suitable for immunological studies. Various sensitivities to infection can be obtained by using different inbred strains of mice. Some discrepancies in the results according to the so-called 'sensitivity' or 'resistance' of a given strain of mice[8,9,23,26] could be due to differences in the genetic background of these strains in the different countries. The 'sensitivity' of our strain of C57BL6 mice appeared to be higher compared to that of mice[23,26,27] used in previous studies.

The major interest of the comparison of the immune reactions in strains differing in their resistance to the infection by a parasite has been emphasized[28]: our experimental model of AE allows such a comparison between 'resistant' and 'sensitive' strains; the analysis of different pathological forms of sensitivity (frequency versus weight of metastases) could also be performed. Moreover, the mouse represents a fairly good model for immunological studies since its immunological status is well known; monoclonal antibodies for phenotype determinations are readily available; inbred stains are genetically well defined and recombinant and congenic mice can be obtained in order to study the relationship between resistance to *E.m.*, development of cellular immunity and genetic control. Our observations in C57BL6 and C57BL10 mice respectively 'sensitive' and 'resistant' to infection by *E.m.* although sharing the same H2 (b) determinants argue against a direct link between H2 and resistance to the parasite. Expression of cell-mediated immunity, and natural or acquired resistance to mycobacterial infection, have been shown to be controlled by, at least, two different genes, one being H2 linked and the other one not. Such relationships have to be studied in alveolar echinococcosis.

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Parenteral soya bean fat emulsions potentiate the hepatotoxicity of *E. coli* endotoxin in suckling rats

K.M. Heinonen, V. Kataja and M. Laitinen

Children's Hospital, University of Kuopio, SF-70210 Kuopio 21 (Finland), 8 March 1982

Summary. A dose of soy bean fat emulsion which was injected i.v. in suckling rats accumulated in the cells of liver parenchyma, both in hepatocytes and in reticuloendothelial cells. Subsequent i.p. injection of *E. coli* endotoxin was followed by extensive liver tissue necrosis and increased activities of serum aspartic and alanine aminotransferase. These signs of liver damage were markedly more pronounced than those observed after the administration of *E. coli* endotoxin only.
Key words. Rat, suckling; *E. coli* endotoxin; endotoxin; hepatotoxicity; soya bean fat emulsion.

Parenteral fat emulsions are widely used in parenteral nutrition. They provide high amounts of energy in small volumes of fluid, without inappropriately high osmotic loads[1]. Parenteral soya bean fat emulsions also contain sufficient essential fatty acids[2]. However, recent observations have confirmed that there is accumulation of lipid pigment in hepatocytes and reticuloendothelial cells during the parenteral use of soya bean fat emulsions in young children[3-5]. Lipid pigment deposition has been shown to persist for years after parenteral infusion of fat[5]. During and after parenteral fat infusion, various liver disturbances have been reported in human beings[6-9]. Whether or not this is caused only by the parenteral fat emulsion, or by the latter in combination with other factors, has not been thoroughly evaluated. A potentially important hepatotoxic factor, often associated with parenteral feeding, is infection[3,6-9]. In this paper, we present observations on liver damage associated with the use of parenteral fat emulsions, alone and in combination with experimental endotoxinaemia, in suckling rats.

Material and methods. 10 litters, each containing four suckling male Wistar rats, 15 days old, were divided into four groups of 10 animals. There were no significant differences (±1 SD) between the mean weights of the animals in the 4 groups (table). The groups were treated as follows.

Group I. Each animal received a parenteral injection of a 20%

Serum aspartate aminotransferase (S-ASAT) and alanine aminotransferase (S-ALAT) activities in sera from suckling rats after parenteral administration of fat (group I), *E. coli* endotoxin (group II), fat and *E. coli* endotoxin (group III) and in controls (group IV).

Study group	Weight (g)	Enzyme activities (U/l) S-ALAT Mean	SD	p_1	p_2	S-ASAT Mean	SD	p_1	p_2
I	31.4 ± 1.1 (n = 10)	65.3 (n = 7)	27.4	ns	< 0.005	160.0 (n = 7)	31.2	< 0.01	< 0.001
II	32.2 ± 0.6 (n = 10)	167.9 (n = 7)	61.4	< 0.01	< 0.01	568.0 (n = 7)	150.2	< 0.01	< 0.01
III	32.9 ± 0.4 (n = 10)	384.0 (n = 7)	128.9	< 0.001		2914.3 (n = 7)	2115.8	< 0.001	
IV (controls)	32.6 ± 0.4 (n = 10)	42.3 (n = 7)	37.6			98.4 (n = 7)	37.4		

p-Values were determined using Student's t-test ($p > 0.05$ = not significant (ns)). Values represent mean ± 1 SD.
p_1 = Statistical significance in comparison with the control group (group IV); p_2 = Statistical significance in comparison with the fat and *E. coli* endotoxin group (group III).

soya bean fat emulsion (Intralipid) (Kabi Vitrum, Stockholm, Sweden) at a dose of 0.06 mg. This dose corresponded to 2 g of soya bean fat/kg of b.wt, a proportion commonly used in the parenteral feeding of neonates and infants[6–9]. The lipid emulsion was injected into the tail vein.

Group II. Each animal received an i.p. injection of endotoxin (purified lipopolysaccharide from *E. coli* 011:B4) (Difco Laboratories Inc., Detroit, USA), at a dose of 0.040 mg[10].

Group III. Each animal received first a parenteral injection of soya bean fat emulsion, as in group I, and then an i.p. injection of *E. coli* endotoxin, as in group II.

Group IV. Each animal received an injection of physiological saline corresponding in volume to the volumes of soya bean fat emulsion and endotoxin administered in the experimental groups.

Blood samples for analysis were drawn by cardiac puncture 24 h after injection, after which the animals were killed. Blood samples were centrifuged at 5000 rpm. Alanine aminotransferase (ALAT) and aspartic aminotransferase (ASAT) activities in serum aliquots were determined kinetically, using an IL Multistat III Micro Centrifugal analyzer at 37 °C (two determinations per sample)[11]. Samples of liver taken immediately after the animals were killed were deep frozen and subjected to histological examination. Frozen sections of liver tissues were stained with Sudan black, in order to assess accumulation of lipid in the liver parenchyma.

The data were analyzed statistically using Student's t-test.

Results. Histological examination. Lipid emulsion, administered as a single i.v. bolus injection, accumulated in the cells of the liver parenchyma, as shown by the presence of Sudan black-positive vacuoles in both hepatocytes and liver reticuloendothelial cells (RES). In animals which received endotoxin, there was evidence of focal hepatic necrosis. The administration of both lipid and endotoxin resulted in extensive liver necrosis and accumulation of lipid-staining material in hepatocytes and RES. Control animals exhibited no histological signs of liver damage.

Enzyme activities. The activities of the live enzymes in the serum samples paralleled the histological findings relating to liver tissue damage and necrosis. In the serum samples from animals to which only lipid emulsion had been administered (group I), ASAT activity was significantly higher than in serum samples from control animals. ALAT activities were similar in both groups. In the animals to which only endotoxin had been administered (group II), both ASAT and ALAT activities in the serum samples were significantly higher than those in animals to which only lipid emulsion had been administered. The highest ASAT and ALAT activities were observed in serum specimens from those animals to which both lipid emulsion and endotoxin had been given parenterally (table).

Discussion. The accumulation of lipid in hepatocytes and RES of liver parenchyma has been reported to occur in man after parenteral feeding[6–9]. Even short periods of parenteral lipid administration have been shown to lead to accumulation of lipid-staining material in the liver parenchyma[9]. The present data are consistent with these earlier observations, and confirm the accumulation of lipids in hepatocytes and RES following parenteral injection of a lipid bolus.

Earlier studies have shown the importance of the protective of filtering functions of liver RES, e.g. in destroying damaged red cells, in relation to uptake of endotoxins, in relation to antigens and antigen-antibody complexes and in relation to the clearance of bacteria, viruses and other particles[12]. Previous experiments[10–12] also indicate that blocking of the hepatic RES may enhance the destruction of liver cells resulting from injection of endotoxin into the portal circulation. The present data showed that liver cell damage was more pronounced and liver enzyme activities markedly higher in sera from animals to which endotoxin and parenterally administered lipid emulsion were administered than in sera from animals given only endotoxin or parenteral lipid emulsion. In way of explaining of these phenomena, we suggest that lipid blockade of liver RES may interfere with the ability of the RES to remove and detoxify endotoxins, leaving the liver parenchyma unprotected against the latter. The shelter offered by intact liver RES may be especially important in neonates, because the immature gut in newborn animals has been shown to possess increased permeability to enzymes, toxins and micro-organisms[13]. On the basis of these observations, the use of parenteral lipid emulsions during acute septic infections in human neonates would seem to be inadvisable.

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