petent persons, it is in this age. The old simples of our fore-fathers have given away to complex preparations, active and poisonous principles, heretofore unknown and now in daily use. The pharmacist of to-day must be a pharmacist, chemist, and analyst combined.

I am aware that these few thoughts will call forth a good deal of criticism. They are deliberately written for that purpose and hostile, as well as favorable criticism, will be welcome, as it is only by criticism of proposed or accepted methods that we can ever hope to arrive at even a partially successful conclusion.

BACTERIAL *v.* VEGETABLE TOXINS.

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In these days when the value of such products as antidiphtheria serum and antitetanus serum are recognized on all sides as being unique in their respective spheres, it is interesting to recall that it was as the result of the study of a product obtained from a purely vegetable source that these biological products assumed a practical form. The substance referred to is ricin, the tox-albuminoid principle found in castor-oil seeds, and a comparison of this and allied substances, both of vegetable and animal origin, with similar products elaborated by bacteria may not be without interest.

It is only comparatively recently that the existence of poisonous proteids or tox-albumins has been recognized. The idea that a proteid can produce dangerous or even fatal symptoms or act in any way except as a food dates only from 1884, but, according to Cushny, most of the animal poisons are now believed to be of proteid nature, and the toxins formed by micro-organisms of disease are almost certainly of the same class.

The most important toxins or toxalbumins of the vegetable kingdom are ricin, abrin, and crotin. The two latter are obtained respectively from the seeds of *Abrus precatorius* (jequirity) and *Croton Tiglium,* but they closely resemble ricin, and it will only be necessary here to refer at any length to this last-named substance.

Ricin is an intensely poisonous phytoalbuminose, which may be obtained from castor-oil seeds after the removal of the oil. It occurs only in the endosperm and embryo, where it is present to the extent of 2.8 to 3 *per cent.,* and may be obtained from fresh decorticated and strongly expressed seed by percolation with a 10 *per cent.* saline solution in which it is soluble. The percolate is filtered and saturated at 20° to 22° C. with magnesium sulphate, and the resulting white precipitate separated from the crystallized salts by dialysis. This preparation is not pure ricin, and probably contains a large proportion of albumins. As thus obtained, ricin is a white, odorless, strongly toxic, ash-yielding powder, insoluble in alcohol, ether, and chloroform.

The chemical nature of ricin appears to be analogous to that usually ascribed at the present time to the bacterial toxins and ferments, and the name toxalbumin, originally suggested by Kobert and Stillmark, who first investigated the substance,

is abandoned. Ricin differs in a marked manner from the bacterial toxins and snake venoms by its relative stability towards the natural fluids and ferments of the alimentary tract. For this reason it appears to be absorbed by the intact alimentary tract, and thus may act as a poison when administered by the mouth. The action of ricin is, however, much less powerful in the stomach than when injected hypodermically. The toxicity of the substance is enormous, and it may certainly be regarded as among the most powerful vegetable poisons when injected directly into the blood.

According to Ehrlich, 1-2000th grain per 2 lbs. body weight is fatal; 1 gm. (15.43 grains) subcutaneously is sufficient to kill one and a-half million guinea-pigs, while the lethal dose for man is supposed to be 0.30 gm. by the mouth or 0.003 gm. subcutaneously. It should, of course, be remembered that these figures do not refer to pure ricin, but to ricin contaminated with more or less albumin. Smaller doses, injected hypodermically, soon produce immunity, antiricin being formed.

As previously stated, the observation of Ehrlich of this protective reaction laid the foundation of serum therapeutics. Before discussing the production of antiricin it may be as well to briefly consider the toxins elaborated by bacteria. When pathogenic bacteria grow and multiply in the body, symptoms of poisoning (toxæmia) are manifested; consequently it was inferred that bacteria either produced poisons during their growth or contained poisons. Subsequent experiments proved that the poisonous effects of a few bacteria which passed out into the surrounding media, and the poisonous effects of the other class, seemed to be due to the actual constituents of the bacterial cells. The former are termed exotoxins or extra-cellular toxins, and the latter endotoxins or intra-cellular toxins. Some bacteria, on the other hand, notably the tubercle bacillus, elaborate both exotoxins and endotoxins. These toxins are substances of a very complex composition, probably allied to the proteins. In some instances they appear to be of the nature of enzymes or ferments, and they are direct products of the bacterial cells.

Among the few bacteria producing extra-cellular toxins or exotoxins the bacillus of diphtheria and the bacillus of tetanus are the most important. They are extremely poisonous; in fact, it has been computed that the toxin elaborated by a virulent culture of the bacillus tetanus is the most potent poison known to science to-day. These exotoxins being excreted by the bacteria, are found in solution in the liquid culture media containing the growing micro-organisms. Serum from an animal immunized by injecting into its body small and increasing doses of these soluble toxins, administered at regular intervals and given over a long period of time, is rich in antitoxin. This antitoxin, when properly prepared and standardized, constitutes the antitoxin of commerce. Diphtheria and tetanus antitoxins are prepared in this manner.

In the case of the bacteria which do not secrete a soluble toxin, the killed bacteria themselves are used for immunization. They constitute what are known as the antimicrobial serums, a familiar example of which is antistreptococcus serum, and should be distinguished from antidiphtheria and antitetanus serums, which are strictly antitoxic in nature.

Antiricin may be produced in exactly the same way as an antitoxin; in fact, an-

tiricin might be described as a vegetable antitoxin. Rabbits have been immunized by gradually increasing doses of ricin until they have obtained an immunity of 5,000, or, in other words, have developed so much antiricin in their blood serum that they are not affected by 5,000 times as much ricin as would have killed them had no preliminary treatment been instituted.

The immunity acquired for both ricin and bacterial toxins is entirely different from the tolerance acquired for morphine and other drugs. According to Cushny, the latter is due to the cells of the body becoming accustomed to being constantly bathed in a fluid containing the alkaloid. The same tolerance is acquired by various marine animals, which would be killed if suddenly changed to fresh water, but which are gradually acclimatized if the change is made more gradually by adding increasing proportions of fresh water to the sea water of the aquarium. In the case of ricin and bacterial toxins the immunity is due to formation in the body of a substance which antagonizes the original poison and constitutes what is known as an antitoxin. This antagonistic substance circulates in the blood, and can be withdrawn from the immune animal and injected into a second, which then acquires a certain degree of immunity, although less than that of the first. Just as diphtheria antitoxin and tetanus antitoxin are antagonistic only to their respective toxins, so also antiricin is antagonistic only to ricin and does not protect an animal from any other form of toxin.

Various animal poisons, such as snake venom, spider toxin, and eel serum, have been found to act in a similar manner although, apart from bacterial toxins, snake venom is the only one used for therapeutic purposes. By means of this an antitoxin has been produced which has marked prophylactic properties against snake bites, and is used extensively in countries where poisonous snakes abound. In addition to the vegetable toxins—risin, abrin, and crotin—toxins have also been obtained from poisonous mushrooms.

While antiricin has no practical therapeutic value, yet it was as the result of the study of this remarkably interesting substance that Ehrlich arrived at a practical method of standardizing the bacterial antitoxins, thus establishing a definite antitoxin unit value for these products.

It is not within the province of this article to discuss the physiological methods employed in standardization or the ingenious side-chain theory which Ehrlich evolved to explain the probable action of the antitoxins in producing immunity. Suffice to say that the discovery of ricin paved the way for some of the most wonderful products used in medicine to-day. It is only necessary to consider the tremendous number of lives which have been saved by the timely use of antidiphtheria serum, and particularly antitetanus serum in the present campaign, to fully appreciate its importance.

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"Education is a companion which no misfortune can depress; no crime destroy; no friend alienate; no despotism enslave; at home, a friend; abroad, an introduction; in solitude, a solace; and in society, an ornament—without it, what is man?"