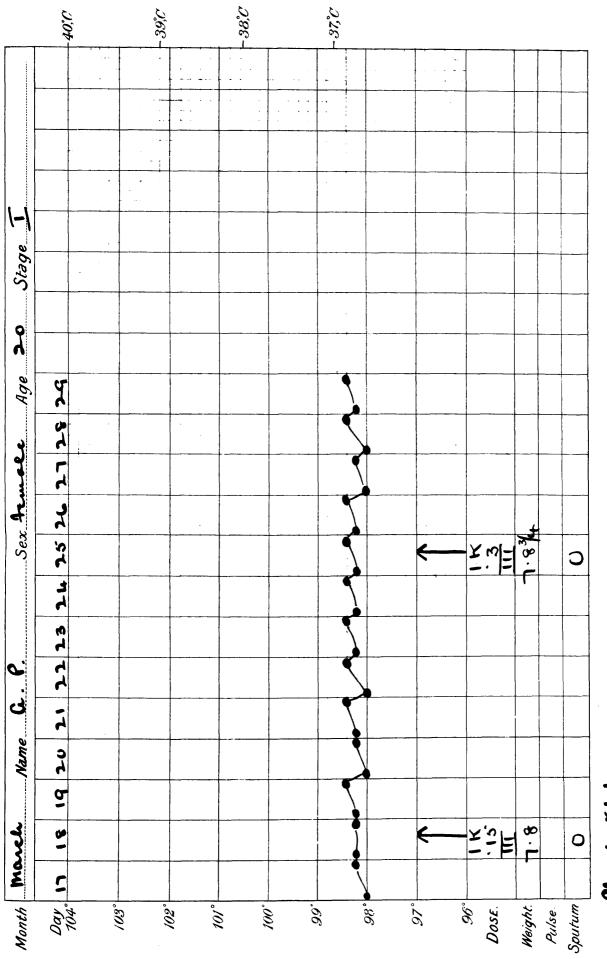


Chart XLI

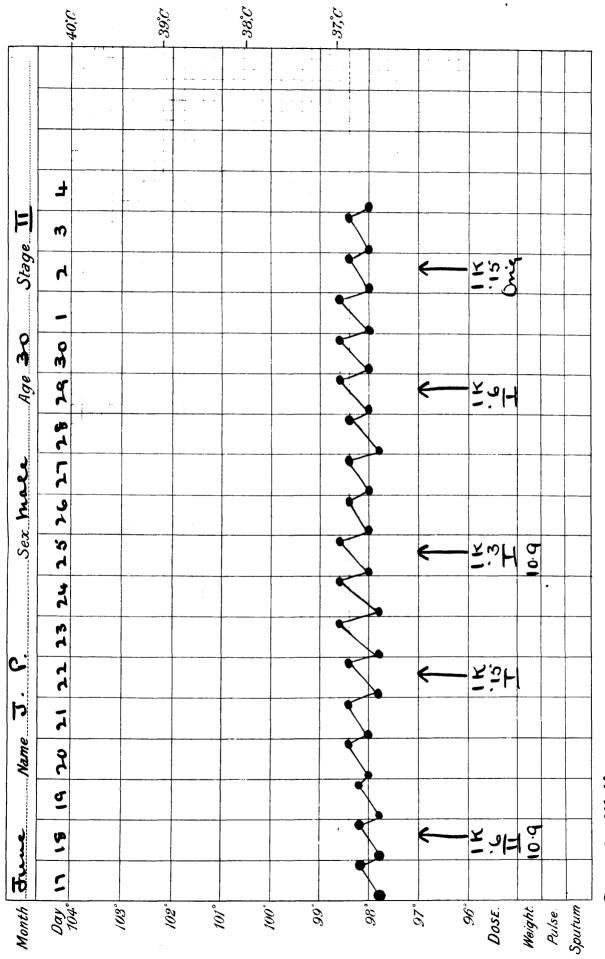


Chart XLII.