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TYPHOID SHOCK THERAPY

Results of Fifteen Years' Experience

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A survey of the medical literature for the past five years reveals that the use of typhoid shock therapy is less popular than during the preceding decade. This is probably due to lessened need for non-specific protein in treatment of infections and inflammatory processes. This is indicative of medical progress and reflects better understanding of the cause and treatment of disease. Yet in spite of the amazing bactericidal and bacteriostatic effects of the sulfa drugs and penicillin, we are confronted still with many medical conditions which are refractory to ordinary therapy. It is among these that nonspecific protein shock therapy has a useful place in clinical medicine.

In some instances typhoid vaccine given subcutaneously or intravenously merely relieves painful symptons, but in many cases it shortens the course of disease and contributes to recovery. Experience with its use in several thousand patients during a fifteen-year period has determined the course of administration and indications and contraindications for its use.

We know relatively little about chemical and biological changes that take place in the body during this type of shock therapy. However, it can be rightfully assumed that fever produced by proteins injected intra-

venously or subcutaneously causes active participation of cells of the body in production of a rise in body temperature. Furthermore, experience leads me to believe that defenses of the body against infection are mobilized not only by increased cellular oxidation but also by modification of cellular permeability, increased chemical exchange between the cells and body fluids, and favorable effect on the formation of defensive enzymes and antibodies. Many investigators have emphasized these effects and have shown that following such shock reactions there is increase in total leucocytes and improved phagocytosis as well as improvement in minute volume of blood through the capillaries.

The favorable effects of intravenous typhoid therapy point to increase in the defense against diseases which have remained at a subacute or chronic level. On the other hand, except in cases of Sydenham's chorea, the results are rarely dramatic.

Production of fever by typhoid shock has certain advantages over passive hyperthermia induced by the heat cabinet. In the latter form of therapy discomfort and dangers from prolonged maintenance of high body temperature have led me to discontinue its use. In experience at Cleveland Clinic few, if any, diseases have been found that cannot be treated with greater benefit by typhoid vaccine or by therapeutic methods other than the hypertherm.

In an earlier trial with various methods of administering typhoid vaccine intravenously a definite therapeutic program proved to be essential for safe and satisfactory results. The principles of treatment outlined by Howard were those adopted.[1]

Formerly typhoid and paratyphoid vaccines as found in the open market were routinely employed, but in recent years a vaccine prepared in the Clinic laboratories has afforded better and more uniform results.

The routine treatment begins with an initial dose of 25 million typhoid and paratyphoid organisms for adults and 15 million for children under 10 years. The bacteria are diluted in 10 cc. of sterile physiologic saline solution and given in the vein of the forearm. In one to three hours the patient has a chill followed by fever of 102.5 to 103. If a chill does not occur promptly, it may be because the patient is refractory or the injection has been given extravenously. Under such conditions the chill may not occur until a second dose is administered.

With prompt rise in temperature the patient has no feeling of depression but rather the sensation which accompanies a slight attack of "flu." Within two or three hours the fever may drop rapidly or be followed by a secondary rise. As soon as the temperature remains fairly normal for twenty-four hours, the second dose, consisting of 50 million bacteria, is given. Each subsequent dose is double the preceding dose

until a total of six injections has been administered. In other words, the adult patient receives successively 25 million, 50 million, 100 million, 200 million, 400 million, and 800 million. An afebrile period of approximately twenty-four hours is allowed to elapse before the next dose is given.

From a careful selection of cases, there have occurred no serious, unfavorable effects with use of intravenous typhoid vaccine in either children or adults. Among the contraindications to its use, however, are such conditions as advanced arteriosclerosis and hypertension, myocardial weakness, angina pectoris, chronic renal disease, diabetes mellitus, active tuberculosis, severe allergy, and pronounced undernourishment with fatigue. In acute rheumatism or chorea the presence of carditis or endocarditis does not increase the hazard of treatment.

The advantages of this treatment are:

1. Safety.
2. Economy—approximately two weeks hospitalization.
3. Little, if any dehydration.
4. Prompt reaction after injection of vaccine.
5. Active participation of the cells, resembling an immunizing process.
6. Repetition of the course of treatment without hazard; with intravenous method the patient does not seem to be sensitized to typhoid bacteria.

In dealing with clinical application of intravenous typhoid vaccine to certain disease processes it must be emphasized that this form of treatment does not lend itself to accurate statistical study. Many times one cannot be certain whether the patient is cured or merely relieved of uncomfortable symptoms. Furthermore, the disease may be still in progress or may recur at a later date. However, since this type of therapy is employed in conditions that may be unresponsive to other forms of treatment, and since many statements in this paper are based on fifteen years of experience, I have the temerity to be rather dogmatic.

Nonspecific shock has been produced in this Clinic for a multitude of pathologic states, but at present it is utilized largely in the following conditions.

1. Acute virus infections of the central nervous system—encephalitis and encephalomyelitis.
2. Chronic rheumatoid arthritis.
3. Chorea.
4. Various eye and skin disorders.

In untreated cases of acute encephalitis recovery occurs in almost 25 per cent while death occurs in slightly more than 38 per cent. Of the remaining 37 per cent there are mild or severe complications. Since the neurotrophic virus, whether chemical or bacterial, is an obligate parasite which lives and multiplies within the grey matter of the central nervous system, it is understandable why no specific treatment is available. The cell protoplasm of the host probably acts as a barrier to viricidal substances such as antibodies and chemicals. Theoretically nonspecific protein shock therapy by influencing cell metabolism might stimulate the grey matter to attenuate or destroy the virus.

In an effort to evaluate the results of intravenous typhoid injections we have not been able to make a satisfactory statistical study. This is due to several reasons among which are the relatively few cases of acute lethargic encephalitis that have come to the Clinic. Apparently this disease is not as prevalent in this locality as elsewhere. Then, too, the diagnosis is often difficult. Such conditions as benign lymphocyte choriomeningitis, acute disseminated sclerosis, and even brain tumors, especially in children, have caused some mistakes in early diagnosis. The general impression has been, however, that the fever induced by typhoid reactions has reduced headache, somnolence or irritability, and spinal fluid cell count within a week.

In the treatment of 49 patients with acute encephalitis by roentgen ray therapy Portmann found that 29 (59.1 per cent) recovered and 15 (30.6 per cent) improved. This treatment resulted in improvement in 13 cases as early as three or four days after radiation.[2] In 1 of these patients who recovered consciousness following x-ray therapy I administered a course of typhoid shock therapy. After the third reaction the patient became quiet and relaxed and completely recovered. Three other cases recovered even more rapidly with the combined roentgen ray and typhoid shock treatment.

In Sydenham's chorea, on the other hand, immediate results of typhoid therapy are often spectacular. After as few as two or three reactions the purposeless movements of the body are quieted, and the patient becomes generally subdued. While the average patient recovers from acute chorea in six to eight weeks without treatment, some patients included in this study are known to have had the disease for two to five months.

In a series of 29 patients with Sydenham's chorea treated at the Clinic recovery was obtained in 18 (67 per cent) after three to six shock treatments, decided improvement in 6 (23 per cent), and no relief in 3 (10 per cent). In this group 5 patients had had one previous attack;

1, two earlier attacks; and 1, six recurrences of short duration over a period of two years.

In our follow-up study only 2 patients had recurrences of chorea, and both had mild attacks. These excellent results may have been due, to a large degree, to carefully followed instructions given to the parents of the patient upon dismissal from the hospital.

The etiology of chronic rheumatoid arthritis is unknown. There is no evidence to prove that it is due to any known infection. Removal of infective foci is of little if any value. This serious, progressive, and deforming type of arthritis presents a most difficult and disappointing therapeutic problem. Gradual destruction of joint cartilage characterized by proliferation of the synovial membrane, small round cell infiltration and growth of granulation tissue over the joint cartilage usually ends in ankylosis.

Six years ago 40 cases treated with intravenous typhoid vaccine (six reactions) were reviewed. In 72.5 per cent of these there was immediate subjective relief resulting in amelioration of joint pain, restlessness, and fever. However, this improvement was not permanent, since it did not shorten the course of the disease or contribute materially to a "cure." But the patients who responded with temporary improvement were grateful for this relief and were content to remain in the hospital for special therapy, such as blood transfusion, neoarsphenamine, physical therapy, dietary regulation, and other measures to build up general resistance of the body. These shock treatments are used in patients who have acute exacerbations of rheumatoid arthritis, but rarely is it found necessary to give more than six successive typhoid injections at any particular attack.

In ophthalmology intravenous typhoid vaccine is administered in the following conditions:

1. Retrobulbar neuritis of unknown cause.
2. Infectious retinopathies which have failed to respond to other forms of treatment.
3. Keratitis and iritis of rheumatic origin.
4. Keratitis in congenital syphilis.
5. Uveitis with secondary glaucoma (before and after surgery).
6. Presence of foreign bodies (before and after surgery).

The results have warranted a continuation of shock therapy in the foregoing diseases. Likewise, nonspecific therapy with the use of typhoid vaccine or milk protein are employed with some frequency in dermatology. Persistent pustular acne and pyogenic dermatoses, severe

psoriasis, especially when accompanied by arthritis, and erythema nodosum improve as a rule after protein shock treatments in conjunction with other therapeutic procedures. Shock treatment has been discontinued, except in rare instances, in otolaryngology and urology.

It is obvious from this brief review of the experience of fifteen years with intravenous typhoid shock therapy that a strong endorsement of this measure cannot be presented. Yet in properly selected cases it is helpful, and in Sydenham's chorea it definitely hastens recovery. Until specific therapy is available for many diseases of doubtful etiology or those in which ordinary treatment is unsatisfactory, we are justified in utilizing nonspecific measures.

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THE USE OF TANTALUM FOR REPAIR OF CRANIAL DEFECTS IN INFECTED CASES

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The primary purpose of this article is to demonstrate that presence of a tantalum implant does not impair healing of an infected wound. Secondarily the author wishes to describe his experience with a hitherto untried method of dealing with abscess of the brain.

Tantalum, a newly available metal, has proved to be the most satisfactory material for repair of cranial defects.[1-10] Thus far it has been employed chiefly in secondary repair of cranial defects resulting from war wounds. A few surgeons have advocated its use in contaminated wounds, as in immediate repair of compound comminuated fractures of the skull.[11,12,13,14] Infection, however, has been generally considered an absolute contraindication to the use of any metal implant.

Treatment of brain abscess by complete excision rather than drainage has yielded a lower morbidity in the author's experience, but the danger of cerebral fungus following radical excision has been a deterrent to the universal application of this method. Since cerebral fungus can be entirely prevented by closure of the skull defect with tantalum, the use of this material naturally suggested itself. Furthermore, tantalum has proved so inert by past experience[13] that its use in infected cases seemed