Discussion. These experiments suggest that passively administered antiserum may suppress or enhance antibody formation to Toxoplasma. The outcome seems to be dependent on a number of variables including the infecting strain and the antigen-antibody ratio. Previous studies with sheep red blood cells have also shown that prior treatment of animals with IgG or IgM can both enhance and suppress antibody production[7]. The suppression in present experiments may have been due to action of passive antiserum on antibody-forming cells. This was indicated in a recent study of kinetics of antibody-mediated suppression of humoral immune response to Toxoplasma at a cellular level[8]. A marked reduction in the number of spleen rosette-forming cells was revealed in antibody-treated group. Using defined lymphoid populations, majority of the rosette-forming cells in Toxoplasma immunized mice have been identified as B-cells (Masihi and Werner, unpublished observations). The mechanism of enhancement is at present not completely clear. However, much experimental data suggest that T- and B-lymphocytes are heterogenous in their composition and that T-cells consist of helper and suppressor subpopulations. The exact conditions under which these subpopulations may be triggered are not fully elucidated. It is of interest that differences in the degree of lymphocyte stimulation by 11 strains on challenge with virulent Toxoplasma have been observed in mice[8]. Maternal antibody passively acquired by the newborn is catabolized within a few months. To what extent this antibody may influence the immune response of human foetus or newborn to Toxoplasma infection is not known. In a recent study with rats, Toxoplasma IgM antibody response could not be detected by immunofluorescent test during the 7-week observation period in newborns infected with the parasite 1–2 days after birth from chronically infected mothers[9]. In the offsprings from normal mothers, high IgM antibody titres were present 2–3 weeks after similar infection. Newborn rats from mothers with chronic infections had high Sabin-Feldman and IgG immunofluorescent test titres. This suggests that their IgM response may have been suppressed by passively acquired maternal IgG antibody. In the case of humans, it is not unlikely that the alteration of immune response to suppression or enhancement could occur but would depend on time and magnitude of foetal and maternal infections, amount of circulating antibody formed by the mother and the infecting strain of Toxoplasma.

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Villus growth and cell replacement in the small intestine of the neonatal pig

M. W. Smith and L. G. Jarvis

ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT (England), 3 May 1977

Summary. Cells produced in the crypts of newborn pig ileum migrate onto villi during development. There is little or no corresponding loss of cells from villus tips during the first week of postnatal life. Villus growth during this period is largely responsible for the slow rate of cellular renewal seen to take place.

Intestinal absorption of immunoglobulins in the pig at birth is associated with an immediate increase in sodium transport[1]. This is followed 5–24 h later by a marked inhibition[2]. Immunoglobulin brought into contact with the newborn pig intestine initially increases the rate of oxygen consumption but this effect disappears some 4 days later[3]. Removing piglets from the sow overnight restores sodium transport to levels found in the newborn animal. This effect disappears 10 days after birth[2]. The purpose of the present work was to try to establish which if any of these changing parameters might be associated with the physical appearance of a different population of cells upon the surface of the developing intestinal villus.

Materials and methods. Pigs taken at birth were injected s.c. with an aqueous solution of [6-^{3}H] thymidine obtained from The Radiochemical Centre, Amersham, England (1 μCi/g b.wt, 20,000–30,000 mCi/mmole). Piglets were then returned to the sow to be killed 2, 24, 48, 96, 144 and 192 h later. The small intestine was dissected out, portions of the mid-intestine being fixed, prior to embedding, in phosphate-buffered formalin, pH 7.0. Sections taken at 2 μm, coated with Ilford K2 emulsion, were allowed to develop for 127 days before being stained with haematoxylin and eosin. Total and radioactive cell counts were then carried out from base of crypt to tip of villus.

Results and discussion. Villus height and crypt depth, together with the mean position of the fastest migrating thymidine labelled cells, is shown for different times following injection of thymidine in the table. The depth of crypts remained virtually constant up to 6 days after birth. Additional measurements on 10-day-old pig intestines taken from the same region show a crypt depth of 24.9 ± 1.1 cells. The height of villus plus crypt showed a 3fold increase over the same time period (80–231 cells). Thymidine labelled cells were confined initially to the crypts. They moved onto the villus after 24 h reaching cell position 189 some 7 days later. Cells produced by

Villus growth and cell migration in the pig intestine measured during the first 8 days of postnatal life

Time after birth (h)	2	24	48	96	144	192
Height of villus and crypt	80.3 ±4.6	82.3 ±4.6	99.5 ±3.7	136.9 ±5.7	215.2 ±8.7	231.0 ±7.6
Depth of crypt	24.7 ±0.9	26.2 ±1.1	27.1 ±1.2	27.0 ±1.0	28.2 ±1.8	33.5 ±1.4
Distance from crypt base to leading labelled cell	11.9 ±0.7	26.4 ±1.7	46.1 ±2.4	78.1 ±4.2	172.8 ±7.6	189.2 ±7.5

Numbers give cell counts from base of crypts. Each value gives the mean ± SE of 12 determinations.

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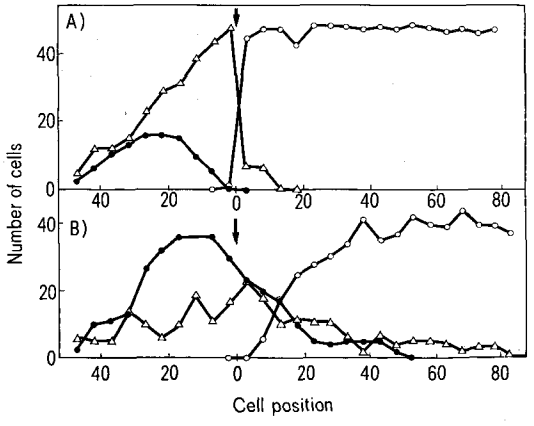
mitosis during the first 6 days are added to an already existing cell population. Villi from the intestines of 8-day-old pigs are, however, similar in size to those seen in the 6-day-old animals. This also applies to the 10-day-old animal (crypt + villus height 211 ± 7.1 cells). If labelled cells continue to migrate at the same rate, one can predict that they will reach the tips of the now nongrowing villi by day 10. It is clear though that any loss of physiological function seen to take place up to 6 days after birth must be explained on the basis of an already existing cell population changing its properties. This includes the ability to change sodium transport as well as to react with immunoglobulins in such a way as to stimulate oxygen consumption.



Cell migration during early postnatal development in the pig small intestine. Measurements taken *A* 2 h and *B* 48 h after the injection of [^{3}H] thymidine. Cell position 0 (↓) corresponds to the junction between crypt and villus, cell positions to the left and right referring to distance into crypts or onto villus respectively. The number of cells at positions greater than 30 in crypts is small since few crypts have depths greater than this value. 3 types of cell are considered: those labelled with thymidine which never become vacuolated (–●–); unlabelled cells which never become vacuolated (–△–) and unlabelled vacuolated cells (–○–). Values give the means of 10 observations.

Experiments showing the relative distribution of thymidine labelled and vacuolated epithelial cells on the villi of 2 and 48 h old piglets are illustrated in the figure. Vacuolation, caused by the endocytosis of immunoglobulins within 2 h of ingesting colostrum, is confined to cells on the villus (figure, A). Labelled cells first appear towards the base of the crypts. Trapped between labelled cells and vacuolated cells on the villus lies a population of nonlabelled crypt cells. The way these 3 populations redistribute themselves in the succeeding 46 h is shown in the figure, B. The total number of nonlabelled vacuolated and nonlabelled unvacuolated cells remains constant while the population of labelled cells increases by a factor of 4. Considerable cell mixing takes place during this period of development. After 48 h one can find some labelled cells ahead of nonlabelled unvacuolated cells and some of both of these populations ahead of some of the vacuolated cells. This leads to a rather inefficient displacement of the original cell population. Some of the originally vacuolated cells will, nevertheless, have been displaced by day 10. This is the time at which the small intestine ceases to respond to a period of starvation by increasing its transport of sodium[2].

The fact that little or no cell replacement takes place up to day 6 allows to conclude that deficiencies in function arising within this time period must occur within the original population of cells. Functional changes occurring with a time course greater than 6 days, probably arise from the physical displacement of some of the original population of cells from nongrowing villi.

Effect of histones from brain on DNA-synthesis in vitro[1]

G. Jahn, I. Szijan and J. A. Burdman

Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, Buenos Aires (Argentina), 11 October 1976

Summary. The results of these experiments demonstrate that histones from brain inhibit the replication of DNA in vitro. A similar effect is observed with polylysine or polyarginine. The reversion of inhibition by polyglutamic acid or acidic proteins is completed in all cases except when the DNA is previously complexed with histones, polyarginine or polylysine. This suggest that histones masking of DNA towards the polymerases involves electrostatic forces.

Several studies have shown that histones inhibit various DNA-polymerase systems in vitro[2–4]. Lysine-rich histones were the most effective and arginine-rich histones the least effective inhibitors of DNA-synthesis[4]. The histones can cover the DNA-strand or change its conformation in such a way as to render it unrecognizable by the polymerases.

In our laboratory we are interested in the role of nuclear proteins in the regulation of DNA-replication in the brain. We demonstrated in our previous experiments a close relationship between the rate of DNA-replication and the synthesis of chromatin proteins[5]. Lately, we have demonstrated the presence of DNA-polymerase and endonuclease activity within the nonhistone proteins of the brain chromatin[6,7].

As histones have a high positive charge, their interaction with DNA could be due, at least in part, to electrostatic forces between the positive charges of the histones and the negative charges of the phosphoric acid groups in DNA. In this way, polypeptides of high positive charge such as polyarginine and polylysine can be used as histone analogs.

In the present study we investigated the effects of unfractionated brain histones, polyarginine and polylysine on DNA-synthesis in vitro. We also studied the effect of polyglutamic acid, a highly anionic polypeptide and acidic proteins, that could compete with DNA in the binding of the basic molecules of polyarginine, polylysine or histones. This will provide evidence on the degree of affinity of the histones, polyarginine and polylysine for the DNA. We can also see if the inhibition of the DNA-polymerase activity produced by these can be reversed with polyglutamic and acidic proteins.

Material and methods. 8-day-old rats of either sex from a highly inbred Wistar strain were used. They were killed by decapitation and unfractionated histones and acidic de-