

respect to CCP levels. A marked increase in ACP hemolytic titers was found to occur in the last few weeks of gestation (see Figure), thus suggesting that pregnancy time-course and ACP titers are closely related, as also seen in the significant correlation coefficient ($r = 0.61$; $p < 0.02$). The results of the hemolytic assays were further strengthened by the rocket immunoelectrophoresis finding of higher C3-proactivator concentration in sera of pregnant subjects.

In an effort to extend these observations, and to reduce the variability inherent to data on hospitalized patients, we investigated ACP levels in pregnant mice. As shown in Table II, the trend in mice is fully consistent with the one found in humans. Sera from pregnant mice display a higher hemolytic efficiency which significantly differs ($p < 0.001$) from the one of the control sera. Somewhat surprising was the likeness of the hemolytic behaviour among animals belonging to allogeneic and syngeneic pregnancy groups.

Increase in ACP and in C3-proactivator concentration, as it occurs in pregnancy, may be interpreted, from an immunologic viewpoint, as reflecting the preferential depletion of selected ACP components, namely properdin, properdin-convertase and factor D (C3PAse), as a consequence of their consumption by weak but continuous humoral or cellular immune reactions. This hypothesis suggests that antigenic differences between mother and conceptus are of relevance in pregnancy, as mainly supported by several data, such as hypertrophy of the regional uterine lymph nodes, which attest to the pregnant female's awareness of her fetuses². On the other hand, it cannot be excluded, pregnancy being characterized by a different hormonal balance, that hormones more than

immune reactions are responsible for the observed patterns. To cite an example, it is well established that sex-hormones influence the homeostasis of certain plasma proteins¹⁷ among which, and to a higher extent, late-acting complement components^{18,19}, and acute phase reactants may attain twice the normal levels during preparturition period²⁰. Consistent with this opposite view, our findings of an identical behaviour in inbred and outbred pregnancies cast doubts on whether hystocompatibility differences should be considered partially responsible for the high ACP-activation found in pregnancy. However, even in inbred pregnancy, mother and conceptus may present different antigenic specificities, due to foetal antigens and/or to sex-linked determinants.

It is difficult and unproductive, at this preliminary stage of our investigation, to relate present findings to any one of the several physiological changes which occur in pregnancy. Conclusive evidence must await more extensive studies on humans and on suitable animal strains with well defined major and minor hystocompatibility differences. The possible relevance of alternative and classical complement pathway behaviour in monitoring pregnancies, either in normal or in pathologic conditions should be emphasized.

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Mast Cells in the Pinna of Balb/c 'nude' (nu/nu) and Heterozygotes (nu/+) Mice¹

K. WŁODARSKI^{2,3}

Department of Immunology and Microbiology, Wayne State University, School of Medicine, 540 E. Canfield Street, Detroit (Michigan 48201, USA), 30 June 1976.

Summary. The relative number of mast cells in the ear lobes' skin (pinna) of nude (athymic) nu/nu and normal (thymic) nu/+ heterozygotes of Balb/c mice was similar. The results obtained contradict some suggestions about the general influence of the thymus on the number of mast cells in the skin and suggest the existence of some local factor(s) in regulation of skin mast cell numbers.

Although there is some evidence that the thymus may contain precursors of mast cells (MC)⁴⁻⁶, it is hard to accept the hypothesis that the precursors of these cells are of thymic origin. CSABA et al.⁷ reported a decrease of circulating MC in the blood after neonatal thymectomy of rats, but such an effect was not observed by WALKER⁸ in the mouse. VIKLICKY⁹, in extensive experiments employing chimeras, showed that precursors of mouse MC are radio-resistant reticular cells. The presence of MC in athymic 'nude' mice seems to be the best evidence against the concept of thymic origin of MC¹⁰. It was found that in the skin of 'nude' mice there is nearly three times more MC than in normal animals^{10,11}. The abundance of MC in the skin of 'nude' mice lead VIKLICKY et al.¹⁰ to the conclusion that the frequency of MC is regulated in some way by the thymus. The absence of this regulation in athymic mice is, according to them, responsible for the high frequency of MC in their mice.

Searching for the role of thymus in regulating lymph node mast cell populations, we examined a number of popliteal lymph nodes of normal and athymus 'nude' Balb/c mice, but we could not demonstrate significant

differences in the absolute number of MC between these animals. As an additional control, we have analyzed the relative number of MC in the 'nude' and normal Balb/c mice. This analysis was performed on the pinna (the auricle of the ear), as this organ seemed to be more uniform and thinner, thus making the quantitation of MC

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² Permanent address: Department of Histology, Institute of Biostructure, School of Medicine, PL 02-004 Warsaw, Poland.

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Relative number of mast cells (MC) in pinna of nude and normal Balb/c mice

| nu/nu ^a Total count of MC | No. of scale projected | Average No. of MC per 1 scale unit (250 μm) | nu/+ ^b Total count of MC | No. of scale projected | Average No. of MC per 1 scale unit (250 μm) |
|--|---------------------------|---|---|---------------------------|---|
| 1115 | 96.0 | 11.60 | 864 | 88.8 | 9.72 |
| 641 | 56.2 | 13.20 | 423 | 43.7 | 9.67 |
| 789 | 52.0 | 15.17 | 796 | 69.8 | 11.40 |
| 638 | 53.0 | 12.78 | 435 | 43.0 | 10.10 |
| 1263 | 104.5 | 12.08 | 661 | 71.5 | 9.24 |
| 639 | 70.5 | 9.06 | | | |
| 638 | 64.0 | 9.96 | | | |

^aMean 11.9 ± 1.92; ^bmean 10.02 ± 0.84.

easier to perform. Contrary to earlier reports of elevated numbers of skin MC in ‘nude’ mice^{10,11}, we did not find any difference in the number of in the pinna of ‘nude’ and normal mice.

Materials and methods. 11-week-old Balb/c ‘nude’ (*nu/nu*) and litter-mate, normal heterozygotes (*nu/+*) mice of both sexes were used. The lower one-third of one pinna was removed, fixed 4–6 h in Bouin solution, embedded in paraffin and 7 μm sections were stained with 0.1% aqueous solution of toluidine blue, pH 7.6. Under 40 × 10 magnification, the total number of MC on both sides of elastic cartilage was counted alongside the projection of the Zeiss microplate (1 cm divided into 100 units) inserted in the ocular. Between 10 and 32 length of scale was projected into one section of pinna and, from each specimen, the number of MC was counted in 3–6 sections. Total number of MC from each section was pooled, divided by the number of scale projected, and the value obtained represented the average number of MC per length unit (250 μm). The mean values for both groups of mice were counted, and data obtained were statistically analyzed using Student’s *t*-test at the level of *p* = 0.05.

Results and discussion. The table shows the number of animals used and the results obtained. The mean number of MC in pinna of nude mice was 11.98 ± 1.97, and, in those of normal heterozygotes, 10.02 ± 0.84. This difference is not significant at *p* > 0.05. The distribution of MC in both cases was similar. They were distributed homogenously in the skin of pinna.

¹¹ R. KELLER, M. W. HESS and J. F. RILEY, *Experientia* 32, 171 (1976).

The results are in contrast to those obtained by others^{10,11} in skin taken from the back. KELLER et al.¹¹ reported nearly 4 times higher concentration of skin MC in ‘nude’ Balb/c mice than in normal mice. VIKLICKY et al.¹⁰ found 3 times more MC in skin of ‘nude’ B₁₀LP than in control mice.

The histology of pinnae in both ‘nudes’ and heterozygotes was similar, and the number of hair follicles and glands is equal. The only difference was lack of or retardation of hair development. The mitotic activity in the epidermis and glandular follicles, although not examined systematically, seemed to be identical in both cases.

We do not have an explanation for the discrepancy of skin MC content in regard to the site (back skin, pinna skin). The presence or absence of the ‘nu’ gene may be more important in determining the number of MC than skin site. The presence of this gene in both ‘nude’ and control mice may be responsible for similar MC content. KELLER et al.¹¹ used normal Balb/c (+/+) for their controls, while in the present study *nu/nu* were compared to *nu/+* animals.

It would be interesting to find whether the presence of large amounts of cartilage in pinna tissue exert some modifying effect on MC content. This possibility will be examined. At present, we are inclined to consider the local factor(s) or ‘nu’ gene in regulation of skin MC numbers more than the influence of the thymus itself. This assumption is based on the more pronounced histological difference of back ‘nude’ skin and hair-covered skin in contrast to pinnae, and on the lack of drastic differences in the absolute number of MC in lymph nodes.

Foetal Blood Abnormality Associated with Hypodactyly in the hd Strain of Rat

C. PETTER

Laboratoire de Physiologie du Développement du Collège de France et de l'Université Pierre et Marie Curie, 4, place Jussieu, F-75 230 Paris-Cedex 05 (France), 1 June 1976.

Summary. The homozygous fetuses of hypodactyl rats (hd strain) present an obvious red blood cell macrocytosis (day 14 of gestation). This blood abnormality could give rise to thrombosis leading to early necrosis of the extremities.

Some mutations are known to affect the number of digits in mouse¹, or to lead to limb amputations in rabbit², cat³ and man⁴. Among them, the strain of br rabbit (brachydactylia), first described by GREENE and SAXTON² has been studied by several authors^{5–8}.

In that strain, a blood abnormality has been shown: the foetal primordial red cells are especially large and numerous, and could give rise spontaneously, between days 15 and 16 of gestation, to thrombosis, haemorrhages and necrosis of the extremities⁷. The lesions can be pre-