Translation from the French of a paper by Professor J. Maisin, published in "*L'Europe Medicale"*, September 25, l938, No. 5, pg. 52, entitled:

NEOPLASMS, INFECTIONS AND ALLERGY

Although our knowledge of the subject of the etiology of cancers and tumors in general has made truly important progress during the past several years, we are still ignorant of the intimate mechanism of the cancerization of the cell. We know the exact formula of a large number of carcinogenic substances and we know of certain carcinogenic "viruses". Recent research seems to have arrived at the conclusion that these "viruses" are large protein molecules of a molecular weight in the tens of millions—a sort of enzyme with a perverted action. But we do not know what essential reaction in the biochemistry of the normal cell these carcinogenic substances, or those viruses, modify, in order to transform it into a biologic unit more or less differentiated and autonomous. Many scientists think that the difficulty resides in an alteration of the carbohydrate metabolism.

Infections caused by all sorts of microorganisms, protozoa, cocci, bacilli, spirilli and viruses are in the last resort organic chemical disturbances caused by poisons coming from such microorganisms.

Since the memorable work of Pasteur, a world of bacteriologists has devoted itself to a study of the mechanism of immunity. Such terms have, been created as vaccines, serums, antigens, antibodies, antitoxins, agglutins, precipitinis, bacteriotropins, opsonins and many others, in order to explain in simple language facts discovered in the course of immune phenomena. It was impossible to do otherwise, but those expressions do not explain anything of the chemical mechanism of these infections. This is what has inspired a large modern group of biochemists, who have attempted to translate in chemical terms these others terms which, though imprecise, are so useful of the language of bacteriology.

The fine researches of Ramon on antitoxins; of Avery on the nature of pneumococcal toxins (polysaccharides); those of Landsteiner are magnificent practical impressions on the maquis of classic immunology. These works, for the first time, attempted to concretize chemically some of the bacteriological findings.

Such terms as allergy, energy and hyperergy are oven more vague from the standpoint of bacteriological chemistry than those of which we have just spoken. They imply the idea of a state of immunity (allergy), or a lack of defense (anergy) towards various pathogenic agents, either chemical or microbic, without giving any idea as to what particular function or functions of the biochemistry these states are due.

Actually, when one studies the complex types of reactions of living organisms, one is struck by the large number of enzyme reactions that have been discovered and more or less studied. The principal processes of metabolism--carbohydrates, fats, proteins-are affected by the intermediary of a complicated set of enzymatic reactions, which include the addition or the subtraction of an atom of oxygen, hydrogen, or nitrogen, from the compounds involved; reactions which could never take place at the temperature of the body without the catalytic function of these enzymes.

In fact, the most important physiological functions are in the end dependent on enzymatic reactions and when, we speak of an organic defense of allergy, it is incontestable that these states derive, at least in part, from fermentation reactions.

Susceptibility to disease (whether a cancer, an, infection, or a toxicity), simply shows that our organism is not capable of transforming into an inoffensive substance a carcinogenic substance, or a microbic toxin, or a foreign protein, or a chemical substance of some sort. If one of our enzymatic functions is capable of changing the toxic nature of those foreign substances, then the latter are rapidly used by breakdown, or by synthesis, for our organic needs.

A chemical substance is carcinogenic because our normal functions are unable to "digest it". It is the same with the poisons of pathogenic organisms and other substances.

In the case of carcinogenic substances this intoxication eventuates in the creation of a type of autonomous cell; in infectious diseases it shows up by the appearance of reactions, inflammations, etc. and in hyperergic reactions by phenomena similar to the last group. However, the response of the organism to these various pathogenic, toxic, agents is fundamentally a method of defense on the part of the organism, in an attempt to rid itself of the cause of the lesions. The organism is doing its utmost not to succumb, after having been unable to neutralize chemically the pathogenic agent. It attempts to rid itself of it through the production of the various lesions which are the only means remaining at its disposal.

Such defense reactions may by their intensity become dangerous to life. A large pleural inflammation may compress the lungs or this heart and cause death. A cerebral abscess, or pulmonary edema may also result in death. This is what has caused certain authors to remark that inflammation in the larger sense is a dangerous reaction, of which the final end is not understood, whereas other authors say that inflammation is a remarkable defense of the organism which is always adequate to the type of lesion.

Quite objectively, one may say that inflammatory reactions of a hyperergic character are often dangerous.

Just as a hyperergic reaction is a danger, so is a neoplastic proliferation. Nothing proves that the neoplastic proliferation is not an ultimate means of defense of the cell, which is trying to escape death from the carcinogenic poison, an inadequate and dangerous means, just as the hyperergic reaction, although a means of defense, is also dangerous.

These are the last resorts of organisms in distress, which have been able to oxidize or reduce a chemical substance, which has been introduced into them or which is found within them.

We all know that a microbic poison may be extremely toxic for a given species, although it is quite inoffensive for another; that a substance is carcinogenic for one species, whilst it is not for another. This is to say that the living organisms have within themselves the means to "metabolize" the substance.

Such means as recently mentioned are often enzymatic means. It may, therefore, be that by

modifying the enzymatic functions of a living thing, one might change its receptivity, not merely from the standpoint of a single disease, but a whole group of affections.

Our efforts, during the last several years, have been directed toward this end and we regret that we do not have the necessary space here to express at greater length the results we have obtained in this direction.

By introducing into living organisms traces, in the order of a fraction of a gamma of very reactive substances, such as peroxides (for example, the peroxide of diformaldehyde) or of simple, unsaturated substances of the general formula R=C=R, one modifies profoundly, among other functions, certain enzymatic reactions of the blood, for example, the activity of catalases and peroxidases.

These modifications last a long time-several days, or several weeks--following a single injection. As a consequence, one notes a series of interesting changes in the injected organism--a modification of the hyperergic state reflected in the reaction to foreign substances, and a modification of the receptivity to carcinoma provoked experimentally by a given chemical substance.

This has resulted in some curious applications, therapeutic and prophylactic for a series of disease conditions quite different from each other by one single substance of simple, chemical composition, such is the peroxide of diformaldehyde in such diseases as: asthma, eczema, infections, cancer.

In the domain of cancer, this therapy is particularly interesting in connection with radiation therapy. We have examined this aspect of the subject for more than four years. Doing absolutely nonspecific, the treatment relieves not only the general cancerous state, but it also diminishes the untoward aftereffects of X-ray therapy, such as fatigue and the alteration of the blood picture. It often makes it possible to reduce the dose of X-ray or of radium in important proportions. In our eyes, it is the best adjuvant to X-ray therapy or radium therapy, an adjuvant which is by no means illusory, but of which the good effects are obtained a few hours, or a few days after the first injection.

Thanks to medical work of the kind, we may be able, we think, to enlarge considerably the field of application of X-ray and radium therapy.

Our work in this controversial field is continuing, with a view to finding out not only the mechanism of the bacteriological reactions started by the injected substances, but also with a view to differentiating between types of reactions started by substances of two types—R=O=O=R, or R=C=R.

These reactions, at first apparently similar, may finally prove more applicable, we think, to different organic conditions-perhaps one group for allergy and another group for hyperergy, which will enable us one day to understand the chemical mechanism of these particular conditions.