ONTOGEN OF THE BOVINE IMMUNE SYSTEM

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The understanding of the immune system of the newborn calf makes it necessary to first look at the development of this system in the bovine embryo and fetus. Certain phases of immunological development have been studied by several investigators and some of the facts that emerge from these studies shall be discussed (SCHULTZ, 1973; SOLOMON, 1971).

Like in all birds and mammals, the ontogeny of the immune system begins with the development of haemopoetic stem cells in the yolk sac and the liver. In the bone marrow these cells differentiate into lymphoid stem cells. It is clearly established that the lymphoid stem cells need to migrate into so-called primary or central lymphatic organs for further differentiation.

One population of lymphoid cells migrates to the thymus to become immunocompetent there, most likely under the influence of the thymic hormone thymosin. Immunocompetence means that the lymphocytes now possess so-called surface receptors that can react specifically with antigens. After the passage through the thymus we call these lymphocytes T-cells or thymus derived lymphocyes. T-cells colonize the peripheral lymphatic system (i.e. lymph node, spleen) where they can be identified in certain compartments. As a population of long-living lymphocytes they also recirculate via the lymphatics into the blood and back to the lymphoid organs. T-cells are responsible for the various functions of cell-mediated immunity (i.e. delayed hypersensitivity, graft rejection, graft versus host reaction, effector cells, lymphokine production).

Another population of lymphoid stem cells requires the Bursa of Favricius in birds or the so-called Bursa-aequivalent in mammals. What exactly represents the Bursa-aequivalent

is uncertain: it may be both the bone marrow and the gut-associated lymphoid tissue. During processing in the Bursa-aequivalent lymphocytes develop on their surface antigen-specific immunoglobulins which remain firmly attached to the cell. Again, the lymphocytes, now called B-cells, migrate to the peripheral lymphatic organs where they settle in compartments such as germinal centers of spleen and lymph nodes. The function of B-cells is to develop further into plasma cells which synthesize and secrete immunoglobulin or antibody. The immunoglobulins sofar detected in the bovine species are IgG_1, IgG_2, IgM, IgA, and IgE. Thus, B-cells are responsible for the humoral or antibody-mediated immunity.

For some of the topics in this seminar it is of considerable interest to point out that a systemic immune response will occur when the antigen penetrates through some portal of entry into the body. As depicted on this schematic representation B-cells often require the help of T-cells (helper cells) to be activated. Within germinal centers B-cells differentiate into plasma cells which actibely synthesize antibody, which eventually reaches the circulation. If, however, the antigen remains confined to a mucosa, the local type of immune response will develop in the so-called lympho-epithelial system. IgA is the predominant immunoglobulin of tracheo-bronchial and gastro-intestinal secretions. Knowledge of the local immune system is particularly important in immunisation programs based on oral or intranasal administration of vaccines. The local lympho-epithelial systems are also called.

- BALT (Bronchus-associated lymphoid tissue in the lung) and
- GALT (Gut-associated lymphoid tissue in the gut.

There is evidence that these systems function in the following way: Antigens taken up by BALT seem to stimulate locally the formation of IgA precursor cells, i.e. B-cells.

These circulate through the lymphatics into the blood and return ("homing") to their appropriate milieu in the bronchial and intestinal mucosa, where they eventually mature into IgA-producing plasma cells.

IgA is synthesized by interstitial plasma cells and selectively transmitted through secretory epithelia. During this process IgA becomes conjugated with a glycoprotein called secretory component (SC) (BIENENSTOCK et al., 1973). The SC is synthesized by the epithelial cell. The conjugation of two IgA molecules with the SC is of biological value,since the dimeric IgA, SC-IgA, is highly resistent to proteolytic degradation.

In TABLE I, the time sequence is summarized how the immunological competence develops in the bovine fetus. We can see the dates at which the primary lymphoid organs,thymus and bone marrow, are colonized; that the structure of the peripheral lymph nodes develops at 55 and 60 days post conception. Minute quantities of serum IgM become first detectable at 130 days, and IgG at 145 days.

Ontogeny of T and B cells (SENOGLES et al., 1979).

	90 days	280 days (at term)
Thymus	60-70% T, 1% B	60-70% T, 1% B
Spleen	11% T, 3% B	40% T, 3% B
Periph.Blood	1% T, 1% B	45% T, 5% B

It becomes apparent that the precolostral calf is not absolutely agammaglovulinaemic. Low levels of IgM and/or IgG were detected in most serum samples examined after 200 days of gestation (KLAUS et al. 1969; SAWYER 1973; SCHULTZ et al., 1971). In cases of in utero infection a significant rise in immunoglobulin has been observed.

TABLE II summarizes some data concerning the onset of immunocompetence in the immunologically stimulated fetus. The assumption is that if a fetus is infected in utero with

microbial antigens or stimulated with non-microbial antigens and produces specific antibody,the animal was immunologically competent at the time of initial stimulation.

Some 14 different viruses are known to infect the bovine foetus or the placenta. Immunological competence begins not earlier than 90 days post conception. Examples of viral infections: BVD-MD, Parainfluenza-3, IBR, Bluetongue, Bovine enteroviruses. (Antibodies to the latter proved to be "non-specific inhibitors to bovine enteroviruses ", ROSSI et al., 1976). The immune response to several bacteria has also been studied, one of the earliest being Leptospira saxkobing. In advanced gestation the bovine fetus may also produce antibody against microbes such as Vibrio fetus, Aerobacter aerogenes and E.coli (0 16:K 60:NM) (OLSON and WAxler, 1977). Immunological competence of the fetus also includes antibodies against erythrocye antigen, ferritin plus Freund's adjuvant, and ovalbumin plus Freund's Adjuvant.

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Table 1: ONTOGENY OF THE IMMUNE SYSTEM IN THE BOVINE FETUS

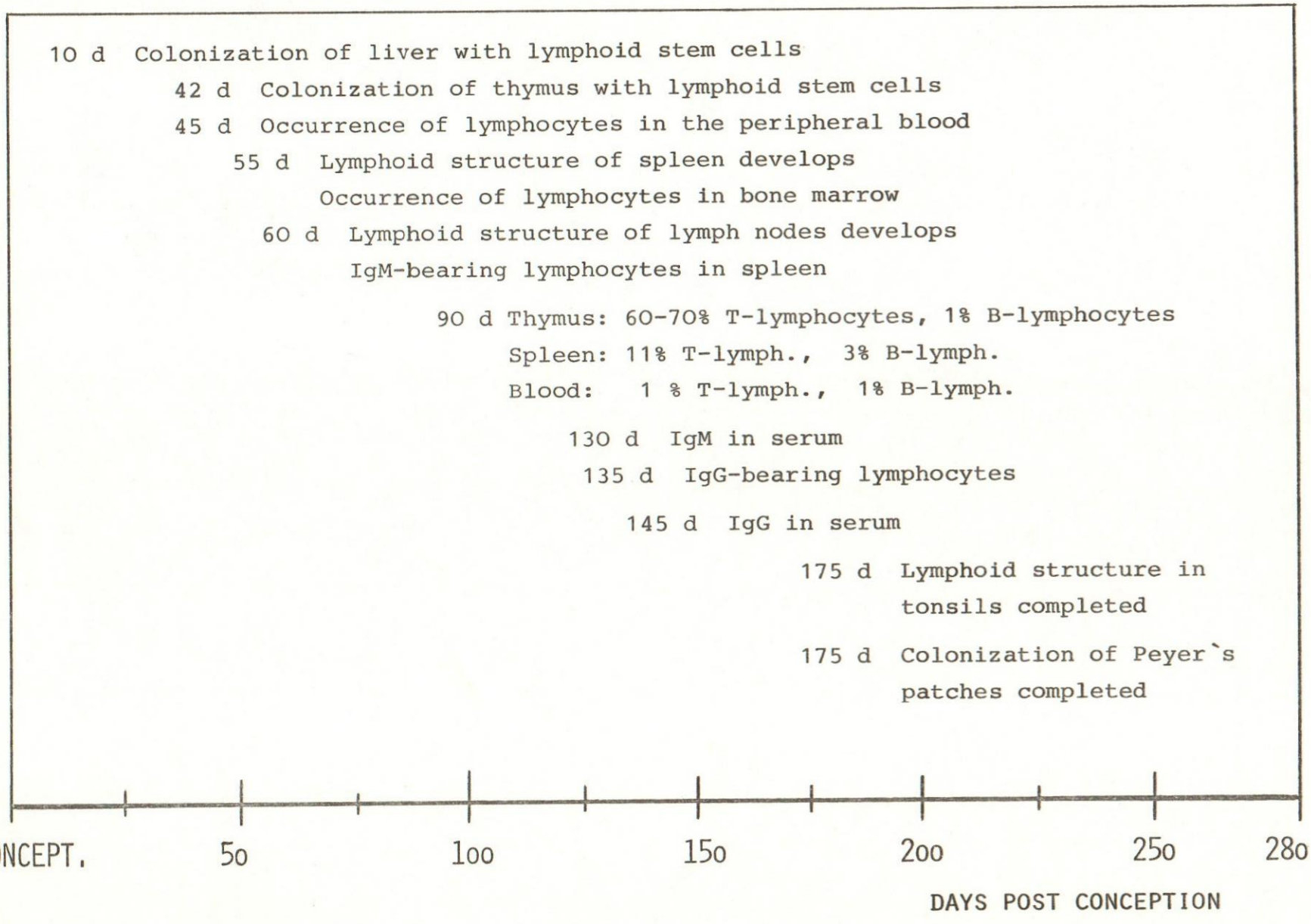

Table 2: ONTOGENY OF THE CELLULAR AND HUMORAL IMMUNE SYSTEM IN THE BOVINE FETUS