A SURVEY OF THE MODERN DEFINITIONS OF ANTIGENS AND ANTIGENICITY, IMMUNOGENICITY AND SPECIFICITY OF ANTIGENS, HOMOLOGOUS, HETEROLOGOUS AND CROSS-REACTING ANTIGENS

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The definition of the antigens before: «Every matter which enters the organism and induces the production of antibodies is an antigen» is not actual any more and does not define exactly the new aspects of immunology. Antibodies are not obligatory produced only after antigen irritation (stimulation); specific cell reactivity of hypersensitivity of delayed type or immunologic tolerance are often responses. Therefore, according to the old definition, no antigens are the reason for the latter. It must be pointed out that except antibodies we have to consider some other specific immunologic reactions too. The biologic nature and origin of the substances inducing the aforementioned reactions must also be concerned. That is why, the new definition indicates that: Antigens are all substances which possess genetically different information which entering the organism induce specific immunological reactions. This definition is a result of the immunity content: a way of defence of the organism against living microorganisms and substances possessing genetically different information.

The nature and origin of the antigens have been the object of a long-term discussion. It was accepted before that only proteins and their derivatives could be antigens. Recently new data of the non-protein origin of many antigens were reported by great number of authors. Now we know that antigens can be proteins, but together with them complex polysaccharides, lipopolysaccharides, polypeptides, even nuclear acids with high molecular weight. Having in mind that simple elements (Fe, Mn, P, Na) can not be antigens, it is logical to accept that compounds of chemically same-type molecules possess no antigenicity (glucose, acids, aminosaccharides, salts of metals, etc.). However, aminoacids in a polypeptide chain with certain complex structure and enough length can show definite antigen activity. The molecular weight plays certain role as well: MW above 10 000 provides antigenicity (egg albumin — 40 000; serum albumin — 70 000, etc.). There are some proteins with lower MW (insulin 6000, even vasopresin — 1000) which can be also antigens only if applied together with some stimulators in the organism. Until now there is no definite explanation about the role of MW: it is very possible that macrophages are able to swallow larger molecules and the latter stay longer in the organism, thus exerting longer influence. Recently, after the role of both T- and B-lymphocytes was precisely determined, specially for their cooperation in the immune response (B-lymphocytes for the determinant groups, T-lymphocytes for the base carrier part of the antigen molecule), it is accepted that the molecular weight is quite important.

In order to define any substance as an antigen it must have the following characteristics: genetically different origin, antigenicity, immunogenicity and specificity. All these features are obligatory: genetically different is any antigen, otherwise it has no antigenicity. For example, albumin of guinea pig is not antigen for the same animal, because there is no genetical difference, but this albumin is antigen for any other organism (animal, man, etc.). Antigenicity is the ability to induce synthesis of antibodies; it is more or less expressed, but obligatory. Immunogenecity is the capacity of forming (creating) the immunity. Of course, it is a matter of microbes most of all, because their antigens with their own immunogenecity induce immunity against infections. Specificity is a feature showing the peculiarities of the antigens and their differences. Often there are specific substances which can not induce production of antibodies in the organism, but possess the ability to interact with synthesized antibodies. These substances are named haptens, which are genetically different to the organism but have no immunogenecity, antigenecity. They can be complete antigens only if combine with other substances having great molecular weight (molecular structure).

What is most important for the specificity of antigens and what structures of the antigens interact with the specific antibodies? The experiments of Landsteiner shew that even the protein of the own organism can be an antigen if only one different element or radical is added to its periphery: 2 rabbits injected with veal and horse serum will have synthesized antibodies towards both sera (one for the first rabbit, second for the other one). There is no cross-reactivity between corresponding antigens and antibodies. However, if both sera (antigens) are influenced preliminarily with iodine and after that they are applied to another 2 rabbits, the produced antibodies have no more specificity: both groups antibodies (from both rabbits) are able to interact with either iodine horse serum or with iodine veal serum — there is cross-reactivity. These experiments show that the protein is undoubtfully necessary for antigenecity, it is the base part of the antigen, its outer half. But if the periphery structure is changed it looses the specificity. Landsteiner, by applying iodine, changes and displaces the specific differences betwen the horse and veal serum, replaces their surface chemical radicals (determinant groups) which are the factors of specificity. It is obvious that the determinant groups with their chemical structure, various combinations of aminoacids, their number and surface location, i. e. optical activity, determine the specificity of any antigen. Jerne gives the name «epitopes» to these groups and when the epitopes are similar they form epitype. For example, all patients suffered typhus have antibodies which can agglutinate simultaneously the epitopes of R. prowazeki and Bact. proteus OX_{19}, although these microorganisms (Rickettsia, Proteus) are quite different and far in taxonomia. This is a result of the fact that their antigens have similar, perhaps even same, epitopes (determinant groups) while the antigens themselves are considerably different. Various antigens possess various number of surface determinant groups and due to that, one molecule antigen is able to interact with several molecules antibodies. This is the so-called valency of the antigens.

Full characteristics of antigens requires their genetical difference for the organism. The antigens are heterologous for the organism. Principally, the macromolecules of own organism have no antigenecity and no antibodies against them are synthesized. It is known, however, that crystaline of the eyes, sperm

cells and other molecules are homologous to the organism (their own organism) and have no contact with the apparatus of the normal organism responsible for the synthesis of antibodies. But if the same molecules are applied parenterally to their own organism they are able to induce production of antibodies (autoantibodies). With certain pathological conditions the organism is capable of synthesizing autoantibodies against number of own organs and tissue antigens. It can be explained only by the influence of definite physical and chemical factors which transform their own normal molecules in «foreign» and different. The remarkable ability of the organism — to establish which is own and which is not is still a discussed problem. One substance is not always antigen only because it is genetically different for the organism. It has a possible dependence to the organism itself (animal or man), type and individual features, etc. Thus, pneumococcal polysaccharides are antigens for man and mouse but not for rabbits.

It is obvious that there is a big variety of antigen variants. Therefore, it is worth-mentioning the classification scheme of Kwapinski for the antigens:

ANTIGENS: complete (total) and incomplete (haptens)

COMPLETE ANTIGENS: proteins, nucleoproteins, lipopolysaccharides, polysaccharides

INCOMPLETE (HAPTENS): complex haptens and simple haptens

SIMPLE HAPTENS: disaccharides, elementary organic compounds

COMPLEX HAPTENS: polypeptides, nuclear acids, polysaccharides, lipides

Regardless of their type, origin and synthesis, the specificity of the antigens can be considerably changed by applying temperatures above 60° C, denaturating agents, enzymes, chemical compounds (iodine, nitrogen, etc.), oxydation and reduction, etc. Various antigens show various sensitiveness towards different physical and chemical factors. For example O-antigen of the Enterobacteriaceae can be subjected 2 hours to 100° C, whereas H-antigen of these bacteria is far from this resistance; it is very thermo-unstable. The influence of numerous factors upon antigens is very important for the practical immunology.

ОБЗОР СОВРЕМЕННЫХ ПОНЯТИЙ «АНТИГЕН И АНТИГЕННОСТЬ», «ИММУНОГЕННОСТЬ И СПЕЦИФИЧНОСТЬ АНТИГЕНОВ», «ГОМОЛОЖНЫЕ, ГЕТЕРОЛОЖНЫЕ И ПЕРЕКРЕСТНО РЕАГИРУЮЩИЕ АНТИГЕНЫ»

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РЕЗЮМЕ

Сделана попытка выяснить основные понятия иммунологии на базе последних открытий в этой области и в свете современных концепций. Указывается на значение антигенов и антигенности для имунного ответа, на их иммуногенность и специфичность, как и на гомоложность, гетероложность и перекрестную реакционную способность антигенов в различных условиях индуцирования специфического иммунного ответа.