THE EFFECT OF MATERNAL ENVONOMATION BY NAJA HAJE (EGYPTIAN COBRA) SNAKE ON THE DEVELOPING CENTRAL NERVOUS SYSTEM

N. N. Y. Nawar

Faculty of Medicine
Ein Shams University
Cairo, Egypt.

SYNOPSIS

The effect of maternal envenomation by Naja haje venom (Egyptian Cobra) on early and late stages of the developing central nervous system was studied in mice. The venom passed the placental barrier in both stages. In the stage which corresponded with closure of the neural tube, the venom caused congestion of the brain leptomeninges, cortical atrophy together with increase in the size of the ventricular system. However, in the foetuses which were envenomated late in pregnancy (15th day of gestation) the spinal arteries were dilated and the anterior horn, posterior horn and posterior root ganglionic cells showed chromatolytic changes.

INTRODUCTION

The effects of Egyptian Cobra (Naja haje) venom on the foetal nervous system has not been studied although some workers described lesions produced by other venoms (Ruch and Gabriel-Robez-Kremer, 1962 and Gabriel-Robez and Clavert, 1969). Therefore, it is the aim of this work to study the effect of maternal envenomation on the developing central nervous system. Of relevance is the observation that pregnant women living in areas bordering the Sahara in this country are liable to be bitten by the above serpent.

MATERIALS AND METHOD

Albino mice of the Rockefeller strain were used. In each prospective mating one oestrous female was kept overnight in a cage with one male. The next day all the females showing vaginal plug were considered to be in the first day of pregnancy. The pregnant mice were divided into three groups. Animals of group I and II received a single 1 m dose of Naja haje (Egyptian Cobra) venom (0.15 ug per 20 g body weight). The LD_{50} is 10 ug per 20 g body weight. Group I was injected on the tenth day of gestation and group II was injected on the 16th day of gestation. Group III served as a control. All the females that showed vaginal bleeding were eliminated from this study. From each group, six animals were chosen 48 hr after being injected and sacrified by an overdose of ether together with their control. The foetuses were removed, fixed in Bouin's fixative, dehydrated, cleared and embedded. Serial transverse and longitudinal sections were taken of the brain and spinal cord (10 um thick) and stained with cresyl violet.

RESULTS

The main lesion in foetuses, following maternal envenomation during the period that corresponded with closure of the neural tube (group I), was on the brain vascular system. The leptomeninges were congested, the cortex exhibited generalized atrophy as manifested by diminution of its thickness (18% as compared with the control) and there was an increase in the size of the ventricular system. A case of ventriculo-encephalocoele was also observed. The choroid plexus of the fourth ventricle seemed to be extruded and came in contact with the foetal membranes (Fig. 1). On the other hand when maternal envenomation was late in pregnancy (group II) the foetal lesion appeared to be in the vascular system of the spinal cord. The spinal arteries were dilated, the pial ring congested and the central canal dilated (23% as compared with the control) (Fig. 2). The neurons of the anterior horn, posterior horn and the dorsal root ganglion had chromatolytic changes (Fig. 3, 4 and 5).

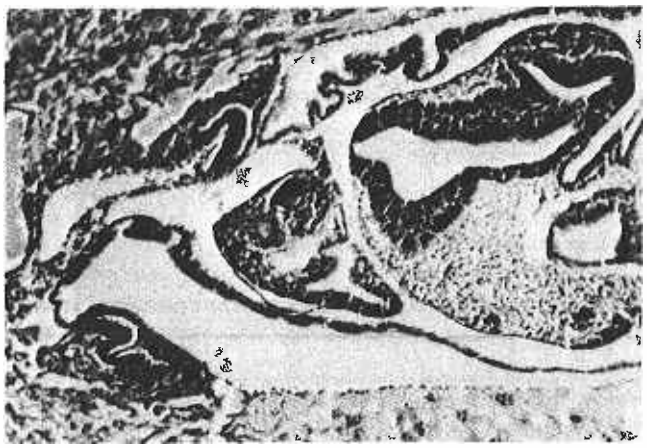

Fig. 1 Photomicrograph showing a sagittal section of the brain of a foetus which was maternally injected on the tenth day of gestation with Naja haje venom and sacrified two days after. The choroid plexus of the fourth ventricle was extruded and came with the foetal membranes. Cresyl violet stain (X 40).

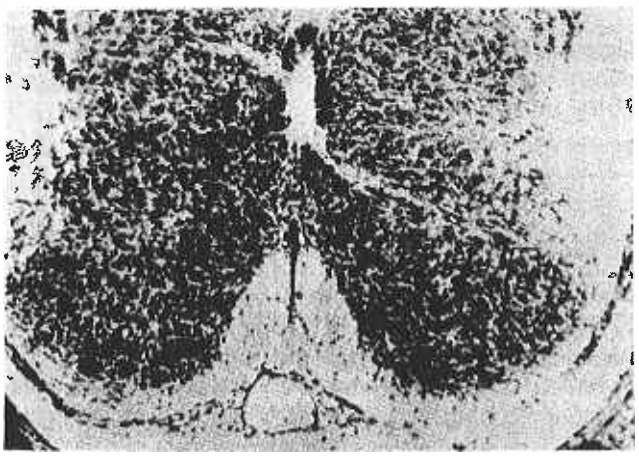

Fig. 2 Photomicrograph showing the dilated central canal and the anterior spinal artery in the cervical segment of the spinal cord of a foetus maternally injected on the 16th day of gestation with Naja haje venom and sacrified two days after. Cresyl violet stain (X 60).

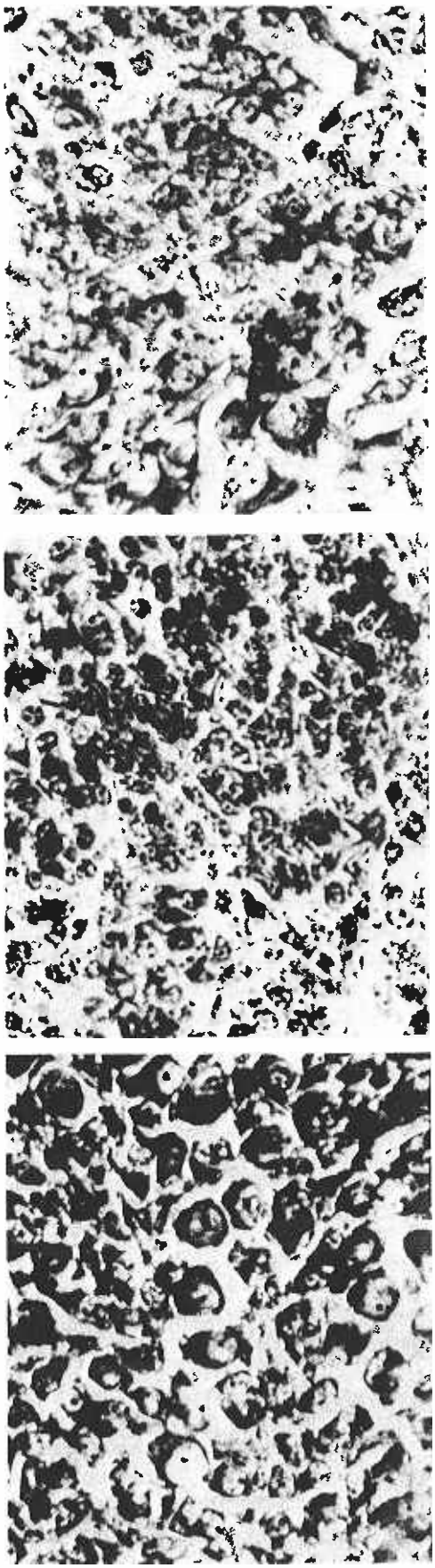

Fig. 3, 4 and 5 Photomicrographs showing the chromatolytic changes in the anterior horn, posterior horn and posterior root ganglionic cells respectively of the spinal cord of foetuses of the above group. Cresyl violet stain (X 400).

DISCUSSION

Although a single low dose of Naja haje venom (65th LD_{50}) was injected maternally, the dose was toxic to the foetal central nervous system both in early and late pregnancy.

In a comparative study on experimental envenomation, exencephaly was described with Vipera aspis envenomation in the mouse (Gabriel-Robez and Clavert, 1969) and with Naja envenomation of the chick embryo (Ruch and Gabriel-Robez-Kremer, 1962). The mechanism by which the envenomation induced such malformation was not described. Giround (1960) noticed in anencephalic embryos the choroid plexus was plentiful and in direct contact with the amniotic fluid. Therefore, it seemed probable that in cases of maternal envenomation with Naja haje venom the growth of the foetal choroid plexus would be stimulated, resulting in an increase of the volume of the amniotic fluid. That might explain the ventriculo-encephalocele and the dilatation of the central canal of the spinal cord observed in the present study.

Naja haje venom when injected into the mother can pass the placental barrier and exert a toxic effect on the vascular system of the brain and cord. Similar vascular effects were noticed in adult (Taube and Essex, 1937; Fidler et al, 1940; Okonogi et al, 1961; Mohamed et al, 1974 a) and foetal tissues (Mohamed et al, 1974 b). The chromatolytic changes observed in the anterior horn, posterior horn and posterior root ganglionic cells could be considered secondary to such vascular effects.

REFERENCES

1. Fidler, H.K., Glasgow, R.D. and Carmichael, E.B.: Pathological changes produced by the subcutaneous injection of rattle snake (Crotalus) venom into Macaca mulatta monkeys. Am. J. Path., 16: 355, 1940.
2. Gabriel-Robez, O. and Clavert, J.: Action d'une injection de venin de Vipere (Vipera aspis) a la souris gestante sur la formation des embryons. C.r. Seanc. Soc. Biol., 163: 1576, 1969.
3. Giround, A.: Causes of morphogenesis of anencephaly. Ciba Foundation Symposium on Congenital Malformations 1960, pp 199 (Churchill, London).
4. Mohamed, A.H., Nawar, N.N.Y. and Fatma, A.: Influence of hydrocortisone on the microscopic changes produced by Naja nigricollis venom in kidney, liver and spleen. Toxicon, 12: 45, 1974 a.
5. Mohamed, A.M., Nawar, N.N.Y. and Hanna, M.M.: Some effects on Naja nigricollis envenomation on developing fetal tissue. Toxicon, 12: 477, 1974 b.
6. Okonogi, T., Hoshi, S., Honama, M. and Lizaka, H.: Experimental histopathological studies on the serum therapy against Habu snakebite. Gumma J. med. Sci., 10: 46, 1961.
7. Ruch, J.V. and Gabriel-Robez-Kremer, O.: Action teratogene du venin de Naja sur l'embryon de poulet C.r. Seanc. Soc. Biol., 156: 1508, 1962.
8. Taube, H.N. and Essex, H.E.: Pathological changes in the tissues of the dog following injection of rattlesnake venom. Archs Path., 24, 43, 1937.