Promintic – A Promising New Anthelmintic

One of the most interesting new therapeutics to be introduced in the veterinary field during the past year is a research discovery of Imperial Chemical Industries, England. This material which has the generic name of methyridine is an organic solvent which possesses strong anthelmintic properties against a wide variety of gastrointestinal nematodes, particularly in sheep and cattle. Since the first report of these properties by Broome and Greenhalgh (1) a number of additional clinical and pharmacological papers have appeared. The purpose of this review is to summarize the salient features of these reports for Canadian veterinarians who may wish to employ this drug in practice.

Chemistry

Methyridine as mentioned earlier is an organic solvent which bears the chemical name 2(β-methoxy ethyl) pyridine. It is a colourless and sweet-smelling liquid. For clinical use it is supplied as a 90% v/v solution in water.

Tissue distribution

Methyridine is able to pass freely through most of the barriers which maintain body integrity. Thus it is rapidly absorbed through unbroken skin. For this reason direct contact with the drug should be avoided. Following systemic injection or oral administration it is rapidly distributed throughout the body tissues. Particularly important for its anthelmintic action, an equilibrium is set up between the concentration in the blood and the fluids of the alimentary canal. In this way an effective anthelmintic concentration is obtained in the gut after a subcutaneous injection. For this reason too, even immature parasitic forms deep in the intestinal mucosa are reached by the drug. Methyridine is rapidly eliminated from the body in the form of pyridine -2-acetic acid. Twenty-four hours after administration no drug residues may be found in the milk or tissues.

Made of action

Studies on the pharmacological action of this drug by Broome (2) have shown that it produces neuromuscular block of the decamethonium type. There appears to be sufficient difference between the sensitivity of nematode and vertebrate nervous systems to this drug to allow a wide safety margin for its use in animals. Studies by Broome (2) have also shown that in the vitro anthelmintic activity of methyridine is decreased by lowering the pH. Apparently acidity reduces the entry of the drug through the cuticle into the worms. It has been suggested that this factor may explain the occasional poor efficiency of the drug in the abomasum.

Range of activity

The range of anthelmintic activity of methyridine in cattle and sheep has been established in a series of clinical studies (3, 4, 5, 6, 7, 8). A comparison with phenothiazine is summarized in Table I (3, 4, 5, 6, 7, 8).

Methyridine appears to be particularly outstanding in its ability to remove im-
mature forms of a wide variety of species. Also notable is its strong anthelmintic activity against Trichostrongylus in the abomasum, Ostertagia, Cooperia and Nematodirus in the small intestine and Trichuris in the caecum and large intestine. In this respect the compound is a significant advance over existing anthelmintics. In a recent paper McGregor et al (9) described the use of methyridine, in dogs. In twenty-one animals whipworm infestation was completely eliminated while at the dose given no effect was seen against ascaris or hookworm infestation. Wally (3) studied the effect of methyridine against a variety of parasitic infestations in sheep and cattle. Against lungworm (Dictyocaulus) the compound was active but slightly less so than cyanacethydiazide. No activity could be demonstrated against liver fluke (Fasciola hepatica) in sheep or against a variety of species of Coccidia in sheep or cattle.

Toxicity

Signs of toxicity, principally dullness and lassitude, may be produced by overdosage of the drug. Symptoms appeared half to two hours after dosing and disappeared within 24 hours. Twice the therapeutic dose may cause death from respiratory depression. No effective antidote to the drug is known. When given subcutaneously methyridine may cause local pain, and swelling; in the absence of infection these swellings will disappear without abscess formation or ulceration. These reactions are diminished by dividing the dose and giving no more than 20 ml. at one injection site.

REFERENCES


Scene of Joint Meetings

A combined meeting of the Canadian Veterinary Medical Association and the Ontario Veterinary College Centennial celebrations will be held in Guelph, Ontario, on July 15, 16, 17, 18, 1962. Plans have been made for an excellent scientific and social program. Many of the 5,976 graduates of the Ontario Veterinary College will be returning for the celebrations. Write Dr. N. A. Fish, Ontario Veterinary College, Guelph, Ontario, for reservations.
Abstracts

Homologous Transplantation of Canine Neoplasms

Sixty-seven implants prepared from canine neoplasms were implanted into 48 dogs. Two factors, facilitating the growth of the transplants, were considered in this study: treating the recipients with corticosteroids and with total body irradiation. Two corticosteroids were used: cortisone in a dose of 25 mg, daily to 500-Gm. pups, and prednisolone in doses of 5 and 10 mg. daily or 20 mg. every other day to weanling pups. Thirty-one dogs were irradiated with 170 to 600 r.

In 5 dogs, there was successful growth of the transplant. They were all irradiated, 1 dog with 465, 1 with 500, and 3 with 600 r. In addition, 2 dogs were treated with 10 mg. of prednisolone daily and 1 with 10 mg. of prednisolone every other day. The successfully transplanted tumors were an osteosarcoma, a mixed mammary tumor, and an ovarian adenocarcinoma. The histologic characteristics of the transplanted tumor in the subcutis of the recipients were indistinguishable from those of the donor's tumor.

It can be concluded that depression of the reticuloendothelial system by adrenocortical hormone and the total body irradiation were necessary for the successful growth of the canine transplants thus far attempted. Adrenocorticosteroid treatment alone and total body irradiation in doses less than 465 r were insufficient to permit growth of the transplants, but in combination some degree of success was achieved. The most efficient method appeared to be high-dosage radiation at the 465 to 600 r range.


The Pathogenesis of Rabies

This is a report on studies of the method of invasion of rabies virus on the central nervous system which causes the irreversible lesions that makes this disease so serious.

Mice were infected, some intramuscularly, with a fixed strain of virus and others intracerebrally with street virus. Mice were then sacrificed at varying intervals and the virus content of infected organs estimated.

It was found that during incubation there was an interval in which virus was not demonstrable in either brain or muscle. After this interval and until death the virus concentration was low in muscle tissue, whereas it increased quickly within the C.N.S. and soon reached titres of 10 LD50. Moreover, the virus was demonstrable in muscular tissue only after having multiplied and reached titres higher than 100LD50 in the C.N.S. No viraemia was demonstrated. It was concluded that the virus does not multiply in muscular tissue and that its presence in skeletal muscles in the later stages of incubation is the consequence of its multiplication in the C.N.S. The following observations were cited in support of the neural transference theory:

1) The absence of viraemia.
2) The short incubation period when inoculation was into muscles near the C.N.S. rather than those at a distance.
3) The finding of virus in the spinal cord earlier than in the brain following intra-muscular injection into one hind leg.
4) The presence of virus in the peripheral nerves.


Hemodynamic Responses Following Reserpine Feeding to Turkeys

The authors state that an association apparently exists between increased blood pressure and aortic rupture in broad-breasted bronze turkeys. An experiment was therefore prepared to study the hemodynamic pattern of the turkey following oral administration of reserpine (a drug having hypotensive as well as tranquilizing properties). Reserpine was used in an attempt to minimize stress and reduce hypertension, thus affording protection against aortic rupture.

At levels of 0.1 ppm and 0.3 ppm in the
ration, reserpine increased weight gains and reduced blood pressure. Levels above 0.3 ppm reduced blood pressure but were approaching toxicity as shown by lowered weight gains.

No noticeable effects of tranquilization were observed. Circulatory effects were a gradual, moderate drop in blood pressure and heart rate. These effects were most pronounced in males approaching sexual maturity. Hemodynamic responses were more pronounced during longer feeding trials as the blood pressure of untreated lots increased phenomenally with age.

It was felt that reserpine as a low level feed additive may be beneficial in increasing feed conversion, reducing stress and blood pressure sufficient to protect against aortic rupture.


Urethral Occlusion in Lambs on Feed Containing Stilbestrol

This article is a report on the occurrence of urethral occlusion in lambs in a commercial feedlot which were given feed containing stilbestrol at the rate of 0.5 mg per pound. Feed was fed in a self-feeder and the lambs consumed about 4 lb. per lamb per day obtaining an average dose of 2 mg stilbestrol per day. After 4 weeks on feed clinical signs of retention of urine appeared in the form of “water balls”. No evidence of calculi was seen at autopsy. Urethral occlusions found were due to plugs of precipitated mucoprotein.

The Seminal vesicles and bulbo-urethral glands were enlarged but histological examination showed no marked metaplasia. The authors suggest that stilbestrol in the feed was a major factor in the development of urethral occlusion. It was presumed that the affected lambs consumed more than 2 mg per day as the method of feeding allowed greedy lambs to eat as much as they wanted.


The Use of Oxytetracycline in the Prevention of Neonatal Scouring in Piglets

Neonatal scouring and deaths in young piglets due to Escherichia coli were a major problem in the authors' practice when it was decided to try the effect of injecting the sow at the time of parturition with 1 gm of oxytetracycline. Half the sows on one farm were treated and half left untreated. Prior to the start of the trial there had been severe losses due to neonatal scouring and septicaemia caused by E. coli. Deaths due to E. coli infection were significantly reduced in piglets from the infected group, 0.88 per cent in the treated group as opposed to 18.29 per cent in the untreated group. Unfortunately once it appeared that the treatment was effective the owner of the pigs insisted that all his sows should be treated so that the experiment was not as well controlled later in the trial. There were no losses attributable to E. coli in the group that were all treated. The authors conclude that this method offers a useful, practical procedure for the control of this condition in piglets.


Birds and the Spread of Disease

Between 1956 and 1960, workers in the Nile Valley captured and examined 8,379 birds of many species migrating from Europe to Africa or from Africa to Europe along this well defined migration route. Of these 7,381 harboured ticks, especially Haemaphysalis punctata the vector of Rickettsia conorii the causative organism of tick typhus or boutonneuse fever which is widespread throughout Africa and found in Southern Europe. Two other species of ticks found, H. marginatum marginatum and H. marginatum, are associated with Crimean haemorrhagic fever, Q fever, tularemia, tick typhus and brucellosis as well as organisms pathogenic to domestic animals. The authors state that, though limited, these studies serve to show the fundamental role migrating birds may play in the dissemination of tick-borne virus diseases.