THE PHYLACOGENS.*

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As time goes on we appreciate more and more the wisdom and farsightedness of the immortal Pasteur, who prophesied that the day would come when it would be possible to eradicate the infectious diseases by vaccination.

Bacteriology, from the time of Leeuwenhock in the latter part of the seventeenth century to the present day, is as interesting in its evolution as any subject which medicine provides. Its development extends over a period of two hundred years and, during this time, the foundation was laid for the rapid and important progress which has been made in the last three decades.

Bacteriology has revealed that certain micro-organisms produce certain diseases and to-day we are using, in the preparation of a variety of agents, these same bacteria for their own destruction. The value of these products, in the treatment and prevention of disease, is too well known to require emphasis.

Some may think that biologic therapy has grown like the proverbial mushroom, and that the workers in this field have been over-enthusiastic in bringing into use the many products of bacterial origin. But reflect, we have been using Antidiphtheric Serum for twenty years; bacterial vaccines have been in use almost fifteen years and Koch presented his first tuberculin to the profession twenty years ago.

Therefore, while at first thought, it may seem that discoveries and methods of treatment have been presented with unusual rapidity, the therapy has in fact grown but slowly.

At the beginning of the present decade much interest was manifested by the medical profession, in and about San Francisco, concerning the reports of the extraordinary results following the use of a new class of bacterial derivatives in the treatment of acute and chronic infections. The products used were originated by Dr. A. F. Shafer of California, who presented his discovery to the profession through the San Joaquin Medical Society at Fresno, California, in October, 1910, and later through the San Francisco Medical Society in January, 1911.

These products, derived from bacteria, were denominated Phylacogens, from the Greek words, φυλαξ and γενναν, meaning "to produce a guard."

The principle upon which Phylacogen Therapy is founded, is that of mixed or multiple infection. Three theories are advanced by Shafer. First, that the human subject is at all times the host of a great variety of micro-organisms, and harbors pathogenic bacteria without harm to itself, during periods of physiologic resistance at or above par. When physiologic resistance is subnormal, and especially when solution of tissue-continuity occurs, the bacteria harbored assume pathogenic activity. Second, that practically all infections are mixed; that only in rare instances, is there infection by a single species of micro-organism;

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that while one species may, and usually does, predominate, the pathologic process engendered by it is accelerated and intensified by organisms of other species which are present. In other words, that in the course of an infectious disease, manifestations are due, not only to the effects of a single species of organisms, the specific infection, but also in part to the influence of other organisms, whose pathogenic role is not insignificant, and which must be combated in any successful scheme of therapeutics. Third, the growth of micro-organisms, infecting the human subject, can be arrested, and their effects neutralized, by the administration of metabolic substances generated during the development of germs in artificial culture media.

Shafer does not contend that these premises are original with himself, but that he has recognized their pathologic and therapeutic significance, and that his system of therapy by means of Phylacogen is new and a great step forward.

Instances of mixed infections will occur to all of you, as for example, gonorrhea shortly after onset, tuberculosis, and coryza. In tuberculosis, for instance, secondary infection is generally admitted to be the cause of fever, loss of weight, purulent expectoration, destruction of tissue and such other manifestations as appear in advanced tuberculosis. Further evidence of the existence of mixed infections, is the extensive use of so-called combined bacterial vaccines. Physicians many times have had cases of infection that they could improve but could not cure, through the use of a vaccine prepared from a single organism, while cure was rapidly established through the employment of a vaccine containing the predominant organism and such other bacteria as were associated therewith.

The Phylacogens are neither bacterial vaccines nor serums. They are sterile aqueous solutions of substances generated by bacteria grown in artificial media. They are prepared by cultivating a number of the common pathogenic organisms, such as the several staphylococci, streptococcus pyogenes, streptococcus rheumaticus, diplococcus and pneumoniæ, bacillus coli communis, etc. The cultures are incubated at 37° C. for a specified time, the organisms are then killed, a preservative consisting of .5% phenol added and the fluid is then filtered through porcelain. This filtrate is basic Phylacogen and commonly known as Mixed Infection Phylacogen. It is used in the preparation of the specific Phylacogens.

The specific Phylacogens for the treatment of rheumatic and gonococcal infections, erysipelas and pneumonia, are prepared by adding an equal quantity of the basic filtrate, (Mixed Infection Phylacogen), to a filtrate obtained from the predominating organism. In other words, in the preparation of Rheumatism Phylacogen, 5 cc. of a filtrate made from the streptococcus rheumaticus, is added to 5 cc. of basic Phylacogen.

Culture tests are made of each lot of Phylacogen prepared, to determine whether the completed product is sterile. Co-incidentally, safety tests of the same preparations are made by injecting relatively large doses subcutaneously, into a series of animals. Should these investigations result satisfactorily, the product is passed as safe.

As to the physiological action of these preparations, little is known, and, for that reason, Phylacogen Therapy may be objected to under the charge of empiricism. While knowledge of the action of Phylacogen is highly desirable,

the absence thereof is not a valid criticism. Pasteur knew nothing of the action of his virus for the prevention of hydrophobia; Jenner knew nothing of the action of vaccine for the prevention of smallpox; the Jesuit Fathers knew nothing of the action of cinchona bark in the treatment of malaria. These men were empirics, but who at this date minimizes the value accruing to the human family from the use of smallpox vaccine and quinine?

Investigators are busy in attempting to reveal the mysteries in the physiological action of Phylacogen. Progress in research of this kind is slow, but progress has been made, and in all probability considerable light will soon be shed upon this most interesting subject.

Clinically, Mixed Infection Phylacogen is indicated in infections classed as surgical. In this connection, it must be understood, of course, that the Phylacogens are not what might be called "pus absorbers." When pus is present, it must be liberated. Mixed Infection Phylacogen is being used with success, in the treatment of infections in a variety of locations following surgical procedure and other injuries, in puerperal infections, empyema, osteomyelitis, otitis media, carbuncle, etc., etc. It is also being employed in the treatment of hay fever and bronchial asthma. A short time ago one would hesitate to suggest the use of a bacterial product in the treatment of hay fever or asthma, as their causative factors have for years been considered other than bacterial. Suffice it to say, however, that a number of patients have received benefit from the use of appropriate vaccines or of Mixed Infection Phylacogen, and a number have been cured. So-called "asthma," due to cardiac or renal disease, or produced reflexly through pathology in the nose or throat, are not appropriate cases for Phylacogen treatment.

Gonorrhea Phylacogen is indicated in the treatment of acute and chronic complications of gonorrhea. Reports of its efficacy in acute urethritis have appeared but their number is too few to establish its value in this condition. The common complications amenable to Gonorrhea Phylacogen, are acute and chronic prostatitis, vesiculitis and the arthritis, commonly known as gonorrheal rheumatism.

Erysipelas and Pneumonia Phylacogen, as their names imply, are used respectively in the treatment of erysipelas and pneumonia, the latter only when due to the pneumococcus.

Rheumatism Phylacogen is the one of the series that has been used most largely. It is indicated in the treatment of acute and of chronic arthritis due to the streptococcus rheumaticus, and such sequelæ as chorea and neuritis.

The Phylacogens are administered either subcutaneously or intravenously. The subcutaneous method is the one of choice. It accomplishes every purpose in the majority of cases, although the results are not as rapid as from intravenous administration. As a routine measure, the subcutaneous treatment has every advantage and the intravenous method should be employed in those few cases which do not yield to the less heroic procedure.

The injection of Phylacogen is usually followed by reaction, local, systemic, or both. These reactions may be slight or marked, depending principally upon the general condition of the patient and the size of the dose. From intravenous administration, there is no local manifestation other than the slight trauma inci-

dent to injections of this kind. Following the subcutaneous injection more or less local pain, redness and swelling may result. This depends largely, however, upon the site chosen for injection. As a rule injections made slowly into locations of loose tissue are rarely followed by marked reaction, while the reaction is usually greatest when large amounts are given rapidly into the leg or arm.

The systemic response appears usually within six hours. This is manifested by chill, lasting from a few to thirty or more minutes, and an increase in the temperature. Depending again upon the general condition of the patient and the size of dose, the systemic reaction may be mild or pronounced, and following an excessive dose, there may be added to the chill and increase in temperature, nausea, vomiting, diarrhea, great depression and general numbness, etc. Such symptoms, of course, are undesirable, and when they occur, it means that the dose has been in excess.

Clinicians, at this writing, are not agreed as to the necessity of pronounced reactions, but many are of opinion that, with marked systemic response, the cure is more rapidly established. Others hold that mild reaction only is necessary.

The degree of reaction in any patient, it must be remembered, lies entirely in the size of the dose. By well controlled dosage, pronounced reaction can almost always be avoided.

The dose of Phylacogen, as with all drugs, varies with the individual patients, but, as a rule, the initial dose subcutaneously is from 1 to 2 cc. Intravenously, the initial dose is from $\frac{1}{8}$ to $\frac{1}{4}$ cc. Subsequent doses, at intervals of from twelve to forty-eight hours, are to be gradually increased, when given subcutaneously, by from 1 to 2 cc.; when given intravenously by from $\frac{1}{8}$ to $\frac{1}{2}$ cc. The usual maximum subcutaneous dose is 10 cc., the maximum dose intravenously 5 cc.

Before closing this paper, which of necessity is but a brief outline of this new therapy, I wish to take the opportunity to say a few words concerning diagnosis. It has been said that once the diagnosis is established, the treatment is easy and I think we can all agree to the correctness of this assertion in its broad sense. Diagnosis is difficult and the success of any treatment will depend upon the accuracy with which it is established. The development of exact methods of diagnosis, has advanced rapidly during the past few years and the information furnished by various laboratory tests will many times establish the diagnosis and nearly always assist in its determination. In such a protean disease as "rheumatism," for instance, accurate diagnosis is often not easy, and possibly in no other condition are so many errors in diagnosis made. This is due, in great part, to the lack of a satisfactory etiological and pathological classification of the arthritides and in part to the close clinical resemblance between them.

It has been remarked that we, as physicians, are prone to call almost any pain about the joints "Rheumatism," because then we know what we mean, although we do not know what we are talking about. One eminent medical man says, "Rheumatism has sometimes turned out in my experience to mean aortic aneurysm, cancer of the pleura, tabes dorsalis, osteomyelitis, spondylitis deformans, bone tuberculosis, syphilitic-periostitis, lead poisoning, morphine habit, alcoholic neuritis, trichiniasis, and gonorrheal infection.

Acute rheumatic fever and many of the chronic rheumatic conditions are,

beyond doubt, caused by bacteria, but to maintain that all cases of chronic rheumatism are due to germ activity, demands more evidence than we can at this time provide. Naturally, a product of bacterial origin can render no service in a condition in which the causative factor is not bacterial.

The diagnosis being correct and the case suitable, Phylacogen Therapy will, in the great majority of instances, yield prompt and pleasing results, some actually astonishing. These filtrates will produce satisfactory effects more speedily than bacterial vaccines and they are successful in many conditions in which the older agents fail. However, the Phylacogens will not accomplish the impossible—they are not "cure-alls." They have been employed for four years, during which time several thousand cases have been reported, and these indicate a high percentage of successes. Most failures, when they occur, may be considered due to lack of care in diagnosis, to indiscriminate dosage or to faulty technique.

Phylacogen, Vaccine and Serum Therapies, with the possible exception of surgery, are as exact in their scientific application as any therapy which medicine provides. Fulfill the requirements demanded, by a careful selection of cases and intelligent use and they will serve their purpose well.

BUSINESS EXPENSES IN GERMANY.

Apotheker Eugen Roth, of the Ludwig-Wilhelm Apotheke in Carlsruhe, has published for some years in the "Pharmazeutische Zeitung" a table showing the percentage of expense in relation to turnover. Especially interesting in the fact that during the past fourteen years the turnover resulting from dispensing has declined and that from counter-sales increased. The following table shows the percentage participation of the various items of expenditure in 1913, compared with the total turnover:

	Percent		Percent
Drugs and chemicals	13.8	Glass utensils	2.01
Specialties	26.67	Insurance	1.36
Dressings	1.60	Freights and postage	0.85
Indiarubber goods	0.43	Salaries and wages	15.43
Mineral waters	1.55	Heating and light	0.74
Stationery (labels, boxes, etc.)	1.21	Various	0.86

The expenditure, not including taxes, rent, and interest, amount to 65.12 percent of the turnover.—*The Chemist and Druggist* (London).