and SGOT levels which rose significantly, when compared with their respective preoperative values, the former on the 1st, 3rd and 5th, and the latter on the 1st and 3rd postoperative days, did not differ significantly from the respective values following control anesthesia. In the group of patients anesthetized with methoxyflurane, the mean SXO levels, when compared to the preoperative values, were significantly elevated on the 1st postoperative day only (almost 4fold the preoperative value) but when compared with the respective values following control anesthesia, no significant elevation was found at any time. Methoxyflurane anesthesia did not cause a significant alteration in LDH and SGOT activities when compared to the preoperative value, and to the respective control group.

Discussion. We have reported previously that surgical procedures performed on body parts other than the upper abdomen (biliary tract and gastric surgery) are not associated with an increase in SXO activity[22]. None of the patients chosen for the present study were subjected to intraabdominal operations, thus increased SXO activity in the patients studied should be considered to reflect liver damage due to the anesthetic agents involved and not due to the surgical procedures undertaken.

Since halothane and methoxyflurane were administered in addition to N_2O/O_2 mixture, an increase in serum enzyme activity above that caused by N_2O/O_2 administration exclusively was considered to indicate liver damage. According to the change in SXO level, halothane but not methoxyflurane was found to cause hepatocellular damage. The halothane hepatotoxicity was both prompt and transient. These results are compatible with those of several investigators who reported that halothane has a specific hepatotoxic effect[7,9-11], but is incompatible with studies of others who found the hepatotoxic effect of halothane to be comparable with that caused by other anesthetic agents, such as diethyl ether, and chloroform[8,15,16], or failed to demonstrate any hepatotoxic effect of halothane at all[12,14]. The advantage of SXO as a marker for acute hepatocellular damage was again verified in the present study, in man. Out of the 3 intracellular enzymes, SXO, SGOT and LDH, employed for the detection of hepatocellular damage induced by anesthetic agents, only SXO was found to be significantly increased.

Toxicity of *Parthenium hysterophorus* L. to cattle and buffaloes[1]

T. R. Narasimhan, M. Ananth, M. Narayana Swamy[2], M. Rajendra Babu, A. Mangala and P. V. Subba Rao[3]

Institute of Animal Health and Veterinary Biologicals and Department of Biochemistry, Indian Institute of Science, Bangalore-560012 (India), 13 December 1976

Summary. Parthenium hysterophorus L., when fed to buffalo bull calves and cross bred bull calves resulted in acute toxicity leading to death. The former animals developed severe dermatitis. Autopsy revealed ulceration of alimentary tract. Extensive pathological changes were noticed in liver, kidney and skin.

Parthenium hysterophorus L., a native weed of South and Central America, accidentally introduced into India, is posing a threat to agriculture in southern parts of the country where it has invaded food and fodder crops fields[4]. Although Parthenium has been found to be responsible for allergic contact dermatitis in humans in these parts[4,5], its toxicity to domestic animals has not been investigated. Cattle and buffaloes graze occasionally, while goats graze more freely on the weed in areas where waste lands and pasture fields are heavily infested with Parthenium. Many animals, however, graze grass in between Parthenium in the fields. Even in the latter case, the possibility of some Parthenium being ingested can not be ruled out. We therefore studied the toxicity of the weed to cattle and buffaloes, the results of which are presented in this communication.

9 buffalo bull calves and 7 cross bred calves (each 9–12 months old) weighing about 80–100 kg and free of any external and internal parasites in an apparently healthy state, were selected for the study. Feeding chaff cut aerial parts of Parthenium hysterophorus L., ad libitum initially for 48 h was replaced with equal quantities of Parthenium and hybrid napier grass. Control animals throughout the experiment were fed on hybrid napier grass. All the animals received 300 g of concentrate feed mixture every day.

The animals consumed the weed without much resistance but developed diarrhea within 24 h which subsided in 3 to 4 days. 6 buffalo bull calves and 5 cross bred bull calves died within 8–30 days. The controls remained healthy throughout the experimental period. 24 h prior to death, the experimental animals showed signs of excitability and muscular twitching.

The buffalo bull calves developed itching 7 days after feeding Parthenium, followed by the appearance of papular erythematous eruptions involving the tip and base of ears, all along the neck which gradually extended on either side of the thoracic region, dorsal aspects of the abdomen and the lesions extending to knee, hock joints and the brisket region. A few papulae were noticed on the ventral surface of the abdomen. 3 weeks later, the affected areas became alopetic at neck and shoulder region. Depigmentation in patches was marked in these areas. The surviving animals developed oedema around eyelids and the facial muscles. None of the cross bred bull calves, however, suffered from dermatitis.

There was ulceration on the muzzle, on autopsy ulceration on dental pads, dorsum of the tongue, the upper palate extending down to oesophagus was seen in all animals. Liver, gastrointestinal tract and kidney revealed marked lesions on autopsy. There were areas of necrosis with severe congestion in liver and gastrointestinal tract. Ulceration throughout the abdomen and fundic region

1 Acknowledgments. We thank Dr Satish Dhawan and Mr M. A. Sethu Rao for their keen interest. The help rendered by Bangalore City Corporation authorities in the supply of Parthenium is gratefully acknowledged.

2 Institute of Animal Health and Veterinary Biologicals, Hebbal, Bangalore (India).

3 Department of Biochemistry, Indian Institute of Science, Bangalore (India).

4 A. Lonkar, J. C. Mitchell and C. D. Calnan, Trans. a. Rep. St. John's Hosp. derm. Soc. Lond. *60*, 43 (1974).

5 P. V. Subba Rao, A. Mangala, B. S. Subba Rao and K. M. Prakash, Proc. Soc. Biol. Chem. (India) *45*, 12 (1976).

was marked. Congestion and oedema was also observed in the lungs. The hilus of the kidney had gelatenous changes. Histopathological changes were mainly predominant in the liver, kidney and the intestines in both the species. It varied from mild degenerative change in hepatic parenchyma to that of severe hepatic change tending towards necrosis. Kidney revealed extensive haemorrhagic zones at the tubular areas with varied degrees of regressive changes comprising hyaline changes in the tubules and the constricted glomerular tuft. Lesions in the abomasum varied from slight erosion of the epithelial cells to that of haemorrhagic zones on mucosa and submucosa. Intestine also showed severe congestion and erosion of mucous membrane.

On discontinuation of Parthenium after 30 days, the remaining animals which were showing signs of toxicity gained in health. Repigmentation occurred after 3 weeks in buffalo bull calves showing signs of recovery from dermatitis. The ulcerations developed on the muzzle and lips of the surviving cross-bred bull calves showed marked signs of regeneration.

It is not surprising the Parthenium hysterophorus L. is poisonous to animals. Some members of the compositae family to which it belongs, are known to be toxic when eaten by live-stock[6]. Ingestion of Helinium microcephalum, a weed that grows in many parts of Texas, USA, and Mexico was observed to produce acute poisoning and death in cattle, sheep and goats[7]. Toxic properties of this weed have been attributed to helenalin, a sesquiterpene lactone[8]. Similarly tenulin, the major sesquiterpene lactone constituent of Helinium amarum was found to be toxic and was responsible for milk bittering[9]. It remains to be investigated whether the sesquiterpene lactone parthenin from Parthenium hysterophorus L., which has been attributed to be responsible for allergic contact dermatitis in man[10] is responsible for acute illness and death in cattle. Unless effectively checked, the aggressive spread of Parthenium in India may likely to pose considerable danger to live-stock, particularly under drought conditions.

6 J. M. Kingsbury, Poisonous plants of the United States and Canada. Prentice-Hall, Englewood Cliffs, N.J., USA 1964.
7 J. W. Dollahite, W. T. Hardy and J. B. Henson, J. Am. vet. med. Ass. *145*, 694 (1964).
8 D. A. Witzel, G. Ivie and J. W. Dollahite, Am. J. vet. Res. *37*, 859 (1976).
9 G. W. Ivie, D. A. Witzel and D. D. Rushing, J. agric. Fd Chem. *23*, 845 (1975).
10 E. Rodriguez, M. O. Dillon, T. J. Mabry, J. C. Mitchell and G. H. N. Towers, Experientia *32*, 236 (1976).

Influence of oral glucose feeding on endotoxin lethality in mice[1]

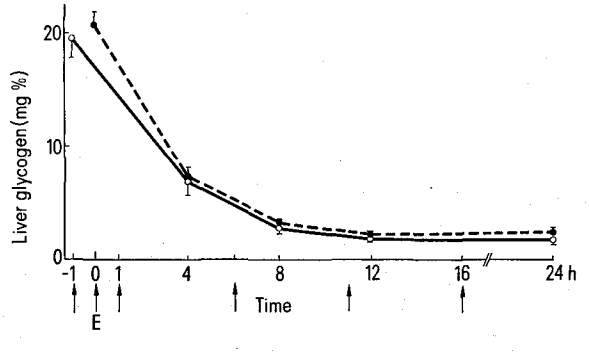
G. Lazar[2] and M. K. Agarwal[3]

INSERM, U-36, 17, rue du Fer à Moulin, F-75005 Paris (France), 3 February 1977

Summary. Prolonged feeding of physiological solutions of glucose (5%) by gavage did not protect against either endotoxin death or liver glycogen depletion in mice.

It is well-known from clinical and experimental observations that one of the most characteristic symptoms of endotoxicosis is the imbalance of carbohydrate metabolism, and many experimental data suggest that loss of carbohydrate reserves may be directly related to the severity of endotoxicosis and thus influence the survival rates[4,5]. If death is directly related to endotoxin-induced carbohydrate loss, it would be logical to assume that survival would be improved by administration of glucose. Several groups of experiments indicate, however, that the administration of exogenous glucose i.v. or i.p., to mice or guinea-pigs, made hyperreactive to endotoxin by BCG[4,5] or CCl_4[6], respectively, or during endotoxin shock in dogs[7], prolongs life but has little effect on the ultimate mortality. Furthermore, significant protection against endotoxin toxicity is not obtained during alloxan-induced diabetes in BCG-sensitized mice, in spite of the fact that diabetes is associated not only with hyperglycemia but also with decreased glucose utilization and with increased gluconeogenesis[5].

The experiments reported below are different from earlier studies at least in three respects: a) since the physiological and pathological reactions of animals rendered hyperreactive to endotoxin are different from normal animals in many aspects[4,5], we studied the effect of exogenous glucose on endotoxin lethality in normal mice; b) glucose was administered by stomach tube in the hope that it would reach the liver directly via the portal venous



Influence of glucose load on liver carbohydrate levels. Mice were injected with endotoxin at time 0 and given an oral glucose (●) or water (○) load at the arrow. Glycogen determination was carried out on liver biopsies taken just before 1st and 2nd feedings and at the indicated times thereafter. All values are an average of 8 separate determinations ± SE.

1 Supported by grants from the INSERM (CL 76.5.001.4), the CNRS (03 7860) and the DGRST. Thanks are due to M. Philippe for technical assistance.

2 International INSERM Fellow.
3 Maître de Recherche au CNRS, to whom all correspondance should be addressed.

4 L. J. Berry, Acad. Press *5*, 165 (1971).
5 J. W. Shands, Jr, V. Miller and H. Martin, Proc. Soc. exp. Biol. Med. *130*, 413 (1969).
6 W. E. Farrar, Jr, and J. G. Watson, Proc. Soc. exp. Biol. Med. *115*, 833 (1964).
7 L. B. Hinshaw, M. D. Peyton and L. T. Archer, Surgery Gynec. Obstet. *139*, 851 (1974).