

ÜLO PAVEL

ON THE DEVELOPMENT OF IMMUNOLOGICAL REACTIVITY IN THE PERINATAL PERIOD

It is widely accepted that the perinatal period (i. e. the embryonic and early postnatal period) in birds and mammals is characterized by low immunological reactivity. Actually, many species do not synthesize antibodies in the perinatal period of life. The opinion that a developing animal is not able to produce any kind of immunological reaction is obviously an underestimation of the abilities of the young animal. Therefore V. Berman (Берман, 1955) is right when objecting to the use of the term "non-reactivity" for describing the low immunological capabilities of a newborn animal. As we see below, the contradictions between various authors are mainly caused by the circumstance that one interprets some basic immunological terms differently, especially resistance and reactivity.

In the perinatal period it is characteristic of developing organisms that they are, on the one hand, susceptible to certain facultative pathogens, such as *Escherichia* and *Proteus* and, on the other, resistant to some obligatory pathogens (Сиротинин, 1938; Poltyev, 1947; Зильбер, 1948; Здродовский, 1961).

Referring to Haeckel's law of biogenesis, V. Poltyev presumes that at early stages of individual development the cellular factors ought to be expressed more extensively than humoral ones. We must say that this is only correct if we keep in mind the phagocytic activity of macrophages. Thus the phagocytic activity is rather well expressed during the early stages of embryogenesis. However, the work of A. Varshavsky (Варшавский, 1938) clearly demonstrates that the excretion function of RES cells is lower in the perinatal period. As seen from the work of K. Karthigasu, C. R. Jenkin and K. J. Turner (1964) and also from the findings of C. Stiffel and collaborators (1964) and J. Sterzl and collaborators (1965) the activity of macrophages also depends on the antigenic structure of pathogens. It is demonstrated that the absence of lysozyme in young animal is the reason of low phagocytic activity of leucocytes (Аршавский и др., 1946; Аршавский, Соколова, 1949). The incompleteness of cellular factors in the perinatal period is further shown by the finding that the inflammation reaction is weaker in newborn animals than in adults (Аршавский, Молдавская, 1949). Supplying the newborn rabbit with humoral factors does not enable it to form an anaphylactic reaction, either (Сиротинин, 1938).

Thus one can see that the cellular defence mechanisms are not yet complete in the perinatal period.

J. Šterzl (Штерцль, 1961) distinguishes three stages in the formation of immunological reactivity. According to his theory, the first stage is limited to phagocytic potentialities; during the second stage, the capacity of forming specific cellular reactions of the type of delayed hypersensitivity is developed. The third and last stage is characterized by the immunological maturation of the individual, which is reflected by the ability to synthesize antibodies.

Thus, the immunological capacities in the perinatal period specialize gradually. The duration of the development of capacities of immunity depends on the animal species. A newborn animal may already approach the stage of maturity, or it is, at the moment of birth, physiologically immature (e. g. rabbits, dogs, etc.).

In general, the perinatal period is characterized by a high sensitivity threshold (Берман, 1955) which, among other factors, is evidently caused by an underdevelopment of systemic factors like the endocrinal system (Verge, Paraf, 1957; Здродовский, 1961). But the main reason is that the mesenchymal tissue itself is subjected to developmental processes (Шварц, 1938). As mentioned above, the high resistance to certain toxins of bacterial origin is characteristic of the perinatal period (Сиротинин, 1949; Пасичник, 1949).

Having in mind the different terms used in immunology to designate similar or even identic phenomena, and also the confusion in the interpretation of some terms, we propose a simple scheme in which we try to present immunological phenomena in a logical sequence, where an argument is followed by its function. As argument will serve the reactivity of organism, and its function will be the result — resistance (or susceptibility). We have constructed this scheme on the basis of the ideas of L. Zilber (Зильбер, 1948), J. W. Gowen (1951, 1961), V. Gostyev (Гостев, 1959), V. Efroimson (Эфроимсон, 1964), N. Sirotnin (Сиротинин, 1951), J. Arshavsky (Аршавский, 1959), P. Zdrodovsky (Здродовский, 1961), S. Moshkovsky (Мошковский, 1947), W. C. Boyd (1956), and others.

The scheme is as follows:

A. Immunological reactivity (recognition of the antigen and the reaction produced).

1. **Non-specific reactivity** (determines the non-specific response of organism). It depends on the individuality (structure and function) of: a) non-specific factors of resistance (barriers, humoral factors, etc.); b) systemic factors (endocrine and nervous systems); c) absence of a certain metabolite.

2. **Specific reactivity** (determines the immune response). It depends on the individuality of lymphatic apparatus and of the presence of antibody-like substances.

B. Resistance, the function of immunological reactivity; it does not depend on the sign (+ or —) of argument; it can be subdivided: a) non-specific resistance (depends on the non-specific reactivity); b) specific resistance (depends on both forms of immunological reactivity), and c) resistance based on hypo-reactivity of the individual. The non-specific (1) and specific (2) immunological processes may appear in the following combinations: a) (1) and (2) have the same direction (individuals with high, *resp.* low non-specific and specific reactivity); b) (1) and (2) have different directions (individuals with high non-specific and low specific reactivity and vice versa).

The value of the scheme consists in the fact that it connects the physiological and genetic grounds of immunological reactivity and that it does not divide immunological phenomena into two different groups (such as

natural and acquired immunity), but indicates that there are two steps in reactivity, the second of which is characterized by high specificity. These specific reactions in most cases only strengthen the resistance of the organism (Гостев, 1959; Gowen, 1948, 1961), and in some cases they play an insignificant role. Thus, the specific humoral factors may enhance the action of barriers (Берман, Славская, 1955).

According to the presented scheme of immunity reactions, the natural immunity corresponds to non-specific resistance and acquired immunity to specific resistance. But we have to assert that the term of natural immunity is very suitable for designating the inborn immunity of a species to a certain pathogen.

Perhaps the term "specific" in the scheme is not the best one for characterizing immunological processes, but we think that such a term as physiological reactivity (instead of non-specific reactivity) does not reflect the sense of these processes to better advantage.

We should call attention just to one thing, namely to the circumstance, that perhaps one must to agree with professor S. Moshkovsky's (Можковский, 1947) point of view that the term "condition" instead of "reactivity" reflects the immunological status of the organism more precisely. Thus, if under the term of non-specific reactivity one can comprehend the non-specific reactive potentialities of an individual as well as the non-specific immunity reactions themselves, the term "non-specific condition" designates the reaction of a certain individual, only.

As may be seen from this arbitrary scheme, the terms reactivity and resistance are not identical in the sense that high reactivity also means a high degree of resistance. In some cases, however, the low reactivity or even the lack of immunological reactivity is the reason of the resistance. It is known that hyper-reactivity does not always coincide with resistance.

Concerning the non-specific resistance, it is worth to call attention to the circumstance that it may be also caused by the absence of a certain metabolite necessary for the reproduction of the parasite.

On the other hand, having in mind the mutational theory of immunity (Эфромсон, 1961), according to which some mutant biopolymers of animal organism may act as antibodies (so-called antibody-like substances), these must be classified as specific substances, though the production of these substances is not dependent on the presence of the pathogen. Therefore, in our scheme, antibody-like substances are placed under the term of specific reactivity. In this instance, we have extended the sense of specific reactivity. Therefore, the former is not only limited to the function of lymphatic apparatus, but it also comprehends some sort of genetic variation of biopolymers.

Having dealt with the weak and strong points of the scheme of immunological reactivity, we may continue to consider some peculiarities of the immunological reactivity in the perinatal period of life. As we have already mentioned, the perinatal period is characterized by a low immunological reactivity, expressed by a raised threshold of sensitivity (Берман, 1955) and the absence of some non-specific resistance factors. For example, the findings of V. Berman and J. Slavskaya (Берман, Славская, 1955) show that facultative pathogens may propagate in a young animal at the same rate as obligatory parasites. Thus, in newborn mice, the *Salmonella typhimurium* and *Salmonella paratyphi B* propagate at the same rate.

They also stated that developmental changes in the barrier function of the gut wall do not take place. But the ability of the microbes to propagate largely depends on the stage of the individual development of

animals. Thus it seems that young animals are lacking some factors limiting the reproduction of bacteria.

As mentioned above, the hypo-reactivity of newborn animals may be the reason of resistance. Thus M. Sirotnin (Сиротинін, 1949) succeeded in demonstrating that newborn rabbits are markedly more resistant to staphylococci than adult animals. As M. Sirotnin showed, this is not correlated with antibodies or phagocytosis. He (Сиротинін, 1938) does not agree with the assumption of Gröer and Kassowitz (1923; cit. Сиротинін, 1938) who explain the refractory condition of newborn individuals with the absence of corresponding receptors in the Ehrlich sense. In his opinion, the reason is the hypoergy of the newborn.

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IMMUNOLOOGILISE REAKTIIVSUSE ARENGUST PERINATAALSEL PERIOODIL

Resüme

Esitatakse immunoloogiliste protsesside järjestuskeem, kus argumentide järgneb funktsioon. Argumentiks on organismi reaktiivsus ja selle funktsiooniks — resistentsus. Mittespetsiifiline reaktiivsus määrab organismi mittespetsiifilise vastuse ning sõltub organismi struktuurilisest ja funktsionaalsest individuaalsusest. Spetsiifiline reaktiivsus sõltub lümfatilisest aparaadist individuaalsusest ja antikehadesarnaste ainete esinemisest. Resistentsus on reaktiivsuse funktsioon, kusjuures see ei sõltu argumenti märgist. Spetsiifiline resistentsus põhineb mõlemal immunoloogilisel reaktiivsuse vormil. Mittespetsiifilised ja spetsiifilised immunoloogilised protsessid võivad esineda erinevates kombinatsioonides.

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ЮЛО ПАВЕЛ

О РАЗВИТИИ ИММУНОЛОГИЧЕСКОЙ РЕАКТИВНОСТИ В ПЕРИНАТАЛЬНОМ ПЕРИОДЕ

Резюме

Приводится схема иммунологических процессов, которая основывается на идее, что резистентность является функцией иммунологической реактивности. Последняя (свойство признать антиген и реагировать на него) подразделяется на неспецифическую и специфическую реактивность. Специфическая реактивность основывается как на неспецифических, так и на специфических факторах и зависит, таким образом, как от индивидуальности лимфатической системы, так и от присутствия антитело-подобных веществ.

Указывается, что иммунологические процессы могут встречаться в виде различных комбинаций.

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