DMSO: An alternative perspective

THE MEDICINAL PROPERTIES of the solvent dimethyl sulphoxide (DMSO) were first examined in the early 1960s. At that time reports suggested that it had considerable potential as a therapeutic agent in musculoskeletal disorders and in a range of other conditions. Additionally, it was recognised that its ability to penetrate the epidermis of skin or mucous membrane, coupled with its use as a water miscible solvent, greatly enhanced the absorption of many drugs for which DMSO acted as a carrier (Jacob, Bischel and Herschler 1964). Although these early reports provoked great interest and some enthusiastic application of this ability to penetrate the epidermis of skin or mucous conditions. Additionally, it was recognised that its typical use is as a carrier, particularly for the antiviral agent idoxuridine. It is in this context that it received its only reference in the fifth edition of Clinical Pharmacology (Laurence and Bennett 1980). Its use in the treatment of renal amyloidosis is also documented. The British National Formulary (Anon 1984) mentions its use for the symptomatic relief of interstitial cystitis by direct instillation into the bladder. After 20 years of use, apart from these indications, it appears to have received little official recognition.

Recognised British reference sources give little information on its potential uses. Martindales Extra Pharmacopoeia (Martindale 28th edn, 1982) mentions its various pharmacological properties and states that its principal use is as a carrier, particularly for the antiviral agent idoxuridine. It is in this context that it receives its only reference in the fifth edition of Clinical Pharmacology (Laurence and Bennett 1980). Its use in the treatment of renal amyloidosis is also documented. The British National Formulary (Anon 1984) mentions its use for the symptomatic relief of interstitial cystitis by direct instillation into the bladder. After 20 years of use, apart from these indications, it appears to have received little official recognition.

The review by Hillidge (1985) suggests a variety of important and, in some cases, potentially life-saving therapeutic applications in man and animals, and indicates a wide range of actions and uses in equine medicine. Although the toxic effects of DMSO are well-known, they are not, as noted by Hillidge, of such severity as to prohibit its clinical use.

We seem to face something of a paradox. Is DMSO, as Hillidge suggests, a drug whose full potential in equine medicine has yet to be established, or is it, as its history tends to suggest, a compound which has failed to establish itself as a reliable and widely used therapeutic agent. Failures are less often reported than successes so it may not be surprising that most of the reports in the literature give support to its use and speculate upon its beneficial mode of action.

Because it is a well-known chemical compound, and most of its biological actions have already been described, it is probably not of great interest to major pharmaceutical companies who may not be able to cover their investment with commercially useful patents. Nonetheless it is still not clear why DMSO has not made a greater impact in veterinary and human medicine. Further reports of its clinical evaluation are awaited with interest; it may be an appropriate time to hold a symposium on its actions and uses in equine medicine to provide a forum in which its real potential can be assessed.

J. SANFORD
Wyeth Laboratories
Maidenhead
Berkshire

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Infectious diarrhoea in foals

DIARRHOEA IS PROBABLY the most frequent clinical abnormality of young foals and up to 80 per cent experience at least one episode in the first six months of life (Urquhart 1981). The majority of episodes are mild, transient and not caused by infectious agents. The most common of these syndromes is 'foal heat' diarrhoea, the cause of which is unclear but may be associated with hormone levels in the mares' milk.

Infectious diarrhoeas in foals are often mild, but may be life-threatening and cause significant economic loss, yet at present there is no prophylactic treatment available. This state of affairs exists partly because so many different organisms have been isolated from foals with diarrhoea that their significance as aetiological agents is often unclear.

Infectious diarrhoea may be caused by viruses, bacteria, fungi, protozoa or helminth parasites, but the first two of these are probably the most important. The major enteric viral pathogen of the young of many species is rotavirus (Cilli and Castrucci 1981) and an increasing number of reports, worldwide, suggest that this may be true also in foals. Clinically, rotavirus infection may be mild to severe, the more severe disease occurring in younger foals. About 20 per cent of the
total incidence are affected severely. Of these, up to 30 per cent may die. Two serotypes of equine rotavirus have been described so far (Hoshino et al 1983) but, in view of the numerous rotavirus serotypes in man and cattle, more may be discovered.

Two other groups of viruses have been detected in foals with diarrhoea, coronaviruses and adenoviruses. There are few reports to date of enteric infection of foals with coronaviruses (Bass and Sharpee 1975; Durham, Stevenson and Farquharson 1979) and the importance of these agents as a significant cause of foal diarrhoea has yet to be determined. In other species, however, coronaviruses are often the second most common viral agent causing enteritis. Adenoviruses are common respiratory pathogens. Equine adenovirus type 1 is no exception, but up to 50 per cent of affected foals may also develop diarrhoea (McChesney, England and Rich 1973). A second serotype, equine adenovirus type 2 (Studdert and Blackney 1982) has been isolated from the stools of diarrhoeic foals and may represent a true enteric pathogen. This virus was shown to be widespread in Australian horses as judged by serological surveys but its significance in the UK is unknown. There are no reports of other viruses associated with foal diarrhoea but it would not be surprising if some do exist and have yet to be discovered.

*Escherichia coli* is perhaps the most important bacterial agent of diarrhoea in the young of many species, but its importance in foals is not clear and specific enteropathogenic *E. coli* serotypes have not been recognised. Indeed, Tzipori, Withers and Hayes (1984) have recently demonstrated that even though equine intestinal brush borders possess receptors for the K88 antigen, which is characteristic of strains of *E. coli* enteropathogenic in other species, strains bearing this antigen were inefficient at colonising the gut of colostrum-deprived foals. *Salmonella*, by contrast, are clearly recognised as enteric pathogens of foal diarrhoea. However, the incidence of diarrhoea caused by *salmonella* infection in foals is low compared to other species, *Salmonella typhimurium* being the most frequently implicated. It has been suggested (Morse, Duncan, Page and Fessler 1976; Gibbons 1980) that *salmonella* induce diarrhoea only in ‘stressed’ individuals.

In recent years, *Campylobacter* species have gained prominence as enteric pathogens in many species and there has been a report of the isolation of *Campylobacter jejuni* subspecies *coli* from five foals with diarrhoea (Atherton and Ricketts 1980). All of the animals showed signs of colic and two were found to have perforated ulcers on post mortem examination. Since Becht, Hendricks and Merritt (1984) reported that up to 30 per cent of foal deaths were associated with gastric and duodenal ulceration and a similar percentage with diarrhoea, the importance of *Campylobacter* species involvement must not be underestimated.

Toxigenic strains of *Clostridium difficile* produce enteritis in several species, particularly in individuals undergoing broad spectrum antibiotic therapy (Gilligan, McCarthy and Genta 1981) but have not so far been implicated in foal enteritis. However, *C difficile* toxin has been detected in horses of unspecified age both with and without acute diarrhoea (Ehrlich et al 1984). *Clostridium perfringens*, on the other hand, has been reported to be an occasional cause of necrotising enteritis in foals (Sims, Tzipori, Hazard and Carroll 1985). Other bacteria, such as *Corynebacterium equi*, which are considered to be part of the normal gut flora have, on occasions, been implicated in foal diarrhoea. However, the importance of such organisms as aetiological agents of foal diarrhoea remains to be clarified.

Apart from infections caused by a single pathogen, a significant proportion of cases of diarrhoea in other species are associated with mixed infections, eg, with two viruses or a virus and a bacterium. Often, such infections are more severe than those caused by each pathogen individually (Tzipori, Makin, Smith and Krautli 1982). A mixed infection of foals with rotavirus and *S typhimurium* (Eugster, Whitford and Mehr 1978) has been described and it is likely that others will be found.

What can be done about infectious diarrhoea in foals? As indicated, a wide variety of potential pathogens has been isolated from foals with diarrhoea but because the reports are based on isolated outbreaks our knowledge of the overall importance of each pathogen is limited. Moreover, the role that other factors, in particular 'stress', might play in determining whether or not an animal develops clinical diarrhoea when infected with a particular pathogen is unclear. It is impractical and not really necessary to introduce prophylactic measures against all the potential pathogens and a large scale systematic survey to determine the most important pathogens should, therefore, be carried out. If such a survey was combined with a carefully compiled questionnaire, the results might suggest measures, such as a change in management practices, that would reduce the incidence of clinical disease. However, if certain infectious agents appear to be the primary problem, once the chief culprits have been identified, it should be possible to begin development of a vaccine. But that is another story.

D. A. Harbour
Department of Veterinary Medicine
Langford House
Langford
Bristol BS18 7DU

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A report on the feasibility of a collaborative study of infectious foal diarrhoea has been compiled under the auspices of the BEVA Trust Equine Research Liaison Committee. This report may be obtained from the Chairman of the Committee, at the EVJ Editorial Office address, at a cost of £2.00 (within Europe) or £4.00 (outside Europe) including mailing.