Acta vet. scand. 1966, 7, 321—329.

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METABOLISM AND DISTRIBUTION OF I^{131}-LABELLED ALBUMIN IN PIGS WITH GASTROINTESTINAL DISEASE*)

By
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Loss of serum proteins into the lumen of the digestive tract is responsible for the hypoproteinemia seen in various gastrointestinal diseases of man. Regional enteritis (terminal ileitis) and hypertrophic gastritis are examples of such protein-losing gastroenteropathies, cf. *Schwartz* (1964).

In cattle suffering from hyperplastic abomasitis (ostertagiasis), Johne's disease and chronic catarrhal abomasoenteritis the metabolism of I^{131}-albumin and I^{125}-immunoglobulin (IgG) appeared to be related to the clinical phase of the disease. Thus, cattle studied during a period with profuse diarrhea showed hypercatabolism due to gastrointestinal protein loss, whereas cattle studied during a quiescent phase or during convalescence had normal or even subnormal albumin and immunoglobulin turnover rates (*Nielsen,* to be published). It was considered important to examine, whether a similar relationship might exist in species other than cattle. The present paper reports data obtained in sows with hypertrophic gastritis caused by Hyostrongylus rubidus infestation and in pigs with terminal ileitis (*Emsbo* 1951).

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*) This study was supported by a grant from Statens almindelige Videnskabsfond.

METHODS

Crystalline porcine albumin (Pentex Inc., Ill.) was labelled with carrier-free I^{131} (*McFarlane* 1958). I^{131} not bound to albumin was removed on a resin column (Amberlite IRA 400). The preparations were diluted with albumin and injected within 24 hrs. after labelling.

Experimental procedure. Lugol's iodine solution was given to prevent thyroid uptake of the label. The radioactive solutions were injected into an earvein (dose: 50—70 μC). A blood sample was taken 15 min. after the injection for calculation of plasma volume. Heparinized blood samples were taken daily from v. cava cranialis. After the eighth day, blood samples were taken at alternate days. In pigs with terminal ileitis, feces and urine were collected during the first four days of the experiment. These pigs were placed in metabolism cages. In sows such collections were not practicable. Medical treatment was not given during the studies.

Total serum protein was determined by the gravimetrical method described by *Højensgaard* (1948). Serum protein fractionation was accomplished by paper electrophoresis in Veronal buffer (pH 8.6) using Schleicher & Schüll paper no. 2043B in a LKB apparatus. Urines were tested for protein by Heller's test. Counting of the radioactive samples was done in a thallium-activated NaI scintillation well counter. Plasma samples were counted in 4 ml aliquots. Urine and homogenized feces were counted in 500 ml bottles over the top of the crystal. All samples were counted together with standard dilutions of the injected preparations. Turnover data were calculated according to the method described by *Matthews* (1957).

RESULTS

A. *Hypertrophic gastritis in sows, caused by infestation with Hyostrongylus rubidus*

During the winter of 1966 four sows (427, 428, 513 and 514) were admitted to the Medical Clinic, Royal Veterinary and Agricultural College. The history was one of weight loss during several months in spite of good appetite. The physical examination had failed to reveal the cause or nature of the disease.

At admission, all sows were extremely meagre. All except one (514) were lively and had fairly good appetite. Apart from a few

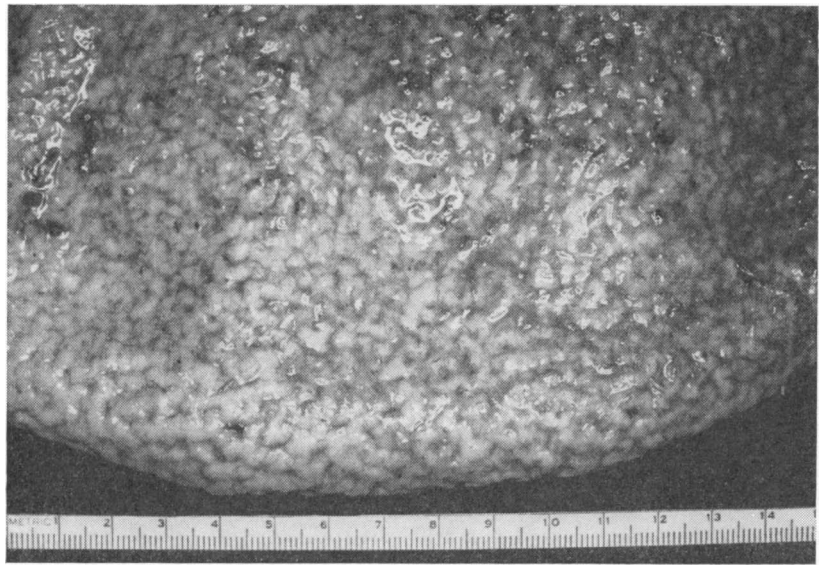

Figure 1. Stomach of sow 513, showing considerable thickening and granulation of mucosal surface. (Courtesy of *Steen Larsen*).

days with soft feces in 513, diarrhea was not a feature of the disease. Moreover it was stated by the owner that the course of the disease in all affected sows of the herd had been non-diarrheal, whereas occasional vomitus had been observed. Biochemical data failed to yield conclusive evidence as to the site or nature of the disease: Serum calcium ranged from 7.8—9.4 mg/100 ml; inorganic phosphate from 6.0—12.0 mg/100 ml; magnesium from 1.8—3.2 mg/100 ml. Sow 427 had uremia (118 mg urea/100 ml) during the terminal phase of the disease, the other sows had normal urea levels (27—43 mg/100 ml). The formolgel test was negative in all sows. Serum protein levels were slightly decreased in 428 (5.9 g/100 ml), and 514 (5.9 g/100 ml) and normal in sows 427 (7.6 g/100 ml) and 513 (6.2 g/100 ml).

Salt water flotation revealed numerous trichostrongylid eggs in the feces of all sows.

Sow 428 eventually recovered; the other three sows were killed. Necropsy revealed chronic hypertrophic gastritis caused by infestation with the red stomach worm, Hyostrongylus rubidus, cf. Fig. 1.

I^{131}-albumin turnover was studied in sows 428 and 513. Sow 428 was examined during a stage of clinical remission: It gained

Table 1. I^{131}-albumin turnover data in two sows with hypertrophic gastritis and in a normal control (450).

Subject	Weight, kg	Plasma volume, ml/kg	Total serum protein, g/100 ml	Serum albumin, g/100 ml	Vascular albumin pool, g/kg	Albumin degradation		Total albumin pool, g/kg	Plasma half life, days	Extravascular:intravascular (Ev:Iv) albumin ratio
						Fractional turnover rate, %/day	Absolute albumin degradation, g/kg/day			
428	108	37.5	5.9	1.72	0.58	9.95	0.06	0.86	10.8	0.49
513	89	56.8	6.2	1.63	0.92	7.73	0.07	2.18	20.3	1.38
450	117	32.4	6.5	2.04	0.65	12.10	0.08	1.62	15.5	1.50

weight (22 kg) during the study and its serum protein concentration increased from 5.4 g/100 ml to 6.3 g/100 ml. Hemoglobin level was low: 55 % (Sicca); serum calcium: 9.4 mg/100 ml; inorg. phosphate: 12.0 mg/100 ml; magnesium: 3.0 mg/100 ml; blood urea: 43 mg/100 ml. The sow eventually recovered (after treatment with Thiabendazole). She was seen in the herd appr. three weeks later. Improvement had continued, she had gained more weight and appeared quite healthy.

Sow 513 was more severely affected: She failed to thrive in spite of rather good appetite (only 1 kg weight gain during the 16 days of investigation). She had occasional loose stools during the middle of the study. Serum calcium was 9.2 mg/100 ml; inorg. phosphate: 6.0 mg/100 ml; magnesium: 1.8 mg/100 ml; standard bicarbonate: 29 meq./l; potassium: 3.1 meq./l; sodium: 150 meq./l; glucose: 75 mg/100 ml; urea: 27 mg/100 ml. There was anemia (hemoglobin: 36 % (Sicca)).

Salient data from the tracer experiments in the two sows are given in Table 1. On comparison with the control sow, 428 had normal plasma volume, whereas an increase was seen in sow 513. Serum protein levels were in the low normal range in both sows. Serum albumin levels were low: 1.63 and 1.72 g/100 ml. The fractional turnover rates of both patients were lower than in the control sow. In sow 513, fractional turnover rate (7.73 %/day) and plasma half life (20.3 days) indicated a state of relative hypocatabolism; the absolute degradation of albumin, however, was 0.07 g/kg/day, which is comparable to the value seen in the control sow (0.08 g/kg/day). Sow 428 had a rather short plasma

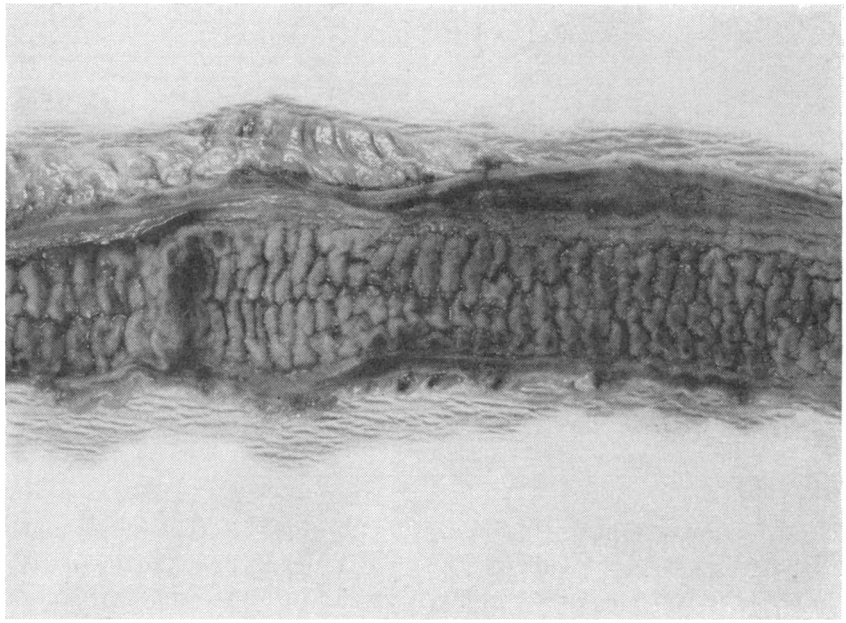

Figure 2. Terminal ileitis (pig 69).

half life (10.8 days). As mentioned above, this animal was examined during a phase of rapid remission. A gastric protein loss was considered unlikely (weight gain, increase of serum protein concentration during the study). Rather, the turnover data of this patient reflect a rapid albumin synthesis, newly synthesized albumin being released into the plasma with resulting decline in plasma albumin specific activity and, possibly, an expansion of plasma volume. The low Ev:Iv ratio in this sow supports this view.

B. *Terminal ileitis in pigs*

Three pigs with terminal ileitis were examined (68, 69 and 301). All pigs were admitted with a history of diarrhea since the time of weaning. They were meagre and had severe diarrhea. Pigs 68 and 69 had normal hemoglobin levels (60 and 70 %, resp.), whereas 301 was anemic (49 %). Standard bicarbonate levels were 26 meq./l (68), 31 meq./l (69) and 24 meq./l (301). Urea levels in blood were measured in pig 68 (43 mg/100 ml) and 69 (38 mg/100 ml).

Table 2. I^{131}-albumin turnover data in three pigs with terminal ileitis and in two normal control pigs (11 and 507).

Subject	Weight, kg	Plasma volume, ml/kg	Total serum protein, g/100 ml	Serum albumin, g/100 ml	Vascular albumin pool, g/kg	Albumin degradation		Total albumin pool, g/kg	Plasma half life, days	Extravascular:intravascular (Ev:Iv) albumin ratio	Fecal excretion of radioactivity during first 4 days, % dose
						Fractional turnover rate, %/day	Absolute albumin degradation, g/kg/day				
301	10.5	98.5	3.8	0.89	0.84	42.8	0.36	1.31	2.8	0.57	4.8
68	22.5	59.0	4.2	0.36	0.22	45.5	0.10	0.29	≈2	0.29	8.1
69	22.1	54.9	3.8	0.38	0.21	50.0	0.11	0.31	≈2	0.45	7.7
11	21.4	70.7	6.2	2.17	1.43	20.0	0.29	3.52	9.5	1.49	1.9
507	27.7	49.1	6.2	2.13	0.96	14.3	0.14	1.85	9.7	0.92	2.9

The pathological findings were similar in the three pigs: There was hypertrophia of the ileal mucosa and the muscular layer (Fig. 2). The lesions did not extend into the cecum or colon.

Turnover data in the three pigs are listed in Table 2. Obviously, all three pigs were in a state of severe hypercatabolism due to gastrointestinal loss of albumin: Their fecal excretion of radioactivity was high (4.8—8.1 % of the administered dose/4 days), fractional turnover rates were very high (42.8—50 %/day) and half lives were extremely short (2—2.8 days). The albumin pools in the three diseased pigs were severely depleted, especially in pigs 68 and 69. This depletion was more pronounced in the extravascular compartments than in the plasma, cf. the low Ev:Iv ratios in the diseased pigs. Thus, these pigs had very rapid turnovers of small albumin pools. E.g. pig 301 had a vascular albumin pool of 8.8 g compared with 30.5 g in control pig 11 (injected with the same preparation). 42.8 % of this pool (3.8 g) was broken down daily, compared with 20 % (6.1 g) in the control.

When pigs 68 and 69 were moved from the metabolism cages their diets were changed: Instead of barley plus water they were now fed barley and milk, supplemented with vitamins (A, D, B) and minerals. Three to four days after this change in feeding managements, diarrhea ceased. In both pigs, this alleviation of digestive symptoms was followed by a change of the plasma disappearance curve, the decline of which became less steep (Fig. 3).

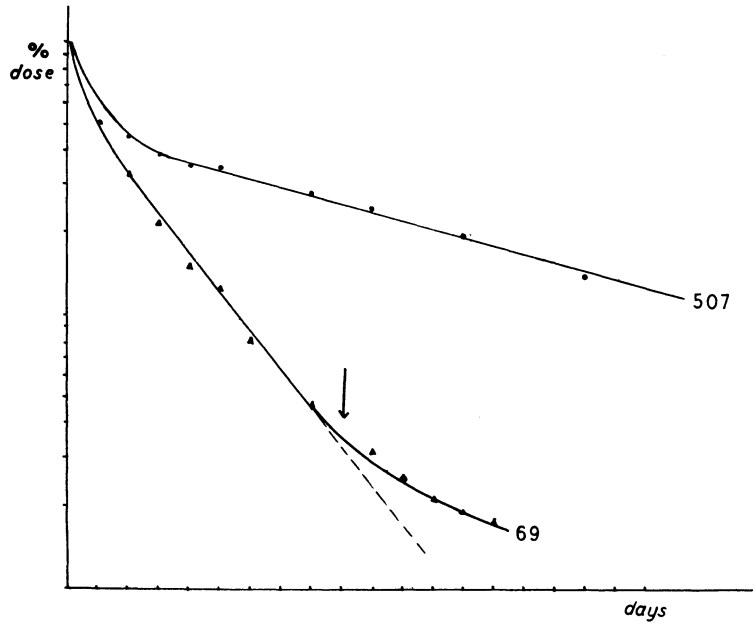

Figure 3. Plasma disappearance curves of pig 69 (terminal ileitis) and normal control pig 507. Arrow indicates cessation of diarrhea.

DISCUSSION

The results reported above lend support to the author's previous findings in cattle, where it was found that the pattern of albumin metabolism is related to the clinical picture of the disease rather than to the pathoanatomical nature of the lesions seen in the gastrointestinal tract. Thus, in the sows with hypertrophic gastritis examined here, albumin turnover data did not indicate hypercatabolism. Clinically, these sows showed very few symptoms of gastrointestinal disorders and above all, diarrhea was not a feature of their disease. In contrast, pigs with regional enteritis (terminal ileitis) showed excessive hypercatabolism, due to gastrointestinal protein loss (Table 2). These pigs had active digestive disorders with diarrhea as the main symptom. When the pigs entered a quiescent phase of the disease (cessation of diarrhea) the slope of the plasma disappearance curve changed markedly and, in fact, approached the decline seen in normal controls (Fig. 3). This effect was seen immediately after the alleviation of digestive symptoms. Obviously, the pathophysiological changes inducing diarrhea exhibit a marked effect upon

albumin metabolism. Short intestinal transit time and the physicochemical properties of the digesta are probably important factors in this mechanism; e.g. it has been shown that instillations of iso- and hypertonic $MgSO_4$-solutions through isolated intestinal loops were followed by increased intestinal transfers of albumin and immunoglobulin (IgG) (*Dich & Nielsen* 1964; *Nielsen & Dich* 1965).

The preliminary results submitted here are in keeping with investigations in humans suffering from ulcerative colitis and regional enteritis, where it was shown that hypercatabolism was restricted to the "acute" phases of the disease, whereas albumin degradation rate was normal in remitting cases (*Wetterfors et al.* 1963).

Studies of serum protein metabolism in animals with digestive diseases are being continued.

REFERENCES

Dich, J. & K. Nielsen: Passage of I^{131}-albumin and I^{125}-gamma globulin into the small intestine of the pig. Canad. J. comp. Med. 1964, *28*, 257—262.

Emsbo, P.: Terminal or regional ileitis in swine. Nord. Vet.-Med. 1951, *3*, 1—28.

Højensgaard, I. C.: Serumproteinbestemmelse med kobbersulfatmetoden. Nord. Med. 1948, *38*, 797—801.

Matthews, C. M. E.: The theory of tracer experiments with I^{131}-labelled plasma proteins. Phys. in Med. Biol. 1957, *2*, 36—53.

McFarlane, A. S.: Efficient trace-labelling of proteins with iodine. Nature (Lond.) 1958, *182*, 53.

Nielsen, K.: Gastrointestinal protein loss in cattle. A clinical and patho-physiological study. To be published.

Nielsen, K. & J. Dich: Passage of I^{131}-albumin and I^{125}-gamma globulin into the small intestine of calves. Acta vet. scand. 1965, *6*, 249—260.

Schwartz, M.: Some clinical aspects of protein-losing gastroenteropathy. I: "Protides of the biological fluids". Proc. 11th colloquium, Brügge 1963. Elsevier Publishing Co., Amsterdam 1964 — Ed. H. Peeters.

Wetterfors, J., S.-O. Liljedahl, L.-O. Plantin & G. Birke: Hypoalbuminemia in ulcerative colitis and certain forms of enteritis. Acta med. scand. 1963, *174*, 529—549.

SUMMARY

The turnover of I^{131}-albumin has been studied in two sows with hypertrophic gastritis (Hyostrongylus rubidus infestation) and in three pigs with terminal ileitis. The sows showed few characteristic

digestive symptoms and their albumin turnover data were essentially normal (Table 1). Pigs with terminal ileitis showed more active symptoms of gastrointestinal disease (diarrhea). Albumin turnover rates were greatly accelerated, with daily degradations of nearly 50 % of the vascular albumin pool (Table 2).

It is concluded that the pattern of albumin metabolism in pigs with gastrointestinal disease is related to the actual clinical phase of the disease rather than to pathoanatomical lesions (hypertrophy etc.). The pathophysiological features determining the clinical picture are, accordingly, of great importance.

ZUSAMMENFASSUNG

Umsatz und Verteilung von J^{131}-Albumin unter gastrointestinalen Krankheiten beim Schwein.

Der Umsatz von J^{131}-Albumin wurde bei zwei Säuen mit hypertrophischer Gastritis (Hyostrongylus rubidus Infestation) und bei drei Ferkeln mit terminaler Ileitis untersucht. Die Säue zeigten nur wenige Indigestions-Symptome und ihre J^{131}-Albumin turnover Daten waren im wesentlichen normal (Tabelle 1). Ferkel mit terminaler Ileitis zeigten mehr ausgeprägte digestive Symptome (Durchfall) und der Albuminkatabolismus war akzeleriert, mit täglichen Degradationen von nahezu 50 % der vaskulären Albuminpuljen (Tabelle 2).

Es wird konkludiert, dass bei gastrointestinalen Krankheiten des Schweines der Albuminkatabolismus mehr mit dem aktuellen, klinischen Bild als mit den pathologischen Veränderungen des Magendarmkanals (Hypertrophie u. dgl.) verbunden ist. Die Relation zwischen den pathophysiologischen Veränderungen und den klinischen Symptomen ist, infolgedessen, sehr wichtig.

SAMMENDRAG

Omsætning og fordeling af J^{131}-albumin hos svin med mavetarmsygdomme.

J^{131}-albumin turnover er undersøgt hos to søer med hypertrofisk gastritis (infestation med Hyostrongylus rubidus) samt hos tre grise med terminal ileitis. Søerne viste kun ukarakteristiske symptomer på fordøjelseslidelse, og deres albumin turnover data var i det væsentlige normale (Tabel 1). Grisene med terminal ileitis viste mere udprægede fordøjelsesforstyrrelser (især diarré), og deres albuminomsætning var stærkt accelereret, med en daglig albumindegradation på nær 50 % af den intravaskulære albuminpulje (Tabel 2).

Det konkluderes, at albuminomsætningen hos svin med fordøjelseslidelser mere står i relation til det aktuelle kliniske symptombillede end til arten af de patologiske forandringer i tarmen (hypertrofi o. lign.). De patofysiologiske faktorer, der er bestemmende for de kliniske symptomer, er derfor af stor vigtighed.

(Received June 9, 1966).