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THE ORGANIZATION OF FIELD TRIALS IN PROJECTS FOR THE CONTROL OF COMMUNICABLE EYE DISEASES

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I. Their usefulness in campaigns of prevention

The public health administrator who starts on mass campaigns against the communicable eye diseases, whether he is the head of a dispensary or of a national department, requires to be informed not only about the material and financial requirements, but also on the results achieved or to be expected. He cannot pledge expenditure, which is often considerable, without having a satisfactory estimate of the results which he expects.

Besides a knowledge of the geographical distribution of the disease and of its epidemiology, which will show him the groups of the population which have the greatest need of medical aid, he must also decide what methods of treatment can be used. What is more, he must be able at any moment to evaluate the results achieved in order to decide how the campaign must be carried on in future.

This information cannot be obtained from routine statistics gathered in mass campaigns, the main object of which is to inform the administrator about the running of the campaign and to enable him to know whether treatments have been administered as planned. An administrator can get very useful information from the experience and the results acquired on other occasions. But if he does not associate with his programme a parallel programme of experimentation and appraisal, he will not appreciate the results. Examples are not rare where such an association enabled the administrator not only to be well informed on the results which were obtained or possible, but also to make substantial economies, by demonstrating methods of treatment which were better adapted and more appropriate under local conditions.

And finally it should be noted that certain campaigns have only been possible because of a previous programme of trials which demonstrated methods of treatment which were sufficiciently economical.

If it is necessary to proceed to a review of the existing literature, we must know how to doubt the doubtful, and be convinced by the evidence of facts. In the publication of results obtained by means of some treatment or other, sometimes contradictions are seen which are often more apparent than real. Some people see in this a reason for considering such comparisons useless. On the contrary, it is just because of this that they are so useful, as these differences often reflect differences of time or place, of environmental or epidemiological conditions, such as the differences between vector agents, a greater or lesser total incidence of trachoma in the community, differences arising from the fact that different stages of the disease or sick people of different ages have been considered, or else differences in criteria of

diagnosis or appraisal, and in the administration of treatment, and by this means demonstrate very useful associations.

In spite of improved facilities for communication, we are still very badly informed about what has been done and found out elsewhere. It is necessary not only to ensure a wider circulation of articles, but also that authors should not limit themselves to listing the results obtained, but also publish the conditions under which these results were obtained : a description of the populations treated, of the treatments administered, their criteria for diagnosis and appraisal, etc.

Let us add finally that these trials are not only useful to find out new methods of treatment, but they also enable us to verify how far results obtained by other experiments in conditions which are often very different can be extrapolated and in addition they are essential to allow a critical personal judgement.

II. Principles governing therapeutic trials

Certain rules and certain fundamental principles of judgement and observation which are by and large much older than the modern statistical methods which have taken them up and developed them and at the same time given them almost an axiomatic value must be strictly respected in organizing therapeutic trials. On their observation depends not only the possibility of analyzing the results by means of modern statistical methods, but also being able to interpret them and drawing valid conclusions. Modern statistical methods are only a supplementary tool in the hands of the experimenter. In no case can they replace his technical knowledge, his good sense, and his critical spirit.

1. Principle I Determining the aims of the trial

The famous French physiologist Claude Bernard summed up this principle when he said: "When you do not know what you are looking for, you don't see what you find". Thus it is not physically possible to undertake a trial to measure the comparative effectiveness of the action of aureomycin and achromycin on trachoma; that is too vague and too vast an aim. For what is meant by comparative effectiveness? Is it the inhibitory power measured on cultures, or the relative effectiveness in reducing the signs of scarring or in cutting down the duration of the illness? Besides, can you talk of relative effectiveness if you do not define the method of treatment? Therefore the aim of the trial must be specified very clearly. In a trial you can study, for example,

if the percentages of cure three months after the end of treatment are higher among trachomatous children on first entering school who have intermittent treatment with achromycin than they are with the same type of treatment with aureomycin.

2. Principle II Comparison with a standard or a control

It is impossible to measure the effect of a treatment or its relative effect as compared with another treatment without comparing the behaviour of a group of patients who have received this treatment with that of a group, similar in all respects, left without treatment or who have received the standard treatment.

For example, with two similar groups of patients or subjects, you can :

(1) Administer the new treatment to the first group and leave the second group without treatment as a control to measure the absolute effect of the treatment.

(2) Administer the new treatment to the first group and administer the standard treatment of known effectiveness to the second to measure the relative effectiveness of the new treatment in relation to the standard.

The use of strict controls is not always possible. No one would leave a patient suffering from a cornal ulcer or gonococcal conjunctivitis without adequate treatment. In trials of long-term treatment, it is difficult to avoid patients getting medicines for themselves from the local chemist or elsewhere. It is always difficult to compare the effect of two treatments which are measured in the course of different experiments because of geographical or epidemiological variations, etc., between the two experiments. The comparison must be made at the same place at the same time by the same experimenters.

Control groups or those who receive the standard treatment must be in every respect similar to those receiving the treatment under study; the same external conditions, same distribution of stages of the disease, of ages, of sexes, etc.

In the case of slowly-developing diseases such as trachoma, it is possible to compare two periods of the disease separated by the treatment, the period before the treatment being taken as the control. Such a procedure generally allows a notable reduction in the individual variations discussed under Principle III.

We should note too that in certain illnesses it is possible to bring about a very appreciable gain in accuracy by applying to the same person either successively or simultaneously the two treatments to be compared in order to

eliminate individual variations in response. In comparing the relief of pain produced by analgesic drugs in cases of advanced cancer it is possible to alternate the two drugs to be compared and to note the apparent alleviation each time. In burns of the eyes we can only take into consideration patients having burns of the same severity in both eyes and try one treatment in one eye and the second treatment in the other.

Such a procedure might also be used with advantage in trials against trachoma or even against seasonal conjunctivitis. However, if the two treatments have different sterilizing qualities or if one eye is left as a control, it is relatively difficult to avoid cross-infection (transfer of germs or even of medicine from one eye to the other by rubbing of the eyes, or from pillows). Besides, such a means of administration requires very great care on the part of the personnel carrying out treatment, as mistakes are easily made. This does not exclude the possibility that in certain trials carried out on smaller series of schoolchildren or on patients in hospitals such plans of administration might be recommended. We are thinking chiefly of trials carried out in communities with a low prevalence of trachoma, where the collection of a sufficient number of comparable cases is not always possible.

3. Principle III Repetition

Variations in sensitivity and in tolerance to a therapeutic agent often vary enormously from one subject to another, and without repeating the experiment it is generally impossible to determine whether a difference found between two differently treated subjects is due to chance fluctuations or corresponds to the superior effect of one treatment as compared with another. It is only by repeating the comparison on a sufficient number of subjects, or conveniently chosen groups of subjects, that it is possible to eliminate, or at any rate reduce, the influence of these individual variations.

What is a sufficient number of repetitions and how can it be determined? In all trials there is an experimental error and the trial should be designed to enable it to be estimated. This error is composed of many intangible causes such as variations in tolerance, variations in the administered dose (by greater or lesser pressure on the tube of ointment certain subjects will receive larger or smaller quantities), variations in measurements and in diagnosis, etc. By repetition these errors tend on the average to balance out, and by increasing the number of repetitions the error affecting the comparison of the two treatments can be made sufficiently small in such a way that if an appreciable difference in effectiveness exists between these two treatments, for example,

a difference of 5% in the number of cures, it should be possible to measure it.

The number of repetitions necessary cannot therefore be fixed in advance once and for all. It depends both on the precision with which it is desired to compare the two treatments on the one hand, and on natural variations or experimental error on the other. For example : the greater the difference of effectiveness between two treatments, the smaller will be the number of repetitions necessary to make it apparent.

4. Principle IV Allocation of treatments at random

This principle is less clear than the others and must be applied with judgement. It can be stated as follows : if a certain number of treatments must be administered to a certain number of subjects or groups of subjects which are a priori indistinguishable, that is to say such that even for a qualified observer it is not possible to foresee that the prognosis will be better or worse among the subjects of the first group than among those in the second group, then the treatments must be allocated at random to different subjects or groups of subjects. Without this proviso that they must be indistinguishable, this principle can give rise to erroneous interpretation. If, for example, two treatments must be compared and there is available a group of 30 subjects of the same sex and the same age, suffering from the same type of trachoma, living in environmental and epidemiological circumstances which are comparable, etc., and thus indistinguishable from the point of view of prognosis, 15 subjects must then be chosen at random who will receive the first treatment, and the other 15 will receive the second. But if certain persons are suffering from trachoma at stage I, and others are at stage III, if some live in contact with other patients suffering from trachoma and others do not, the prognosis is different and it is not possible to speak of random subjects. In such a case, it is generally possible to subdivide the group into homogeneous sub-groups and allocate treatments at random within each sub-group.

5. Principle V Elimination of the psychological effect

A doctor knows that just his presence at the bedside of a sick person may often bring about considerable relief, and the fact of prescribing some treatment may also in certain cases have a similar effect. He knows too that he may have troube in making an impartial diagnosos; if he has prescribed a treatment which he knows to be effective, he may tend to look for signs of improvement and minimize the others. As far as possible therefore steps should be taken :

(a) to arrange the same sequence of examinations whatever the treatment given;

(b) to keep the people treated in ignorance of the type of treatment administered. This is often carried out by giving to control groups a placebo, i.e. a product of the same consistency, the same shape, the same colour and the same taste as the product used for the treatment of the other group, but containing only an inert substance.

(c) to keep those who carry out the examinations in ignorance of the group to which the people examined belong .

We should add that the usefulness of placebos is more evident and necessary in certain illnesses than in others where their usefulness may be questionable.

There is no placebo for a mechanical treatment such as electrocoagulation and a campaign against flies using a placebo by spreading an inert product is difficult to envisage.

It is similarly difficult to imagine a placebo for the treatment of instilling aureomycin ointment, as in the mechanism of action of this means of treatment the ointment itself may play a significant role.

In addition, during prolonged treatment patients receiving a placebo often realize that they have been "cheated" and refuse any further co-operation.

6. Principle VI Need for experimenting in the conditions under which application will be carried out

People will not think of claiming that since one treatment is superior to another against Koch-Weeks conjunctivitis, it must be the same in Morax-Axenfeld conjunctivitis, nor because some treatment brings about a cure in 80 cases in 100 in hospitalized subjects, it will do the same if this treatment is applied to patients at home.

It is no more certain that a treatment which has proved effective against trachoma in the absence of seasonal conjunctivitis will be equally effective in its presence or that methods of intermittent treatment which have been studied in Morocco and the effectiveness of which has been verified in other countries in the Mediterranean Region will also give comparable results among certain under-nourished populations of Asia.

III. Application to trials on trachoma

Bearing in mind the aim which he has fixed for his trial, the experimenter will chose :

(a) an experimental unit

(b) an experimental design

(c) criteria for appraisal and comparison

(d) the type, the frequency and the spacing of examinations as well as forms or cards necessary to record the information gathered

(e) the method of analyzing results which will have to be drawn up at the same time as the choice of points (a) to (d)

It has often been noted that the study of these five points makes it possible to notice certain lacunae in the details of the aim of the trial and thus to express it in a more clear and correct way.

The experimental unit is the smallest unit on which the effects of treatments are compared. When the two eyes of a patient are used to compare two treatments for burns, the eye is the experimental unit. In clinical trials in which pairs of patients are compared, the patient is the experimental unit. In trials of intermittent treatment in schools in Morocco, the class was the experimental unit. In trials of preventive treatment, the unit will normally be an epidemiological unit, in certain cases a family even, more often a district or a village.

Very many experimental designs exist and to review them all would be outside the scope of this work. They have been introduced principally to reduce the variation between the experimental units and at the same time to allow correct evaluation of the effect of different treatments. The choice of experimental design will largely depend on the associated causes which might influence the results of treatment, such as the age of the patients, the presence of complications or associated illnesses, the stage and severity of the disease, the environmental and epidemiological conditions such as the relative abundance of cases of trachoma in the community or the presence of other cases in the family, etc.. Whenever possible, it is useful to adopt an experimental design such that the experimental units compared are made up of subjects of the same age and the same sex, at a similar stage of the disease, and living under similar conditions, in order to reduce the influence of these associated factors.

As we have shown previously (see page 6), the number of experimental units depends on the variability between the units and on the precision with which we require to estimate the differences between treatments. It is impossible to give strict rules for fixing the number of repetitions or experimental units. It is a question where experience, scientific knowledge and the critical spirit of the experimenter play the principal role. The literature on this subject, as on points (a) and (e) is abundant (see the works cited, 1 to 4).

The number of repetitions also depends on the criterial for appraisal and comparison which are chosen. Thus it will generally suffice to take fewer patients to compare the lowering of temperature produced by two treatments in cases of bacterial pneumonia, than are needed to compare their effects on the percentages of complications and sequelae.

These criteria of comparison vary according to the illness and the aims of the trial. For therapeutic trials, the fundamental criteria are : the outcome, the duration, the complications and sequelae, the course of the disease as measured by its severity and by the presence of certain signs.

In trials of preventive treatment, the frequency of new cases must also be considered and the age at onset of the disease, which are measures of the lessening of the risks of transmission or the increased immunity of the subjects.

Relying on one criterion alone can lead to erroneous conclusions. For example, it is not enough to compare two treatments against trachoma solely on the basis of the duration of the illness after the start of treatment, or of the percentages of cure obtained, but the restorative value of treatment based on residual signs of scarring must also be studied. It is often useful to consider a yardstick which takes into account several of these criteria. For example, the frequency of acute conjunctivitis in a community takes into account at the same time the frequency of new cases, and the severity and length of the illness.

Without in any way wishing to minimize the role and the value of trials carried out in hospitals or on isolated patients in outpatient departments, we will exclude them from this work in order to concentrate more especially on trials dealing with the application and the measurement of the effectiveness in the field of mass treatment.

These trials in the field must not be started with the sole aim of measuring the effectiveness of treatment on certain groups of the population under certain conditions, but also - and this aspect is too often neglected - to study the practical nature of the treatments and improvements which can be made to them in order to make their application easier. For example, in Spain it has been noted that intermittent treatment gave excellent results in children who received the full course of treatment, but because of high absenteeism, it was preferable to increase the number of sessions of treatment in order that all the schoolchildren received at least a certain number of doses.

In the following paragraphs as examples we have described certain experimental designs encountered during the course of trials against trachoma. We have

considered only the simplest designs in the case of comparison of two treatments.

1. Application to school trials

In many regions, it has been noted that the majority of cases of trachoma are contracted before the age of 15 and that among young children forms without scarring predominate, and these are the forms in which modern methods of treatment give the most marked results, the active signs often resolving without leaving scars. In these regions, where it is naturally preferable to treat these children of pre-school age and of school age, treatment of children is often carried out in the school itself because of the ease of supervision and administration.

Aim. Principally to compare the curative value of the different methods of treatment.

Experimental unit. The class is often taken as the experimental unit and compared with a class at the same scholastic level or one composed of pupils of the same age within the same school. Theoretically, it would be preferable to administer the two treatments to be compared within each single class, but this method comes up against considerable administrative difficulties and is not always free from error. It is not safe to consider a school as an experimental unit, as between children going to two different schools there are usually environmental and socio-economic differences, and differences in overall frequency of cases of trachoma.

Experimental design. The experimental design generally used is known under the name of randomized blocks. Within the same school treatments are compared on two classes in the same age group or at the same scholastic level in order to avoid differences of response due to age and in order to have comparable distributions of the different stages of trachoma. If classes at different academic levels are considered, comparisons must be made within the same age group. It is necessary that the personnel carrying out the treatment should be the same in the two methods being compared. (In certain cases, however, it may be that we wish to study the relative effectiveness of the same treatment applied by different personnel. For example, comparison of the effectiveness and of the practicability of intermittent treatment carried out either by nurses or by the teachers themselves).

Example of distribution in randomized blocks

(in each block the distribution of classes for various treatments is made at random)

Block	School	Treatment a	Treatment b
I	A	Class 1 (6-9 years) Boys 1st level	Class 2 (6-9 years) Boys 1st level
II	A	Class 3 (6-10 years) Girls 1st level	Class 4 (6-10 years) Girls 1st level
III	A	Class 5 (8-10 years) Boys 2nd level	Class 6 (8-10 years) Boys 2nd level
IV	B	Class 1 (6-7 years) Boys 1st level	Class 2 (6-7 years) Boys 1st level
...	...	.....	.....
...	...	.....	.....
X	E	Class 1 (8-11 years) Boys 3rd level	Class 2 (8-11 years) Boys 3rd level

Leaving aside those cases in which the differences of effectiveness between two treatments are obvious and can be estimated with a small number of patients, it will be necessary to have a minimum of 100 children at the same stage and severity of the disease for each treatment. In certain cases it will be necessary to start the trial with 150 children initially to take into account the possible losses during the trial (6).

Criteria for appraisal. The number of cures is considered as the principal criterion. For more detailed classification, treated cases can be distinguished by :

(a) no improvement or very little;

(b) clear improvement without cure;

(c) probably cure "x cases"; and

(d) clinical cure.

It is also necessary to measure the curative effect of different treatments by comparing the number of active signs and signs of scarring before and after treatment with each.

Type, frequency and spacing of examinations. It is essential to carry out a complete examination of the trachomatous patient before the start of treatment and from 3 to 6 months after the end of treatment. If treatments of different durations are compared, it is a good thing to carry out the two corresponding examinations at the same time. Patients are usually also examined at the end of treatment. When treatments are of different lengths it may be difficult to interpret the results of these examinations.

The individual card with marginal perforations is particularly appropriate for these tests. It is in addition necessary to give to those carrying out the treatment a notebook containing the names of the pupils treated and in which details of treatment actually administered are entered against the name of each pupil.

Analysis of the results. The analysis is carried out by using as a basis a comparative table showing the stages and severity of the trachoma before treatment and after the follow-up period. A separate table must be prepared for each age group, if possible for each sex, for each type of treatment, and, if necessary, for each class. When certain children have not received the complete prescribed treatment, they can be left out. However, when we are interested in the overall results of treatment and not in its effect under ideal conditions, it is necessary to take into account these insufficiently treated cases. Then for each treatment the number of cures is calculated with reference to the stage and the degree of initial severity as well as the number of doses received, usually expressed as a percentage of the number of prescribed doses.

This criterion of appraisal only takes into account the direct effects of treatment among trachomatous children. It is legitimate to ask whether this method of prophylaxis has any effect on the rest of the population. In communities where the standard of school attendance is high, the effect can be estimated by comparing the numbers of trachomatous children in successive school entries. However, this method by itself is not applicable when only part of the children of school age go to school. In this case large annual variations may be found in the prevalence of trachoma among children going to school for the first time, because of annual variations in the number going to school from the different strata of the population.

Finally, it should be noted that in certain areas with a very large total frequency of trachoma and in those where seasonal conjunctivitis is abundant, it is often an advantage to treat all the schoolchildren, whether they are trachomatous or not.

2. Application to curative trials in communities

In certain regions where the number of cases of trachoma is fairly small treatment is carried out on all the cases in the community after systematic screening.

Aim. To compare the curative and the preventive value of different methods of treatment.

Experimental unit. Following systematic screening cases which are discovered are divided into several groups, generally in districts, in blocks of streets or in villages. Within each group the cases are again divided into two homogeneous groups, each of which receives a different treatment. The sub-group is then the experimental unit. Before making this division of cases and groups it is sometimes a good thing to exclude certain extreme cases, e.g. persons suffering from complications, and persons temporarily absent. These cases are nevertheless treated but are not taken into consideration when appraising the results.

The experimental design is a plan in blocks arranged at random as the following diagram shows :

Example of division in randomized blocks

(in each block the allocation of different treatments for the even sides and odd sides of the roads was carried out at random)

Block	Treatment a	Treatment b
I (District A)	Even street numbers	Odd street numbers
II (District B)	Odd " "	Even " "
III (District C)	Odd " "	Even " "
.....	.....	.....
.....	.....	.....
VIII (District H)	Even street numbers	Odd street numbers

The criteria for appraisal and for comparison are generally the same as in the example of the school discussed earlier.

However, such a plan may present difficulties in application. Often in the same street the same health worker will have to treat two sick people with two different treatments, and risks of error and similarly difficulties in appraisal of the practicability of treatments may spring from this. Besides such a method of procedure does not enable an estimate of the preventive value

of treatments to be made. If, in fact, in the years following the treatment a diminution in the number of new cases is noted, it will not be possible to ascribe it to the action of one of these treatments more than to the other.

It is possible to proceed as follows : group the different districts or blocks of streets in towns or large villages, or villages themselves, in homogeneous pairs in such a way that two units of the same pair enjoy similar conditions, the same socio-economic level, the same conditions of life and health, and have the same overall incidence of trachoma. In each pair one treatment is given to one community, and the other to the other, the community being the experimental unit.

Example of a plan of treatment district by district

Block	Treatment a	Treatment b
Block I	District A	District B
Workers, poorer classes	% Tr 65	% Tr 59
Block II		
Workers and small artisans (middle class) old houses	District C % Tr 38	District D % Tr 37
Block III	District E	District F
Small farmers and market gardeners	% Tr 47	% Tr 44
Block IV		
Workers and small artisans recently arrived from the country (newly built houses)	District G % Tr 74	District H % Tr 81

It is desirable that the same personnel should carry out treatment in the two units of the same block. However, it is difficult to eliminate completely the influence of the personnel carrying out treatments as it may happen that the same person can establish excellent contact with one group and fail completely with another.

In these trials, the numbers to be considered must be much higher than in the trials in schools. To estimate the preventive action of treatments, it will generally be necessary to carry out repeated examinations every year, or every two years, of the whole population and to distinguish among the new cases, between those contracted within the community and those imported from outside. It is not safe to estimate this preventive aspect using the indexes of dispensaries

as a basis as they only normally deal with part of the existing cases.

We must remind you also of another type of situation where the sick are included in the experiment as and when they are found by the dispensaries. This method is convenient to compare isolated treatments in communities with a low total frequency of trachoma, e.g. treatments in communities left under observation after a large number of cases have been cured by intensive treatment. The doctor decides the criteria for grouping the cases which are discovered according to age, sex, the stage and severity of the trachoma, and socio-economic conditions, etc. When a sick person in a certain group comes to the dispensary the doctor chooses at random the treatment which he will be given, and the next sick person of the same group to come receives the other treatment. An excellent description of this method, which is very well known, is to be found in Herdan's work (2).

Follow-up examinations and the principles for the analysis of trials of this type are similar to those of the school trials discussed previously.

3. Application to trials of preventive treatment

In regions where the total frequency of cases of trachoma is high and in those where the associated eye infections are numerous, it is usual to treat the whole population.

Aim. The comparative trials of such treatments have as their aim a comparison of their preventive and curative value against trachoma and also against associated infections.

Experimental unit. The experimental unit must be an epidemiological unit. These treatments are applied in particular to rural or semi-rural populations, and the village has generally been considered as the experimental unit.

Experimental design. The experimental design depends on local conditions and on the possibility of finding in a limited area a sufficient number of comparable units. Generally six villages or three pairs of villages which are comparable are the absolute minimum which is adequate to compare two treatments. In the trial which was carried out in 1954 in South Morocco in order to compare the effect of 3 treatments using a control, 16 units were necessary (8).

As far as possible the units compared must have:

(a) comparable distribution of the cases of trachoma and also of those of associated infections;
(b) comparable environmental conditions: number of population, type and density of the inhabitants, climate, altitude, etc...

(c) comparable hygienic and economic levels, ethnic distribution and living habits.

The experimental unit should not be composed of less than 400 inhabitants in order to have a sufficient number of similar cases in each unit.

Often little villages are amalgamated to form a unit, but you should for example avoid comparing a unit made up of two villages with 150 and 300 inhabitants respectively with another unit formed of a village of 450 inhabitants.

If it is necessary to spread the treatment over the whole population of the unit, it will generally be enough to consider only a fraction of the inhabitants of the unit in order to appraise the effect. For example, the agricultural population or people up to the age of 20. In certain cases it has been useful to choose in each unit identical groups of the same size, for example, 100 children from 0 to 6 years, 100 from 7 to 14 years, 100 people from 15 to 24, and 100 of 25 and over, the choice of subjects in each of these groups being made at random after a population census. It is necessary to choose 120 to 150 subjects in these different groups when final comparisons are to be made on 100 people in order to allow for possible losses.

Criteria of appraisal and comparison

Criteria for appraising the curative value of treatments are generally the same as for the school trials described in III.1. The preventive value of treatments is generally estimated by the diminution in the incidence of new cases and the later age of onset of the disease in the different units.

Type, frequency and spacing of examinations and analysis of results

Three examinations are generally adequate, as described in III.1, to evaluate the curative effect of treatments against trachoma. However, their preventive effect often does not make itself appreciably apparent until long after the end of treatment, and it is therefore necessary to carry out follow-up examinations every year or every two years of the whole population, including newborn children and people who have recently arrived in the unit.

The frequency of new cases depends not only on the effect of the treatments, but also on the particular epidemiological situation of the unit. If it has not been possible to eliminate or limit the effects of these peculiarities by an appropriate choice of units and of the experimental design, it will be necessary to compare in each unit the frequency of new cases after treatment with the

frequency observed before treatment. Similarly, it is possible to compare the increase in the prevalence of trachoma with age which is noted in the course of successive examinations.

It will generally be essential to establish a register of the population in which various conditions such as the degree of hygiene, the mode of life, etc... will be recorded for each person. This register will be of the greatest value in research on causes of relapse and new infections.

The appraisal of the effects of treatment against associated seasonal conjunctivitis will necessitate another set of examinations. The frequency of acute forms of conjunctivitis observed at regular intervals during the course of the epidemic period in various age groups has been used to estimate the immediate effect of treatment. It is possible to appraise the long-term effects of treatment by comparing year after year the frequency of acute conjunctivitis at a particular moment, for example at the peak of an epidemic (8).

IV. Summary

Field trials are essential to form a correct estimate of the results of programmes of campaigns against trachoma.

These trials must be carefully prepared. Among other things it is necessary to adhere strictly to certain fundamental principles which are described in part II when organizing these trials, i.e. to choose an experimental unit, the experimental design, criteria of appraisal and comparison, the type, frequency and spacing of examinations, and the method of analysis of results.

These considerations are illustrated in the last pages of this work by a discussion of certain types of field trial in the battle against trachoma.

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