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THE TRANSFER OF SERUM IgG1 ANTIBODY INTO THE GASTROINTESTINAL TRACT IN NEWBORN CALVES

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ABSTRACT

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Transfer of functional blood IgG1 to the gastrointestinal tract was measured in neonatal calves. Radiolabelled immunoglobulin G1 (IgG1) anti-DNP antibody was administered to 2 day old calves by intravenous injection. The serum clearance rate was measured and was compared to the rate of protein-bound ^{125}I excretion in the feces over a 10 day period to determine the importance of transfer to the gastrointestinal tract as a mechanism of serum IgG1 clearance. The amount of protein-bound and DNP-binding ^{125}I present in the gastrointestinal tract of 10 day old calves at necropsy was also measured. Fecal excretion of protein-bound ^{125}I accounted for 32% of the serum ^{125}I-IgG1 clearance.

Protein-bound ^{125}I was present in the gastrointestinal tract at necropsy in amounts estimated to account for 68% of the total ^{125}I-IgG1 clearance, and retained 65% of the DNP-binding ability of the original antibody. The discrepancy between the fecal excretion (32% of total IgG1 clearance) and the GI clearance estimated from protein-bound ^{125}I in the gut (68% of total IgG1 clearance) is explained in part by IgG1 proteolysis occurring after transfer to the gastrointestinal tract but before fecal excretion. These results indicate that transfer to the calf gastrointestinal tract accounts for most IgG1 clearance in young calves, and that the intestinal antibody retains antigen binding function and may contribute to intestinal immunity.

INTRODUCTION

Calves are born essentially devoid of circulating immunoglobulin but are capable of absorbing large amounts of maternal immunoglobulin from colostrum on the first day of life (Pierce, 1962; Butler, 1969). There is considerable variation in the efficiency of this absorption, and a given population of calves will exhibit a broad range of passive serum immunoglobulin concentrations. This is significant because calves with low circulating passive immunoglobulin levels are more susceptible to a number of infectious disease processes (Gay 1983). The relationship between low serum immunoglobulin concentrations and high enteric disease morbidity and mortality rates during the first month of life (Gay 1983) suggests that circulating

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immunoglobulin has an effect on gastrointestinal tract immunity in calves. IgG1 must be prominent in this protection; it is the predominant immunoglobulin in colostrum, and with its relatively long serum half life (approximately 18 days) it is the only passively acquired immunoglobulin persisting in substantial amounts throughout the period of high susceptibility to neonatal enteric disease.

Enteric disease in neonatal calves is most frequently associated with a number of ubiquitous enteropathogens (rotavirus, coronavirus, cryptosporidium, for example) to which older animals are apparently resistant (Morin et al., 1978; Moon et al., 1978). Many infected calves remain asymptomatic, but some individuals develop moderate to severe enteric disease. Calves with high serum immunoglobulin concentrations following colostrum feeding on the first day of life subsequently have lower rates of overall enteric disease morbidity and mortality (Fisher and de la Fuente, 1972; Fisher et al., 1975; Hurvell and Fey, 1970; Blom, 1982; Penhale et al., 1970; Boye et al., 1974; Gay et al., 1965, McEwan et al., 1970). Most studies demonstrating the protective effect of high serum passive immunoglobulin levels have not determined the specific etiology of the observed enteric disease, but specific effects on disease caused by bovine rotavirus (McNulty et al., 1976) and by enteric salmonella (Fisher et al., 1976) infections have been observed. Seemingly, passively acquired serum immunoglobulin, in particular IgG1, influences the occurrence and severity of infectious enteric disease in calves during the first month of life. This association is not simply a correlation between protective lactogenic antibody and colostral antibody content, since a number of studies have involved market calves not nursing their own dams, or have involved calves fed artificial milk replacer (Hurvell and Fey, 1970; Penhale et al., 1970; Boyd et al., 1974). In these situations, dietary (milk) antibody content is not related to the antibody content of the colostrum ingested by the calf.

For circulating IgG1 to affect enteric immunity, transfer of the immunoglobulin into the gastrointestinal tract would presumably be required. Serum IgG1 does appear in the gut lumen: Newby and Bourne (1976) determined that a significant percentage of the IgG1 in normal calves' intestinal contents is serum-derived, and that more serum-derived IgG1 is present in the intestines of calves with higher serum IgG1 concentrations than in calves with lower serum IgG1. Consistent with this observation, Saif and Smith (1985) observed that calves with high serum rotavirus antibody titers have persistent fecal rotavirus antibody titers after cessation of colostrum feeding. In addition, enteritis increases the rate at which serum proteins, including immunoglobulins, appear in the feces (Fisher et al., 1975; Marsh et al., 1969), and immunoglobulin has a shorter serum half-life in animals with diarrhea (Macdougall and Mulligan, 1969).

EXPERIMENTAL RESULTS

Because of the relationship between serum immunoglobulin status and enteric disease, it is of interest to know the concentration of immunoglobulin in the gastrointestinal tract secretions of calves with different serum immunoglobulin levels. Quantitation of immunoglobulins in ruminant gastrointestinal secretions has produced conflicting results (reviewed by Butler, 1983 and Morgan et al., 1981). In young calves, for example, Newby and Bourne (1976) determined that IgG1 decreased from 95% to 48% of intestinal immunoglobulin between two and fourteen weeks of age, while Porter et al. (1972) found only low levels of IgG1 and high relative concentrations of IgM in intestinal loops in a similar age group. The wide range of calf passive serum IgG1 concentrations following colostrum absorption may explain some of the conflicting values reported for intestinal immunoglobulin concentrations in calves.

We used intravenously-injected ^{125}I-labelled IgG1 to quantitate the passage of serum IgG1 into the gastrointestinal tract (Besser, 1986). IgG1 was prepared from affinity-purified anti-DNP antibody, and DNP-binding was subsequently used as a criterion of antibody function of the immunoglobulin appearing in the gastrointestinal tract. The clearance rate of the serum ^{125}I-IgG1 was determined from the time-dependent decrease in serum counts per minute (cpm)/ml. The rate of appearance of ^{125}I-IgG1 in the gastrointestinal tract was measured by: 1) the rate of fecal protein-bound ^{125}I excretion and 2) tne amount of labelled IgG1 in the gastrointestinal tract of calves at necropsy. Fecal excretion of protein-bound ^{125}I accounted for 32% of the total ^{125}I-IgG1 clearance, with fecal and urinary excretion of non-protein bound ^{125}I accounting for the balance. Labelled IgG1 was present in the gastrointestinal tract at necropsy in amounts estimated to account for 68% of the total ^{125}I-IgG1 clearance. The protein-bound ^{125}I in the calves' small and large intestines at necropsy retained 65% of the DNP-binding ability of the antibody originally administered.

The discrepancy between IgG1 transfer to the gut measured by fecal excretion (32% of the total IgG1 clearance) and the transfer estimated from protein-bound ^{125}I in the gut at necropsy (68% of the total IgG1 clearance) may be explained by IgG1 proteolysis occurring after transfer to the gastrointestinal tract but before fecal excretion. The occurrence of such proteolysis was demonstrated by feeding 48-hour-old calves ^{125}I-IgG1. The calves did not absorb measureable IgG1 (protein-bound ^{125}I) to serum and yet excreted only 28% of the ^{125}I dose as protein-bound label in the feces. The remainder was excreted as non-protein bound ^{125}I in the urine.

DISCUSSION

The fraction of circulating, labelled IgG1 transferred daily into the GI tract was similar in calves with a wide range of serum IgG1 concentrations. This agrees with the finding of Newby and Bourne (1976) of higher amounts of serum-derived IgG1 in the intestinal contents of calves with higher serum IgG1 concentrations. Seemingly, transfer to the gastrointestinal tract represents a major mechanism for clearance of passively acquired IgG1 from calf serum, and intestinal IgG1 concentrations are directly affected by serum IgG1 concentrations. From these data, a calf absorbing 100 g of IgG1 from colostrum would be expected to secrete from 2 to 4 g back into the gut each day during the first two weeks of life. This quantity of immunoglobulin could reduce the likelihood of enteric disease in such a calf, and this is a probable explanation for the reduced rates of enteric disease in calves absorbing large amounts of maternal immunoglobulin.

In older cattle and in other species, transfer to the intestine may also account for a substantial amount of IgG clearance and may contribute to intestinal immunity. The similar half-life of IgG1 in calves and in older cattle suggests that a similar clearance mechanism is operating (Butler, 1983; Nielsen et al., 1978; Husband et al., 1972). IgG transfer to the intestine has also been reported in other species: mouse (Fubara and Freter, 1972), rat (Wu and Walker, 1976), rabbit (Fubara, 1972; Wernet et al., 1976), dog (Anderson et al., 1963; Pierce and Reynolds, 1974), and sheep (Husband and Lascelles, 1974; Cripps et al., 1974). In sheep, Cripps et al. (1974) determined that blood-derived IgG makes a significant contribution to the total intestinal IgG. In the dog, radiolabelled IgG transfer into intestinal loops occurred at a rate that explained most IgG clearance (Anderson et al., 1963). Most major enteropathogen infections result in serum IgG antibody formation as part of the body's immune response. If intestinal transfer is a major route of serum IgG clearance and if the transferred antibody retains function, serum-derived IgG may make a significant contribution to the intestinal immunity.

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