INTESTINAL PERMEABILITY TO MACROMOLECULES IN PIGLETS INFECTED WITH TRANSMISSIBLE GASTROENTERITIS VIRUS

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ABSTRACT


The permeability of the intestine of specific pathogen free piglets was investigated by measuring the concentration of 125-I in the blood after oral administration of 125-I polyvinylpyrrolidone (125-I PVP, MW = 40 000 Da) and the concentration of 131-I in the faeces after intravenous administration of 131-I porcine albumin (131-I PA, MW = 68 000 Da). The tests were performed one day before and up to two days after the piglets were infected with the Miller strain of transmissible gastroenteritis (TGE) virus. Biopsies of the jejunum were taken at the end of the experiment and blood samples were taken six-hourly. The piglets became anorexic and had diarrhoea 12 hours after infection; the packed cell volume decreased and the concentrations of urea and total serum proteins increased slightly after infection. However, the marked villous atrophy was not accompanied by an increased permeability of the intestine to PVP or PA.

INTRODUCTION

New-born mammals acquire passive immunity to disease by absorbing immunoglobulins by pinocytosis, a mechanism which probably operates throughout the small intestine (Porter, 1969, 1972; Jeffcott, 1974; Smith et al., 1976). Within a day or two this mechanism ceases to function and the transepithelial transport of macromolecules predominantly occurs across the highly specialized 'M cells', which are associated with lymphoid follicles (Bockman & Winborn, 1966; Owen, 1977; Walker, 1981).

At this stage the permeation of macromolecules through the epithelial layer probably depends upon a number of factors, including damage to the gut mucosa by bacterial or viral agents (Walker & Isselbacher, 1974; Kleinman & Walker, 1984, Vellenga et al., 1985).

The experiments described in this paper were designed to test this hypothesis by looking for changes in the rate of uptake of 125-I polyvinylpyrrolidone (125-I PVP, MW = 40 000 Da) from the gut and in the rate of excretion of 131-I porcine albumin (131-I PA, MW = 68 000 Da) into the gut of piglets which had been infected with transmissible gastroenteritis (TGE) virus.

This virus causes an acute self-limiting diarrhoea which is associated with a marked atrophy of the villi of the jejunum and ileum (Hooper & Haelterman, 1966).

MATERIALS AND METHODS

Animals

Six crossbred (Dutch Landrace X Large White) specific pathogen free (SPF) piglets
were used. They were removed from the sow's uterus by hysterotomy and placed in isolators. On the day of birth they each received approximately 175 ml of irradiated (500 kRad) sow colostrum given in several doses (Vellenga et al., 1986); subsequently they were fed condensed milk* several times a day. After four weeks, when they weighed between 4 and 5 kg, they were transferred to the Clinic for Large Animal Medicine and placed immediately in another isolator. The piglets were observed for signs of illness while they were being reared and during the experiment. Samples of faeces were taken twice while they were being reared and at 0, 24, 45, 55, 61, 67 and 72 hours during the experiment for the determination of the composition of the lipid fraction by thin-layer chromatography (van der Valk, 1979) and for the measurement of 131-I radioactivity.

Experimental infection

One day after their arrival at the clinic, four of the six piglets were fed 5 ml of a culture of TGE virus (Miller strain) containing $10^9$ viable agents per ml mixed into 15 ml of condensed milk.

Permeation of macromolecules

Seven doses of 125-I PVP† (MW = 40 000 Da) (55.3 kBq) were administered orally, the first one 24 hours before and the others 2, 16, 22, 27, 33 and 39 hours after the experimental infection with TGE virus. Two doses of 131-I PA‡ (MW = 68 000 Da) were given intravenously, the first dose of 56.9 kBq 24 hours before and the second dose of 36.6 kBq 24 hours after the experimental infection.

Samples for morphology and biochemistry

Biopsies of the proximal jejunum were taken under halothane anaesthesia from two of the piglets just before the other animals were infected and from the remaining four piglets at the end of the experiment, 48 hours after infection. The formalin-fixed biopsies were examined stereomicroscopically according to Mouwen (1971) and processed routinely for histology.

Blood samples were taken from anterior vena cava when the piglets arrived at the clinic and subsequently at intervals of approximately 6 hours. Two ml of blood was used to measure the packed cell volume and the activity of 125-I; twice a day an extra 2.5 ml of blood was collected to obtain serum for the determination of the concentrations of urea and total proteins by the methods described by Breukink et al. (1974). The radioactivity of 131-I in faeces and 125-I in blood was measured in a Philips P4800 Autogamma counter‡ using a dual label program.

RESULTS

Clinical signs

About 12 hours after infection the four infected piglets developed a profuse watery, green/yellow diarrhoea; they lost their appetite and the faeces of one piglet contained small curds of undigested milk. None of the piglets died and they all started to drink again about 33 hours after infection.

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