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METHODS OF TREATMENT OF TRACHOMA

by

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Treatment of trachoma has undergone a dramatic evolution during the last two or three decades by the introduction of chemotherapy and antibiotics; and great possibilities of further exploitation have been opened up by the recent isolation of the virus of trachoma, the study of its cultural properties, its serological and other reactions, its sensitivity and immunology and by the study of its morphological phases and of the cytological and tissue changes by the electron microscope. When discussing the treatment of trachoma, it may be adequate to reflect back on the old conception of the object of treatment of trachoma, i.e. development of scar tissue with resorption of the follicles or papillae or amelioration of the complications or sequelae of the disease. Such objective was sought mostly by cicatrizing agents or even by escharotics or by rough mechanical treatment which led in many instances to aggravation of the complications and sequelae rather than amelioration. During the last decades, however, the tide gradually turned towards attention to the general treatment, auxiliary factors were brought into play and preventive measures adopted which tended to assume an inter-regional and then an international status. Thus the modern trend is to consider the management of trachoma from both its curative and preventive angles on an international basis and the problem of its control is now one of the objectives of the World Health Organization.

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It is important when considering the various methods of management of trachoma to stress the necessity of early correct diagnosis and early treatment. The criteria for cure must be standardized, not only the clinical cure but also the radical (Mitsui) by laboratory methods which have to be simplified and made accessible for every day use.

In countries where trachoma is endemic and incidence is high, the clinical diagnosis and laboratory investigations are easy but owing to the presence of chronic carriers, reinfection or relapses and viral or bacterial superinfection, it may be difficult to know by a simple method if a trachomatous subject has been rid completely of the trachoma virus. The criteria for cure in individuals have to be more elaborate than those for masses which have to be simplified and adapted to large numbers.

I TREATMENT OF INDIVIDUALS AND MASSES

Treatment of trachoma may not differ fundamentally in individuals, small communities or masses where certain factors come to prominence. Thus in the treatment of communities or masses the method or drug to be used must be cheap, easily applied to a large number of patients and also easily controllable. Since environmental conditions whether economical, cultural or hygienic play an important part contributing to the success or failure of mass treatment, they have to be studied meticulously for local factors usually assume great prominence. To find the ideal method for the treatment of trachoma is still difficult. We have to discuss however the merits of the various methods in common use at present, try to evaluate them and decide which is best and standardize it for each locality according to its environmental factors.

II CHEMOTHERAPY

For more than two decades chemotherapy has been used in acute bacterial eye infections and trachomatous conditions. During these years many sulpha preparations have been used from the earlier prontosil rubrum and album to combined sulpha drugs of very low toxicity. Their value in the treatment of trachoma has been variously described as curative, only ameliorating, or negative. There is no doubt, however, that one of the major effects of these drugs is on the often complicating secondary bacterial infection which takes prominence in countries where

it is of seasonal epidemic incidence followed by a chronic carrier state as in the region of South and Eastern Mediterranean basin.

Since the corneal manifestations of trachoma are in a major part influenced or accentuated by auxiliary factors amongst which is the secondary bacterial infection, which responds promptly to sulpha medication, chemotherapy has a remarkable effect on such manifestations as pannus or deep keratitis, either ameliorating them or lessening their incidence. Moreover, repeated attacks of bacterial infection on a trachomatous conjunctiva often leads to papillary hypertrophy and more tendency to scarring. These also have decreased under chemotherapy. To what extent trachoma virus itself is affected by such treatment is still a controversial issue.

Sulpha preparations have been freed during the last few years from much of their toxic effects, the doses have been standardized and results of treatment in well known acute infections evaluated. Rate of concentration in the blood and rate of excretion of every new sulpha preparation is now an every day laboratory work. Yet though the serious toxic effects of the parental use of the drugs has been brought to a minimum, we still find in certain persons an alarming hypersensitivity. In tropical and sub-tropical regions where hepatopathies and diminished renal efficiency are prevalent due to endemic parasitic infection, chemotherapy may have some limitations. Development of resistance in the infecting agent towards the drugs has to be taken into consideration when the results of any mass treatment are assessed.

Parental use is usually combined with local application to the conjunctiva in the form of drops or ointment in different concentrations that keep stable. It has been suggested to add zinc sulphate to sulpha preparations for local application for the often complicating diplobacilliary infection in trachomatous patients as seen in the southern region of United Arab Republic. The cheapness of sulpha preparations and zinc salts in ointment form, made it possible to put such a combination as a major competitor for topical antibiotic ointments in mass treatment either prophylactic or curative against communicable eye diseases in any proposed campaign for their control. The stability of

the sulpha compounds and their cheapness may turn the scale in their favour since topical use is practically devoid of any general toxic effects with minimum local sensitivity compared with antibiotics. The newer sulpha preparations have more permeability to the deeper ocular tissues which can be further enhanced by spreading drugs.

Method of Administration
Peroral Method

Sulphathiazol, sulphadiazin and sulphamerazin have been used for many years in acute bacterial infections of the conjunctiva either singly or combined and similarly in trachomatous conditions but without the same dramatic result. Of the three preparations, the second and third were less toxic and the second less liable to cause hypersensitivity (Lyons) and has more prolonged action. Treatment of trachoma with sulpha drugs taken internally has to be kept up for at least three or four weeks and may be repeated to have any effect on the virus of trachoma, if any. Usually, in acute ophthalmias, it is a short effective treatment. For individuals and small numbers the single daily dose is not recommended. The calculated dose of 0.50 mgm per kilo body weight per day is better divided into two or even four doses. In mass treatment, where the administration cannot be controlled, a single daily dose may be calculated that can keep the necessary concentration in the blood for the required period. The use of a low dosage, long acting preparations of sulpha, such as the methoxypyridazine, may meet such necessity (Gaspare, Montaldi, Lenzieri and Latte).

Sulpha preparations are usually administered in tablet or powder form or as palatable emulsion (Lyons), mixture or syrup for infants and children.

Topical Use

Sulpha preparations are stable in the form of drops or ointments, the soluble salts and those of a high penetrating power are more effective. The concentrations used vary from 10% to 30% to be used three to four times or more frequently. Many of the soluble salts are combined with antibiotics as penicillin or inorganic salts as zinc. Allergic skin reactions are sometimes seen, due to sensitivity to a particular sulpha preparation, the antibiotic or the vehicle, and has to be stopped or changed.

III ANTIBIOTICS

Since the discovery of penicillin, an overwhelming flood of newer natural or synthetic antibiotics have been added every year yet it has been the dream of every trachomatologist to find the ideal antibiotic that will radically cure trachoma. Every one of these antibiotics has been tried either internally or locally on the conjunctiva. The results claimed have been disputable. The wide range of action of the newer antibiotics has not yet been conclusively proved to include the virus of trachoma.

Since the virus of trachoma could be isolated in only a few instances (T'ang, Taylor and others), the usual laboratory sensitivity tests in vitro for the various antibiotics could not be accomplished yet. Furthermore the recognition of many strains of the virus that may give each a different response to th antibiotic makes the task still more difficult until the amount of available virus for such investigations makes it possible for the virologist to conduct them on a large scale. With such evidence at hand standardized treatment with the effective antibiotic could be assessed. Clinical criteria up till now are not enough to determine the therapeutic value of any antibiotic or trachoma since treatments are mostly conducted under non-identical circumstances.

Method of Administration
Internal Use

Antibiotics given as injections or by mouth have been used for the treatment of trachoma. Foremost was penicillin either in the crystalline form or with procain. Results have never been gratifying with regard to trachoma itself but the complicating secondary infection when it was sensitive to penicillin easily disappeared within a short time and indirectly benefited the evolution of the trachomatous condition specially the corneal manifestation Depot penicillin, such as N-N-' dibenzylendiamine-dipenicillin G (Bietti) gave promising results. Other antibiotics parentally used hardly gave any results worth mentioning. Since the mode of administration of antibiotics by injections or by mouth at definite intervals can hardly be applicable to a disease that tends to take a chronic course and may necessitate thus a prolonged use of the antibiotic and since the cost of such treatment would be high and

because of the side reactions that may be alarmingly dangerous, parental use of antibiotics in trachoma - except perhaps the repository ones - has fallen into disuse unless sometimes for a complicating secondary infection and even then it is better benefited by sulphonamides which can act on all the pathogenic flora of the trachomatous conjunctiva of bacterial origin. Yet recently, Gilkes, Smith and Sowa reported that short courses of massive daily doses of penicillin systematically administered caused cytological changes in scrapings of the trachomatous conjunctiva within 2 to 3 days. There was reduction of the inclusion bodies which ultimately disappeared.

Topical Use

Many antibiotics are used as local applications to the trachomatous conjunctiva. Penicillin which may still be used for secondary infections has been replaced by such antibiotics as chloramphenicol, aureomycin, achromycin, terramycin, erythromycin and other natural or synthetic antibiotics which are marketed under different names though of same group.

Aqueous solutions are unstable and have to be applied several times per day and thus have been discarded. Ointments or oily suspensions are the form in which the various antibiotics are used though there is still an expiry date for every preparation after which their efficiency rapidly falls. Liquid paraffin is better than sesame oil (Tsutsu) for suspension for it is chemically stable and less irritating to the conjunctiva. Terramycin, aureomycin and achromycin are supposed to affect the virus of trachoma more than chloramphenicol, streptomycin, erythromycin, bacitracin, tyrothricin, magnamycin and similar antibiotics. These have been used single or in combination of two or more antibiotics or with sulphonamides or recently with the provocative diagnostic steroid, hydrocortisone which is supposed to promote early subsidence of inflammation in the acute phase of trachoma (Matsui-Yamashita-Tsutsu-Giuffré).

The usual concentration of the antibiotic is 1/2% to 1% but the frequency of applications has been a subject of controversy for the last three years particularly when the question of mass treatment arises. The original schedule of treatment by 2-4 applications or even 6 per day for at least three months to be repeated if necessary has been replaced by 2

applications daily for three consecutive days to be repeated every month until cure is effected (Scott, Taylor and others). The variance of opinion has certainly arisen from the fact that treatment is applied in different phases of trachoma, thus giving different response.

Proper assessment of the therapeutic value of any antibiotic necessitates comparison of the effect in one phase only, which should be the early phase, with meticulous follow-up of its evolution.

Other methods of administration have been tried by various observers; thus, Holland reported good results from subconjunctival injections of chloramphenicol and Carricaburu, Sunyaeva, Dogorova from dihydrostreptomycin. Spreading drugs, such as hyaluronidase, have been added by others, as Francesco.

I suggest trying the injections in the lachrymal gland and sac in individual treatment to enhance the effect of the antibiotic and to act on a probable latent habitat of the trachoma virus.

IV COMBINED CHEMOTHERAPY AND ANTIBIOTIC TREATMENT

Combined treatment of trachoma with sulphonamides and antibiotics has been practised for the last few years with reports of a fair amount of success. The favourite topical combination of penicillin and sulphas is still used by many, though the question of decreasing efficiency of the antibiotic by time has always been raised and attemps have been made to increase the time of potency of the antibiotic, the sulphas remaining stable The rate of penetration of the preparations in topical use has always been given importance and also the vehicle used specially in tropical and subtropical countries, where the heat may alter the stability of the vehicle and render it irritating. Incidence of local or general sensitivity has been pointed to before and this may increase in combined treatment. Combined local antibiotics and general sulphas treatment gives good results in countries where both trachoma and acute bacterial infections flourish, and the same may be said of local sulphas and general antibiotics treatment where there are obscure complicating viral infections.

Long-term internal chemotherapy or antibiotic treatment is not advisable but if it were necessary, it is recommended to use depot antibiotics and long acting non-toxic sulphas in combination, such as benzathine penicillin G and sulphamethoxypyridazine (Kinex).

V MECHANICAL TREATMENT

Mechanical treatment is still resorted to when there are expressible follicles, papillae or post-trachomatous concretions in addition to the surgery when necessary for the sequelae of scarring. The first two, however, always require treatment with sulpha and antibiotics either topically or orally to hasten if possible their resorption and minimize scar formation. Spreading drugs, such as hyaluronidase, may be used with advantage in the surgery together with local antibiotic application with or without non-irritating subconjunctival injections. Light mechanical treatment is supposed to enhance the penetrating power and efficacy of local antibiotics or sulphas.

Repetition of the mechanical treatment may be required, but now, since the use of antibiotics and sulphas, it has become much less frequent or drastic. Actually, the more potent the medical treatment for trachoma the less the need for surgery.

VI RADIATION THERAPY

Revival of radiation therapy for trachoma has been suggested by using Betarays from strontium 90 applicator. It has limited use and results are not very promising.

VII COMPARISON OF VARIOUS METHODS OF TREATMENT

When we try to make a comparative study of the various methods of treatment of trachoma, we have first to draw a broad line between the old and the new treatments. It is not my intention to discuss the first, for I have already done that in "A review of the treatment of trachoma" with El-Tobgy as far back as 1936. Besides, it has now become a subject of historical interest only with occasional revival of some treatments as radiation therapy or vaccine therapy. In reviewing the recent methods of treatment we have to consider the treatment for individuals, small communities or mass treatment, whether curative or prophylactic.

Individual Treatment

Such treatment as carried out in private practice or hospitals is governed by the treating surgeon's personal impression or experience of one method of treatment or other. There are still some who use the old

cicatrizing agents, such as silver nitrate or copper sulphate, together with the mechanical treatment. This may be the only treatment adopted, or it may be combined with topical or general sulphas or antibiotics, irregularly used and not following a systematized course of sufficient duration to have any beneficial effect. Such an attitude between the old and new may be of value when a decisive assessment of the results of one treatment or other cannot be made.

Sulphas, whether used generally or by local application, have fallen into disuse in the treatment of trachoma. Their main value, as has been repeatedly stated, is in the complicating secondary bacterial infection, when they have an ameliorating rather than a curative effect. The dose and methods of administration of sulphas have been discussed and need no further comment, except perhaps with regard to the correct choice of the preparation.

This is important with regard to toxicity and rate of penetration, concentration in the blood and tissues and excretion.

Topical antibiotics are now the best choice for trachomatous conditions in early stages to be combined with general sulpha treatment if there is secondary infection and later, with very mild mechanical treatment if necessary.

Community Treatment

Such treatment as applied to a small group of people under the same environmental conditions, as in schools or institutions, whether private or under government control, may follow both the usual individual treatment and that adopted for masses, whether it be curative or prophylactic. Owing to the relatively small number to be treated who are more or less constantly under observation, the treatment and the assessment of the results can be easily controlled. Even such may be adopted as a pilot project for the evaluation of any method of treatment prior to the launching of any proposed campaign against trachoma.

Mass Treatment

There are certain basic principles that should be observed in mass treatment. It should be simple, inexpensive, easily assessable and controllable, and devoid of any danger. Attempts have been made to apply the results obtained in the treatment of individuals or small communities to masses. This could be obtained following the investigations of the Expert Committee on Trachoma (first and second reports).

Local treatment with terramycin, aureomycin and achromycin in the form of 1% ointment or oily suspension, comes foremost together with occasional periodic sulphonamides by mouth, when there is seasonal incidence of acute ophthalmias. The minimum effective antibiotic number of applications or courses has not yet been definitely agreed upon. Mass treatment requires perfect organization of mobile and fixed treating units provided with well trained personnel under the guidance and periodic inspection of ophthalmic medical staff.

Pilot projects have been established in many countries to study the planning of campaigns for the control of communicable eye diseases. The basis of such campaigns, apart from the social, hygienic and economic schemes, is the establishment of perfect mass treatment, both curative and prophylactic. Many observers have reported on the value of mass treatment, as Rostkowski, Chen and co-workers, Mitsui, Kobayashi, Tamura, Tsutsu, Mikuni and co-workers, Scott, Taylor.

VIII CONCLUDING COMMENT ON TREATMENT PROPOSED

The treatment to be adopted may with advantage follow the scheme proposed by the Expert Committee on Trachoma (WHO) in its second report. The main objective is the control of the disease and if possible, the eradication of in countries where it is endemic.

The problem, as has been repeatedly pointed out, is not in finding the ideal drug for the virus of trachoma, but also in making it available to individuals and communities at a very cheap cost, or even free. This is one aspect of the problem. The other is concerned with health education, sanitation (including fly control), sterilization of carriers and the establishment of periodic campaigns of mass treatment as has been successfully carried out in Tunisia.

Up till now topical antibiotics, terramycin, aureomycin and achromycin as 1% ointment or oily suspension have given best results. With regard to the frequency of applications and the time necessary to radically cure trachoma, we are still in doubt though the tendency is to diminish the duration of each course and to increase the number of courses. Such courses of treatment is best combined with internally administered sulphas of low toxicity and of prolonged action. This course is particularly valuable when there are secondary infections or when seasonal epidemics of acute ophthalmia are anticipated.

Mechanical treatment, if indicated, must be mild, in order to minimize traumatism and excessive scarring. Mechanical desquamatives are still resorted to in countries where chemotherapy and antibiotics are not yet extensively used.

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