α-Fetospecific Serum Proteins in Bovine Fetuses[1] (36852)

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Pedersen (1) reported that a globulin (fetuin) in the serum of neonatal calves decreased in concentration with maturity. The globulin was shown to be a mucoprotein (2) with at least three distinct fractions (3). Fetuin migrated as an α-globulin on starch gel electrophoresis (4). The fetuin content (5) of serum from bovine fetuses during the latter half of gestation was between 10 and 20 mg/ml, whereas total serum α-globulin content (6) (including fetuin) during this period was determined by another method to be approximately 10 mg/ml. The liver of the fetal lamb was more active in producing fetuin during the first half of gestation (7). Whereas sialic acid groups present evidently have little effect on the structure of fetuin (8), the rate of hepatic removal of the fetuin molecules is increased when the groups are absent (9). Fetuin from fetuses late in gestation contained galactose, whereas specimens from younger fetuses did not (10). An additional α-globulin is present in fetal calf serum and has antigenic cross-reactivity with α-globulin in the serum of fetal goats and sheep (11, 12). Therefore, the following systematic names were proposed: α_1-fetospecific serum protein (fetuin), and α_2-fetospecific serum protein (α-fetoprotein) (13).

Materials and Methods. We examined sera from 82 bovine fetuses ranging in gestational age from 110 to 140 days to term (Table I) by using a modification of the horizontal starch gel electrophoresis method of Quinteros and Miller (14). The modifications were: starch concentration of 16.5%, 21.6 ml citric acid buffer (9.6 g/liter) and 18.2 ml Tris buffer (17.1 g/liter) up to 230 ml with distilled water (pH 6.0) and a run of 3 hr at 300 V. The gel cross-section was 6 × 130 mm with a distance of 125 mm between contacts. The initial milliamperage varied between 60 and 95 mA decreasing to between 20 and 35 mA by the end of the run.

Results. Four bands were detected in the α-globulin–postalbumin region of bovine fetal serum that did not appear in the serum of adult cattle (Fig. 1). Therefore, these bands seem to be α-fetospecific serum proteins. Since Pedersen (1) found fetuin in the serum of neonatal calves, it should be considered a protein found in immature cattle rather than limited to fetuses. Fetuin is most likely represented by the fastest moving band because it is found after the other three bands have disappeared (Fig. 2). The latter three

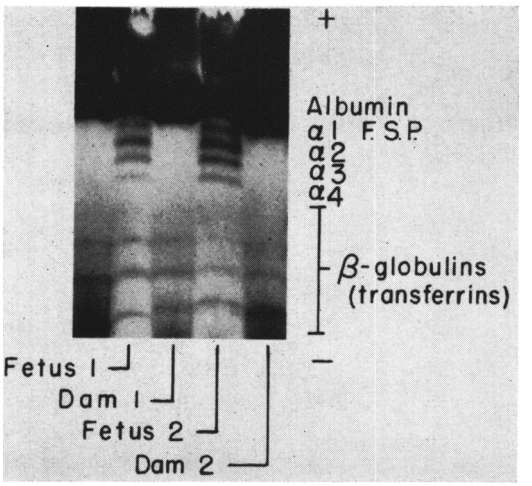

FIG. 1. Comparison by horizontal starch gel electrophoresis of fetospecific serum protein (FSP) bands present in the sera of male and female bovine fetuses (approx 140–150 gestation days) with those of their respective dams.

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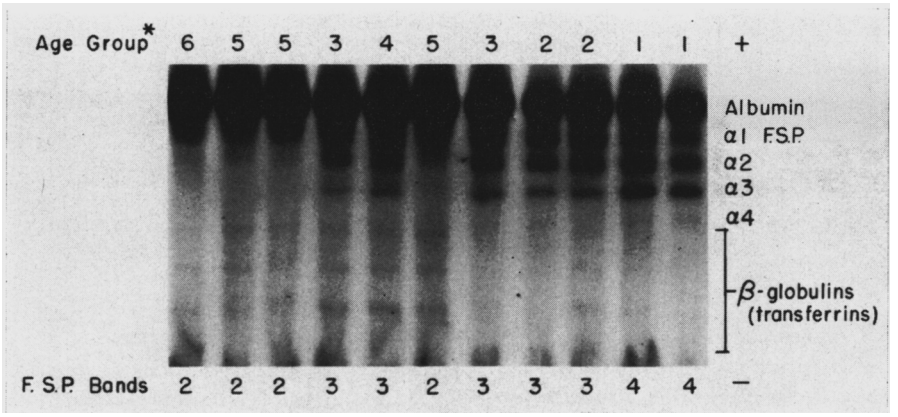

FIG. 2. Bovine fetospecific serum proteins (FSP) in relation to gestational age separated by horizontal starch gel electrophoresis. *Age group (days): 1(110–140), 2(140–150), 3(150–170), 4(170–200), 5(200–230), 6(230–245).

bands disappear sequentially with the slowest-migrating band usually gone by 170–200 gestational days, the middle band by 200–230 days, and the fastest by 245 days (Table I). It is uncertain if one or more of these bands represent the α_2-fetospecific serum protein described elsewhere (11, 12). The bands have been designated provisionally α_1-, α_2-, α_3-, and α_4-fetospecific serum proteins on the basis of decreasing range of electrophoretic migration (Figs. 1 and 2).

Discussion. Although four α-fetoproteins have been detected in bovine fetal serum, there may be more in the serum of younger fetuses or embryos. Much remains to be learned of their function during normal bovine development. Although we have no evidence of a direct carcinogenic association in cattle, there has been a relationship established between human cancer tissues and their ability to produce fetal enzymes (15) or serum proteins (16). An α-fetoprotein synthesized by the normal human fetal liver (17) has been indistinguishable from a protein found in the serum of patients with hepatocellular cancer (18). Perhaps the method used to separate bovine α-fetoproteins would be useful in clarifying the relationships between those proteins found during normal human development and those present in patients with protein-secreting tumors. Five aldolase isoenzyme patterns have been detected in human conceptuses during the sixth week of development that later show a sequential

TABLE I. Number of α-Fetospecific Serum Protein Bands Present in Relation to Bovine Fetal Age.

Gestational age (days)	No. of bands present in serum					
	0	1	2	3	4	Total
110–140	0	0	0	2(2/0)[a]	1(1/0)	3(3/0)
140–150	0	2(2/0)	0	6(0/6)	6(5/1)	14(7/7)
150–170	1(1/0)	0	4(2/2)	13(7/6)	3(1/2)	21(11/10)
170–200	1(0/1)	2(1/1)	1(1/0)	4(2/2)	1(0/1)	9(4/5)
200–230	6(4/2)	0	5(3/2)	3(1/2)	0	14(8/6)
230–245	11(1/10)	3(3/0)	1(1/0)	0	0	15(5/10)
245+	4(2/2)	1(1/0)	1(0/1)	0	0	6(3/3)
Total	23(8/15)	8(7/1)	12(7/5)	28(12/16)	11(7/4)	82(41/41)

[a] No. fetal sera examined (♂/♀).

disappearance with maturity (19) similar to the pattern that we observed for bovine α-fetoproteins.

Summary. Four α-globulins were detected by starch gel electrophoresis in the serum of bovine fetuses of approximately 4 mo gestational age. These proteins were absent from the serum of their dams (α-fetospecific serum proteins) and disappeared sequentially with increasing fetal maturity beginning with the slowest migrating band.

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