Induction of Chronic Diabetes by Streptozotocin in the Miniature Pig*

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Summary. The rapid i.v. injection of 60 mg streptozotocin/kg body weight 8 days after an initial dose of 30 mg/kg was the best method to produce a distinct insulin-deficient diabetes in minipigs. Even in the absence of any therapy the further course of this diabetes remained stable without tending to exhibit ketoacidosis. Besides hyperglycaemia and the loss of insulin response to glucose there was a significant increase of triglycerides and a decrease of plasma albumin. In the oldest animals this diabetes has so far been observed for more than 3 years. Because of some special advantages this experimental diabetes could provide a useful model for studying diabetic angiopathies.

Key words: Streptozotocin diabetes - Miniature pig - Leukosis and streptozotocin


Schlüsselwörter: Streptozotocindiabetes – Miniaturschwein – Leukämie und Streptozotocin

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Despite intensive research, there are still conflicting views and a lack of clarity about the genesis and the development of diabetic angiopathies and especially of micro-angiopathy [1, 4, 6, 13, 14, 21, 22, 23]. Strong arguments have meanwhile been put forward in support of the "metabolism hypothesis" of diabetic angiopathy [13, 23]. However, since the aetiology affects the prophylaxis and therapy of the diabetic angiopathy, a final clarification of these problems must be searched for. A further finding is noteworthy in respect to diabetes mellitus as an "angiopathy risk factor". This is the very varying incidence of (macro)angiopathy among different population groups or races [7], evidently in relation to additional risk factors [15]. These indications demonstrate the necessity of further research into the genesis of the widespread diabetic angiopathies.

Because of the limited availability of human subjects for such investigations, more especially for longterm observations with invasive investigations, we endeavoured to find a model displaying the greatest number of parallels with human insulin-deficient diabetes.

Because of its outstanding advantages for comparative experimental medicine and especially for investigating vascular diseases, we selected the miniature pig as the experimental animal [2, 3, 9, 11]. Because of its relatively specific and dose-dependent beta-toxicity, accompanied by the possibility of producing a latent diabetic metabolism state, streptozotocin (Fig. 1) appeared to be particularly suitable and interesting for inducing diabetes (for further details concerning streptozotocin, see [17]). No reports on experience with streptozotocin-induced diabetes in the pig have so far appeared in the literature. The initial task, therefore, was to work out the over-all basis such as the dosage and form of administration of the streptozotocin, and also the further course of this form of diabetes.

![Streptozotocin](image)

**Fig. 1. Structural formula of streptozotocin [17]**

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**Materials and Method**

Hitherto the results obtained in 17 Hanford pigs of both sexes have been evaluated (♀:♂ = 7:10; male animals castrated. Rearing: Lehrstuhl für Tierhygiene der Universität München). The initial weight was 40.35 ± 9.99 kg (age 3—8 months). Details of the animals' maintenance and feeding and of the operations to be performed (indwelling venous catheter) will be found in [11].

Streptozotocin was dissolved in sodium citrate buffer (0.1 M, pH 4.5) to give a concentration of 30 mg/ml. It was administered to fasted or fed animals in doses of 30—90 mg/kg on one or two occasions either as a bolus or i.v. over 5 min, or s.c. or i.p.

Unless otherwise stated, the humoral parameters were determined with the Technicon Autoanalyzer (Sma Plus, Technicon Instruments, Tarrytown, USA). Glucose was determined...