In this report we shall limit ourselves to a statement concerning the differences which we found in the mitotic proliferation of the epidermis of the guinea-pig in normal adult males on the one hand, and in females in various stages of sexual activity, on the other hand. We found that in adult female guinea pigs during the sexual cycle the mitotic cell proliferation is distinctly less active than in adult males otherwise living under the same conditions. It seems to be weakest at the time of oestrous and then rises very slowly towards the end of the cycle, without, however, reaching the average of the mitotic activity in the male even as late as 15 to 16 days following heat. In castrated female guinea pigs cell proliferation is low; we must assume that castration as such lowers the proliferative activity of the epidermis. On the other hand in pregnant guinea pigs it is definitely higher than in animals during the ordinary cycle, although it does not reach the average of adult male guinea pigs. This rise which takes place during pregnancy, to some extent is maintained during the period of nursing, although it is then not quite so high as during the former period.

We see thus that the changes taking place in female guinea pigs during the sexual cycle and even in pregnancy have a depressing effect on the proliferative activity of the epidermis. This effect is not caused by the sex constitution as such; this is shown by the fact that young, sexually immature female guinea pigs show at least as great a proliferative activity as males of similar age and perhaps an even greater activity.

This is a preliminary report.

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Notes on the Development of Lymphocytes.

MONTROSE T. BURROWS.

From the Research Laboratories of the Barnard Free Skin and Cancer Hospital, and the Department of Surgery, Washington University School of Medicine.

The author has noticed that fully matured lymphocytes, polymorphonuclear leucocytes and many other mononuclear cells will not grow in a tissue culture. Other reactions of these cells when compared with those of fixed tissues indicate that they have suffered decided changes from the mother cells from which they arise.

The migration of fixed tissue cells, including the mother cells of

the lymphocytes and leucocytes, is the result of their liberating a lipoid blood coagulating substance which has been named the ergusia. Their growth is also dependent upon this same substance. The migration of the leucocytes and lymphocytes is not associated with the liberation of this coagulating substance. They migrate apparently by dissolving paths in a solid clotted medium. They possess fermentative reactions, but have lost their power to liberate the ergusia in their differentiations.[1]

They are not important in aiding the body against invading organisms. Bacteria placed in the medium near a fragment of spleen causes this fragment to be disintegrated almost entirely into lymphocytic cells.[2] These lymphocytes show, however, no resistance to the bacteria. They migrate readily and in practically every case directly in and among the growing bacterial cells. Fixed tissue cells on the other hand are strongly antagonistic to these growing bacteria.[1] The fixed tissue cells invade areas of the medium containing bacteria only when their growth activity is greater than that of the bacteria. The bacteria then cease to grow in their presence. This is strikingly seen in cultures of actively growing embryonic tissue or of cancer.[3] When the bacteria are growing very actively the fixed tissue cells cease to become active at the boundary of the zone of activity of the bacteria.[4]

These facts led to the question whether the lymphocyte is any more than the "ashes" of some much more general fundamental reaction in the organism. It acts more as a degenerate cell than one which takes an active part in body defense. It became of interest to study the conditions of the differentiation or formation of these cells.

Several years ago the author placed in tissue cultures fragments of the spleen of a one-week old kitten in drops of the kitten's own plasma, and in drops of plasma prepared from the blood of the mother. The reaction of the splenic cells in these two cases was strikingly different. The spleens of these young kittens show very little differentiation of lymphocytes. In the mother's plasma large numbers of lymphocytes migrated from fragments of them into the medium. In the kitten's plasma no lymphocytes appeared, but there was a most active growth of mesenchyme-like cells. Several repetitions of these experiments have always given the same results.

Last summer Mr. Kramer and I noted in a few experiments that this ability for the plasma of animals to produce lymphocytes from the spleen of young animals appears in kittens to a certain extent as early as two or three weeks after birth.[5]

In other experiments Jorstad and the author[6] noted that vitamin A is probably only the ergusia of plants and animals used for food. The question arose, therefore, can the differentiation of these cells be in any way associated with the loss or the formation of this vitamin in the tissues. Children dying from vitamin A deficiency often show a marked hyperplasia of the lymphoid tissue. Murphy[7] notes an accumulation of lymphoid cells in areas treated with small doses of x-rays or an increased resistance of these areas to cancer. We note that small doses of x-rays protect animals for a time against a vitamin B deficiency, while slightly larger doses protect them also for a time against a vitamin A deficiency. In experiments with growing embryomas of mice, one persisted and grew throughout the life of the mouse.[9] Mouse embryos generally grow for a very short time and are then absorbed. The persisting embryoma showed a marked infiltration with lymphocytes. I have shown that the growth of these embryomas is associated with a low value of the ergusia and the growing cells use ergusia for their growth.

It thus became of interest to study these lymphoid reactions in animals suffering from changes in their vitamin content. Mr. Paul Guttman has studied, therefore, the growth of embryomas of rats on a dietary deficient in vitamin A. In his first experiments he found the embryonic tissue will not grow in animals which were placed immediately on the deficient diet. In later experiments he then placed the animals on this diet after the embryomas had begun to grow. In each case he found a marked infiltration of lymphocytes in these tumors. The lymphoid infiltration in these cases was associated also with hyaline and degenerative changes in the embryonic tissue.

If these embryomas had not degenerated to too great an extent they grow rapidly again when the host is placed on a good dietary. While we do not know the eventual outcome of such embryomas, there has been no evidence to show that the lymphoid cells contained in them prevent in any way their subsequent growth.

In the tissue culture the growth of all cells is dependent upon certain definite supply of lipoid substance, the ergusia. It is only when this lipoid is present in excess in and about the cells that it inhibits their growth.[9, 10, 11] Actively growing tissues remove this lipoid from differentiated tissues about them, producing hyaline and degenerative changes.[10, 12] Hyaline and degenerative changes are associated with the infiltration of lymphocytes in the tissues when the vitamin A is removed from the diet of the hosts.

There has been no evidence from these studies, therefore, to show that the lymphocytes act to resist the invasion of cells. They are

evidently only one of the results of a decrease in those lipoid elements of the tissues which are necessary for the growth of the invading cells.

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Studies on the Mechanism of Gastric Hydrochloric Acid Secretion.

H. A. BULGER AND D. S. ALLEN. (Introduced by D. Barr.)

From the Department of Internal Medicine and the Department of Surgery, Washington University School of Medicine.

The following study was planned to throw some light upon the mechanism by which hydrochloric acid is secreted by the stomach. The serum electrolytes of the arterial and of the venous bloods from the stomach were determined before and during gastric secretion in dogs under amytal anesthesia, histamine being used to stimulate secretion. Venous blood from the acid producing portion of the organ was obtained from the coronary vein. The total base was determined by a modification of Fisk's urine method. The anions are expressed in millimols of base combining capacity, assuming a ratio of primary to secondary phosphate of 1 to 4, and calculating the base combined with protein by a formula determined by Van Slyke. The difference between the total determined acids and the total base is taken as representing the organic acid fraction though it contained the small amount of sulfate which was not estimated.

In studies in this laboratory on human subjects it has been shown that during hydrochloric acid secretion the chloride concentration of the gastric juice continues, as in the fasting condition, to be about the same order of magnitude as in serum, but that there is a de-