

ACUTE TOXICOLOGICAL EXPERIMENT
OF T-2 TOXIN IN RABBITS /Poster/

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Introduction

In two cases of T-2 mycotoxicosis among broiler chicks we detected necrosis of the oral and oesophageal mucosa, and atrophy of the bursa of Fabricius, thymus and spleen /Bitay et al., 1979, 1981/. The lesions produced by T-2 toxin in mammals include congestion of the meningeal vasculature, severe congestion of the jejunal and ileal mucosae, lesions in the jejunum, ileum, caecum, spleen and mesenteric lymph nodes /karyopyknosis, karyorrhesis/, Peyer's patches of the ileum, lymphoid elements of the caecum, lymphoid follicles of the spleen and germinal centres of the mesenteric lymph nodes /Weaver et al., 1978; Sato et al., 1975; Hayes et al., 1979; Corrier and Ziprin, 1986; Pang et al., 1986; Glávits and Ványi, 1988/.

The purpose of this experiment was to study the pathological changes produced by T-2 fusariotoxin in rabbits.

Material and Methods

Thirty-nine clinically normal rabbits, weighing 2.4-2.6 kg, were used. In an acute toxicological experiment, 14 rabbits were given 1-15 mg/body weight T-2 fusariotoxin in dimethyl sulfoxide /DMSO/ solution on one occasion, per os through a gastric tube. Four animals received only DMSO, without T-2 toxin, and served as controls. They were examined

clinically and the survivors and controls were exsanguinated 48 hours after treatment.

In a subacute toxicological experiment 15 rabbits received, in the feed 2 mg/body weight T-2 fusariotoxin daily. The rabbits were killed by bleeding two, or in some cases one, at a time 6, 12, 20, and 48 hours, and 3, 4, 5, 6, 7, 8, 9 and 10 days after treatment. The 6 controls were exsanguinated 20 and 48 hours, and 4, 6, 8, and 10 days after treatment respectively.

Histological examination. Samples were taken from the liver, spleen, kidney, adrenal gland, stomach, small intestine, ampulla ilei, mesenteric lymph node and bone marrow of each animal. After fixation in 5 % buffered formalin and embedding in paraffin, the sections were stained with haemalaun and eosin. In frozen sections prepared from the liver, Fettrot staining was used for the detection of lipids.

Electron-microscopical examination. Spleen and bone marrow samples were taken from two treated /8 mg/body weight/ and two control animals of the acute toxicological experiment. After double fixation in 2.5 % glutaraldehyde and in 1 % osmium tetroxide, both buffered with 0.1 M sodium cacodylate, and dehydration with ethanol, the samples were embedded in Durcupan ACM in the usual way. Ultrathin sections were counter-stained with uranyl acetate and lead citrate, and examined in a Philips 201 CS electron microscope.

Results

The results are shown in Tables I. and II. and are demonstrated in Figures.

Conclusions

Accumulation of serous exudate in the thoracic and abdominal cavity is indicative of disturbed circulation. The acute or subacute catarrhal gastritis and enteritis may be a consequence of the direct cytopathic effect exerted by

the toxin. The damage done to lymphoid cells of the intestinal mucosa is suggestive of a suppressed local immune response, whereas lesions seen in the B- and T-cell-dependent zones of the lymphoid organs are indicative of suppressed humoral and cell-mediated immune responses. Necrosis of cells belonging to the MPS /mononuclear phagocyte system/ indicates disturbed phagocyte function, and impaired granulocytopoiesis in the bone marrow reflects an impaired natural resistance /i.e. inflammatory responsiveness/. The degenerative changes found in the parenchymal cells of the liver and kidneys may be connected with the systemic effect of the toxin, whereas the lesions observed in the adrenals may be attributed, at least in part, to effects exerted by stressors.

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Table I. Pathomorphological changes in rabbits caused by T-2 toxin
(Acute toxicological experiment, 1-15 mg/body weight/one occasion, p.o.)

treatment (mg/body weight kg) and sign of animals		1	1	2	2	4	4	6	6	8	8	10	10	15	15
death							+	+	+	+	+	+	+	+	+
changes (48 hours after treatment)	serum accumulation in the thoracic and abdominal cavity						+			+				+	+
	hyperaemia of lung, emphysema and/or oedema	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	acute gastritis						+	+	+	+	+	+	+	+	+
	acute enteritis						+	+	+	+	+	+	+	+	+
	lymphoid cell necrosis of the intestine ^x				1	2	2	3	2	3	3	3	3	3	3
	pathological fatty liver degeneration				+		+	+	+	+	+	+	+	+	+
	necrosis of liver MPS cells ^x					1	2	2	2	2	3	3	3	3	3
	tubulonephrosis				+		+	+	+	+	+	+	+	+	+
	haemorrhage and diminishing of lipid amount in adrenal cortex		+		+		+		+	+	+	+	+	+	+
	lymphocyte depletion and necrosis in the "B" and "T" dependent zone of the spleen and lymph nodes and lymphoid follicles of the ampulla ilei ^x				1	1	2	2	2	2	3	3	3	3	3
blast cell depletion and necrosis in bone marrow myeloid colonies ^x				1	2	1	2	2	2	3	3	3	3	3	3

x - Remarks: 1 - up to the cell population 5-30 %
 2 - up to the cell population 30-80 %
 3 - up to the cell population 80-100 %

Table II. Pathological changes in rabbits caused by T-2 toxin
(Subacute toxicological experiment, 2 mg/body weight/daily, p.o.)

sign of animals and posttreatment hours until killing		hours						days									
		6.	12.	20.	20.	48.	48.	3.	4.	5.	6.	7.	8.	9.	10.		
changes	loss of weight													+	+	+	
	gastritis								+	+	+	+	+	+	+	+	
	lymphocyte necrosis of small intestine mucosae ^x	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	lymphocyte depletion and necrosis in the lymphoid follicles of ampulla ilei ^x	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	centrolobular pathological fatty liver degeneration				+		+										
	adrenal cortex hypertrophy													+	+	+	+
	lymphocyte depletion and necrosis in the "B" and "T" dependent zone of the spleen and lymph nodes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	blast cell depletion and necrosis in myeloid colonies of the bone marrow ^x	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

x-Remarks: 3-10 % of the cell population is altered

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Rabbits were orally treated once with 1, 2, 4, 6, 8, 10 and 15 mg/body mass kg of T-2 toxin. 4 mg/kg and higher doses caused death within 48 hours. The pathological examinations revealed acute gastritis and enteritis, lymphoid cell necrosis of intestinal mucosa, centrolobular hepatic dystrophy and necrosis of the cells of reticulo-endothelial system in the liver, tubulonephrosis, multiplex focal dystrophy in the adrenal cortex, diffuse lymphocyte-depletion and -necrosis in the lymphoid tissues /both in the "B"- and "T"-dependent zones of the spleen, lymph nodes and in the ampulla ilei/, as well as depletion and necrosis of the myelopoietic cells in the bone marrow. In the survivals, exsanguinated 48 hours after treatment, similar but milder alterations were observed.

AKUT TOXIZITÄT DES T-2 TOXINS IN KANINCHEN /Poster/

Von den mit 1, 2, 4, 6, 8, 10 und 15 mg T-2 Toxin/kg Körpergewicht einmal per os behandelten Kaninchen verendeten die mit 4 mg oder mit mehr behandelten Tieren in 24-48 Stunden. Die pathologischen Untersuchungen zeigten: katharrhalische Entzündung im Magen und Dünndarm, Nekrose der Lymphoid-Zellen der Schleimhaut, zentrolobuläre Leberdystrophie und Nekrose der MPS-Zellen im Leber, Tubulonephrosis, herdförmige Dystrophie in der Cortex-Substanz der Nebenniere; daneben in den lymphatischen Organen /Milz, Lymphknoten, Ampulla ilei/ so auf den "T" als auf den "B" dependenten Gebieten Depletion und Nekrose der Lymphozyten. Auch in dem Knochenmark, besonders in den myeloid Zellkolonien konnten Depletion und Nekrose festgestellt werden. Die überlebenden und nach 48 Stunden verbluteten Kaninchen zeigten ähnliche, aber mindere Veränderungen.



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