Clinical Research Laboratory

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SUGGESTIONS FOR ADMINISTERING TOXIC ANTIGENS ("Vaccines")

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These antigens are prepared from highly specific, highly toxic bacteria and are, therefore, effective in extremely minute doses but are toxic in overdoses. Because of their high potency they should be used according to the following suggestions to get best results and to avoid unfavorable episodes. They should be kept in a cool dark place.

Use a 1/4 cc tuberculin syringe (B.D.), not an ordinary hypodermic syringe. If it is sterilized by boiling, let it dry for a few seconds before putting it together. Also expel any water from the needle.

Do not give an injection in an acute illness, such as a head cold, until it has subsided. After any surgical manipulation of a focus of infection or a tooth extraction, wait at least two weeks and if the symptoms improve wait as long as they continue to improve.

Material supplied. The streptococcus is undoubtedly the common denominator of chronic ill health. Therefore, this organism is the one regularly used in making the antigens. In some instances there is also a staphylococcus infection and a vaccine is made of that organism also. Careful and extensive investigation indicates that other types of bacterial infection are secondary to the streptococcal infection and they clear up when the latter improves. Therefore, vaccines of these other bacteria are not recommended. Since toxins are highly efficient in stimulating the production of antibodies, only the highly toxic organisms are selected. Staphylococci and streptococci are made into separate standard suspensions and then combined into a single series of dilutions. However, in rheumatoid arthritis staphylococcal toxic products, even in minute amounts, cause severe exaccerbation of the arthritic symptoms. Hence, the laboratory should be instructed to use only streptococci in such cases. In a few other instances the dose of streptococci may be quite different from that of staphylococci, resulting in difficulty in adjusting the dose. In such cases return the entire set of bottles to the laboratory and ask to have the streptococci and staphylococci diluted separately.

The standard toxic antigen is a suspension of 1 billion bacteria per cc. For simplicity this is called "dilution #1". When this is diluted 10 times it is called "dilution #2" and the next, "dilution #3", etc. With the present highly effective method for preparing the antigens the optimum dose in most cases is about 0.02 (1/50 th) cc of dilution #46. In hypersensitive conditions such as asthma, urticaria, angioneurotic edema, etc., even such minute doses produce an unfavorable reaction and the laboratory should be instructed to dilute the vaccine still further. A total of 46 decimal dilutions is regularly prepared but only 7 are supplied to the physician. They are: the standard (to be kept for preparing lower dilutions or separate series), #13, 30, 38, 42, 44 and 46. When there are both staphylococci and streptococci the dilution #13 is omitted because it is rarely required.

The initial dose. With most chronic invalids the best initial dose is 0.01 (1/100th cc of dilution #46. If the patient is believed to be hypersensitive or is excessively debilitated or if the non-filament-filament ratio is above 100% or the sedimentation rate is more than 30 mm in 1 hour (Westergren) it is better to build up resistance before beginning the injections. Some physicians prefer to give a preliminary series of our special colon bacillus "implantations" per rectum in such cases because this preparation acts as a nontoxic but highly effective antigen. Special literature is available on this subject.

Administration. The dose and interval must be adjusted each time according to the patient's response. The old idea that an antigen "is working" because it produces an unfavorable effect has no basis in fact. These antigens stimulate the production of antibodies rather than force the patient to produce them.

The best check of the progress of treatment is a white, differential and nonfilament blood count. These require surprisingly more skill and attention than are ordinarily paid to them and for the results to be comparable they should be done in the same laboratory that made the original tests.

The following schedule of weekly doses is suggested for use only until the effective dose is reached. When an effect is noted, no matter how slight or apparently insignificant, adjust the dosage according to the directions given under "Adjusting the dosage".

Test dose	.005 (½ of 1/100th)	#46
Dose no. 1	0.01 (1/100th) of dilution	#46.
2	.02	"
3	.03	"
4	.02	44
5	.01	42
6	.02	"
7	.03	"
8	.04	"
9	.05	"
10	.07	"
11	.10	"
12	.03	38
13	.05	"
14	.10	"
15	.01	30
16	.02	"
17	.03	"
18	.05	"
19	.10	"
20	.01	13
21	.02	"
22	.03	"
23	.05	"
24	.07	"
25	.10	"

If no effect is obtained with this series return the set of bottles to the laboratory and ask to have lower dilutions made.

Adjusting the dosage. As soon as the dose is reached that produces an effect the dosage should be adjusted as follows. If there is slight improvement for a day or so try the next dose in the above schedule. If there is moderate improvement for several days increase the dose about half way to the next in the above schedule. If there is considerable improvement the dose is close to the optimum and should be

repeated, not increased. If the beneficial effect lasts a whole week it is better to omit the next injection until you find out how long the good effect lasts. The injections should then be given at an interval of a day or so less than the length of the good effect. If they are given too soon the accumulation of excess antigen in the tissues will be equivalent to an overdose. If there is an unfavorable effect wait until it has completely subsided, even though it may take several weeks, and then give a much smaller dose. If the initial dose produces an unfavorable effect send the bottle to the laboratory and request still higher dilutions.

One of the gravest mistakes with this type of "vaccine" is to assume that because of the extreme dilution there cannot be any active principle in the preparations. One of the newer findings in colloid physics is that in dilute dispersions the molecules tend to form monomolecular surface layers, probably with some flattening of the molecules. In addition, dielectric effects, the negative colloid charge and "stickiness" of the particles prevent mathematical dilution of the active principle even under the most precise conditions. Until more is known of this subject, proof of the effectiveness of such high dilutions must rest on findings that: (1) the reactions are highly specific and the potency increases with technical skill in preparing the antigens (growing them on special culture media, harvesting in the logarithmic phase and preventing further enzymatic or other chemical change); (2) injection of a minute quantity has a tremendous effect on the nonfilament-filament ratio of leucocytes, often within an hour or so, whereas diluting fluid alone (pyrogen-free, fat-free, 0.5% phenol) has no effect; and (3) such effects are paralleled by other subjective and objective changes.

Criteria of "reactions". For clarity, it is better to refer to an unfavorable effect as a "reaction" and to a favorable effect as a "response". The following may be expected to occur.

No effect at all. In such cases there is no increase or decrease in symptoms, fatigue or drowsiness or other possible effects, particularly within 48 hours. An effect which occurs several days after the injection may be assumed to be due to other causes unless it follows subsequent injections. When there is a doubt as to whether or not a dose has produced a result it is best to repeat it. A favorable response consists of improvement in symptoms or lessening of fatigue or postnasal discharge or a sense of euphoria, no matter how slight, usually beginning within a few hours to a day or so after the injection. An unfavorable reaction consists of increase in symptoms, fatigue or postnasal discharge, no matter how slight and usually comes on within a few hours after the injection. However, the maximum distress may not be noted until several days or even a week after the injection. Hence the desirability of giving longer intervals than usual, particularly when the results are difficult to interpret.

Summary of Suggestions

Select the initial dose according to severity of symptoms and the bacteriological and hematological findings. The more abnormal they are the smaller should be the initial dose.

Increase the amount according to the suggested schedule until an effect is noted. If the effect is unfavorable, wait until it has completely subsided and then give less, and possibly less often. If the effect is favorable, increase the dose cautiously until the favorable effect lasts about a week or longer. In most cases an interval of 2 to 3 weeks gives best results. Give only enough to produce improvement. Do not attempt to force the tissues to produce antibodies by giving large or frequent doses. This overburdens the immune mechanism and prevents response.

Several physicians are acting as consultants in this research. If physicians having problems with these vaccines will submit them to the laboratory (no charge), it will forward them for comment to physicians specially interested in that particular phase of the subject.

Some reasons for failure

The common causes of failure are:-

Leucopenia and neutropenia. Investigation of this subject and methods of correction is in progress, with excellent prospects of success. Notify the laboratory if you are interested.
Endocrine dysfunction, particularly pituitary, thyroid, adrenal and gonad.
Avitaminosis
Liver dysfunction.
Untreated foci of infection. The most commonly overlooked are pyorrhea pockets, caricus or apically infected teeth, nasopharyngeal infection, particularly of the lymphoid structures and mucous membranes, and the gastrointestinal tract.
Unrecognized unfavorable results. Instead of the general question "How are you getting along?" the patient should be questioned minutely about his different symptoms, how soon the effects appeared and how long they lasted. The symptom commonly overlooked is drowsiness.

In some cases, the intravenous method of injection will give better results than hypodermic injections. The dose is similar in both cases but as little blood as possible should be drawn into the syringe or it will displace the vaccine in the hub (about 0.06 cc) and the amount of vaccine injected will be much larger than that calculated.

In giving the injections be sure to compare the first interval on the syringe with subsequent ones. Try to estimate the amount in the first interval and then make adjustment for the amount to be injected. The majority of 1/4 cc tuberculin syringes (B.D.) are accurately graduated and are easier in measuring the small amounts than are larger sizes.