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ЦУКРОВИЙ ДІАБЕТ – МІЖДИСЦИПЛІНАРНА ПРОБЛЕМА СУЧАСНОЇ МЕДИЦИНИ

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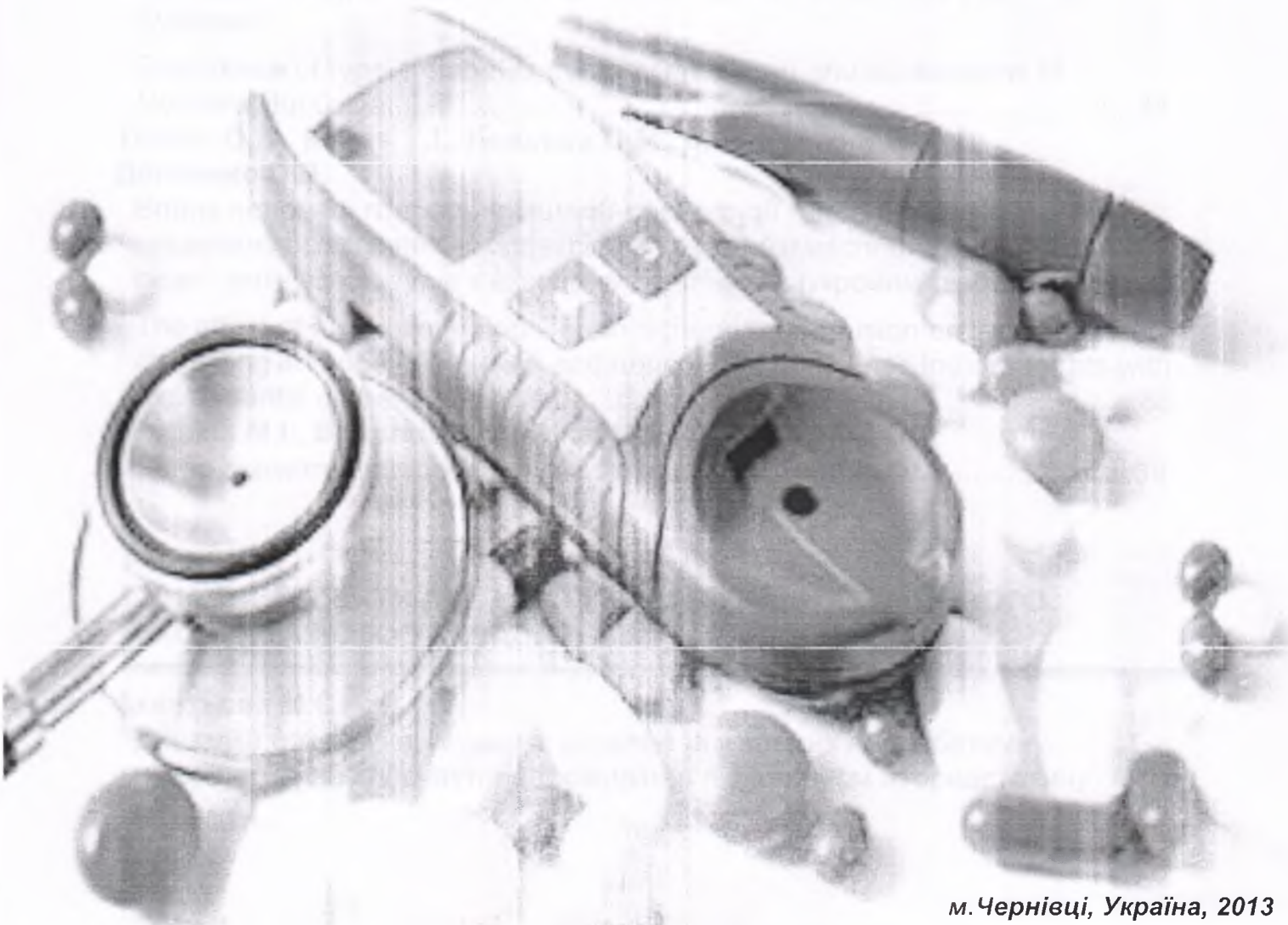

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SOME EXPERIMENTAL MODELS, USED FOR STUDYING DIABETES

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Actuality. Diabetes mellitus (DM) is a potentially morbid condition with high prevalence worldwide thus the disease constitutes a major health concern. Presently, it is an incurable metabolic disorder which affects about 2,8% of the global population. The search for compounds with novel properties to deal with the disease condition is still in progress. This makes the use of experimental models for the disease imperative. Diabetic nephropathy is one of the major long-term microvascular complications and is the major cause of morbidity and premature mortality in individuals with diabetes mellitus. End-stage renal disease (ESRD) in patients with diabetes (first of all type 2) has increased worldwide during the last few decades, and diabetes is associated with worse survival among patients undergoing dialysis.

Aim and object. The existence of experimental animal model of a disease aids not only the understanding of the etiology and pathophysiology of given nosology, but also the development of drugs for its treatment. The use of different experimental animal models of diabetic nephropathy has provided valuable information regarding some aspects of it.

Basic items of information. Experimental models may be divided into two sorts: analogue models and intrimic models. Analogue models are useful as substitutes for some reality otherwise inaccessible to experimentation. Intrimic models do not have to mimic reality, they fascinate on their own. The existing animal models are following. *Normoglycaemic animal model.* Normal healthy animals can be used for testing potential oral hypoglycaemic agents. That is a valid screening method which is often used in addition to diabetic animal models. This method allows for the effect of the drug to be tested in the animal with an intact pancreatic activity. The comparison may give some information regarding mechanism of action. Hyperglycaemic agent may be detected at the same time [Etuk, 2010]. *Oral glucose loading animal model.* This method is often referred to as physiological induction of DM because the blood glucose level of the animal is transiently increased with no damage to the pancreas. In the clinical setting, it is known as Glucose tolerance testing (GTT): a standard procedure often used for the diagnosis of border line diabetic patients. In this procedure, the animals are fasted overnight, then oral glucose load (1-2,5 g/kg body weight) is given and blood glucose level is monitored over a proper period of time. Usually rabbits or male rats are used. Etuk and Mohammed used this procedure to induce hyperglycaemia in Wistar rats. *Chemical induction of diabetes mellitus:* Usually Streptozotocin (STZ, 69%) and alloxan (31%) are the most frequently used drugs and this model has been useful for the study of multiple aspects of the disease. Both drugs exert their diabetogenic action when they are administered parenterally (intraperitoneally, intravenously or subcutaneously). The dose of these

agents required for inducing diabetes depends on the animal species, route of administration and nutritional status [Federiuk *et al.*, 2004]. Streptozotocin (STZ) is a classical antitumor antibiotic and chemically is related to other nitrosureas used in cancer chemotherapy. STZ prevents DNA synthesis in mammalian and bacterial cells. It induces diabetes in monkey, hamster and guinea pig. The biochemical mechanism results in mammalian cell death. Although STZ is the most commonly used drug for induction of diabetes in rats, there are some disadvantages to its use in chronic experiments, such as spontaneous recovery from high blood glucose levels by the development of functioning insulinoma [Iwase *et al.,* 1991] and high incidence of kidney and liver tumors. Alloxan is the next most commonly used chemical for induction of DM [Etuk, 2010]. Alloxan is a urea derivative which causes selective necrosis of the pancreatic β-cells. It is used to produce experimental diabetes in animals such as rabbits, rats, mice and dogs. With this agent, it is possible to produce different grades of severity of the disease by varying the dose of alloxan used: these may be classified by measuring fasting blood sugar (FES) levels. Thus alloxan induced DM served as a pathological biomodel for testing a substance with supposed antioxidant activities *in vivo* [Bartosikova *et al.,* 2003]. It can be administrated by virtually all routes including oral. *Ferric nitrilotriacetate induction of diabetes mellitus*. This is a rarely used procedure. Rats and rabbits parenterally treated with a large daily dose of ferric nitrilotriacetate manifested diabetic symptoms such as hyperglycaemia, glycosuria, ketonemia and ketonuria after approximately 60 days of treatment. *Surgical model of diabetes mellitus*. Another technique used to induce diabetes is complete removal of the pancreas (pancreatectomy). Limitation to this technique include high level of technical expertise and adequate surgical room environment, major surgery and high risk of animal infection, adequate post-operative analgesia and antibiotic administration, supplementation with pancreatic enzymes to prevent malabsorption and loss of pancreatic counter regulatory response to hypoglycemia.

Another way to cause diabetes is genetic models of diabetes (spontaneously develop diabetic rats and genetically engineered diabetic mice or rats). As well as viruses are one environmental factor that is implicated in the pathogenesis of type 1 diabetes. Molecular mimicry is based on two concepts involving pathogenic antigen and reactive lymphocytes.

Conclusions. Chemical induction appears to be the most popularly used procedure in inducing diabetes mellitus in experimental animals. The best known drug-induced diabetic model is the alloxan diabetes. It is capable of inducing both type 1 and type 2 diabetes mellitus with proper dosage selection. But the most commonly used drug is streptozotocin for reasons that are not well specified. Experimental animals must be put to use within seven days after induction of diabetes mellitus or maintain with appropriate doses of insulin to prevent animal death. The surgical and genetic methods require highly technical skills, may be associated with a high percentage of animal death and thus are rarely used. Alloxan induced diabetes model appears to be the most reliable and easily reproducible method of inducing diabetes mellitus in experimental animals.