SHORT COMMUNICATION

KERATOCONJUNCTIVITIS SICCA IN DOGS ASSOCIATED WITH SULPHONAMIDE ADMINISTRATION

D. H. SLATTER*and J. R. BLOGG†

SUMMARY: This report describes the clinical characteristics of 14 cases of sulphonamide-induced keratoconjuctivitis sicca in dogs. Two drugs, sulphadiazine and salicylazosulphapyridine, were associated with the disease. It is recommended that Schirmer Tear Test be performed regularly when sulphonamides are administered long term to dogs. The hypothesis that a nitrogen-containing pyridine ring is responsible for the lacrimotoxic effect is advanced.

The purpose of this report is to draw attention to the relationship between the administration of certain drugs and the occurrence of keratoconjuctivitis sicca (KCS).

In recent years, phenazopyridine and sulphadiazine have been proven to cause KCS in dogs (Todenhofer 1969; Slatter and Bryan 1973; Bryan and Slatter 1973; Slatter and Davis 1974) or have been associated clinically with the presence of KCS (Aguirre 1973). Recently a similar association has been noticed between KCS and the administration of these same drugs in Australia. In addition salicylazosulphapyridine, a sulphonamide not previously associated with KCS (Lorenz 1975) has also been associated with KCS. Circumstantial evidence of a causal relationship between administration of the drugs and the presence of KCS in this study include:

Occurrence of KCS after chronic administration of the drug;

Presence of the disease during drug therapy in dogs younger than would normally be expected to have spontaneous KCS; and

Increase in tear production as measured by the Schirmer Tear Test and clinical improvement after withdrawal of the drug.

Details of referred clinical cases are shown in Table 1. In all except case 1 which was affected with histiocytic ulcerative colitis, the drug was withdrawn after the initial examination and treatment for KCS instituted. In case 1, reduction in dose rate of the drug in question caused an increase in Schirmer Tear Test readings but signs of colitis returned. In all other patients except case 10, cessation of drug administration resulted in return of a discernible precorneal tear film and resolution of the clinical signs of KCS. The period from withdrawal of the drug to resolution varied from less than a week to over a month.

The widespread use of sulphadiazine as a nonspecific 'geriatric stimulant' in aged dogs is of special concern as dogs in this age group are more likely to have lower Schirmer Tear Test readings than normal and be more susceptible to induction of KCS by drug-induced damage to lacrimal and nictitans glands. In cases 3 and 4 (both 6 years of age), clinical signs of decreased tear production occurred within 3 days of the commencement of drug administration indicating a lower functional reserve of capacity to produce lacrimal fluid or a greater susceptibility to the lacrimotoxic effects of the drug.

Previous studies have shown that canine lacrimal and nictitans glands with drug-induced damage do show some repair and regeneration after withdrawal of the toxic agent (Slatter 1973). Residual damage remains, however, and continued administration of the drug would be expected to result in cumulative derangements within the glands. Severe cumulative damage may account for the failure of one dog (case 10) to show increased tear production after withdrawal of the drug.

The original report (Todenhofer 1969) of association between KCS and the administration of this drug in the same product in Germany does not appear to have been followed by obvious warnings of this association in Australia by the manufacturer. Other medications for example Tribrissen®‡ Salazopyrin®§ which contain drugs associated with KCS in dogs should carry similar warnings. Chronic administration of sulphonamides to aged dogs is ill-advised when no specifically diagnosed disease is being treated. If no other drug is suitable and sulphonamides are selected for chronic administration, routine Schirmer Tear Tests should be performed.

Drugs which have so far been associated with

*Murdoch University Veterinary Hospital, School of Veterinary Studies, Murdoch, Western Australia, 6153.
†Animal Eye Clinic, 547 Dandenong Road, Armadale, Victoria, 3143.

‡Tribrissen ® — Burroughs Wellcome & Co. (Aust) Ltd, Kewdale, Western Australia
§Salazoprin ® — Pharmacia Pty. Ltd, Nth Ryde, New South Wales

TABLE 1

Characteristics of Dogs Affected with Keratoconjunctivitis Sicca

Drug	Case No.	Period of Drug Administration Prior to Exam.	Breed	Age (years)	Sex	Initial Schirmer Tear Test Readings mm/minute		Subsequent Schirmer Tear Test Readings mm/minute (Interval from First Examination)	
						OS	OD	OS	OD
*Salicylazo-sulphapyridine	1	6 months	Boxer	4	F	0	0	NA	NA
†Sulphadiazine	2	3 months	Australian Terrier	6	F	0	0	13 (4 weeks)	15 (4 weeks)
	3	3 days	Cairn Terrier	6	M	0	0	5 (2 weeks)	5 (2 weeks)
	4	3 days	Standard Poodle	6	F	NR	NR	NR	NR
‡Sulphadiazine	5	1 year	Miniature Poodle	10	F/S	10	4	14 (12 weeks)	14 (12 weeks)
	6	3 months	English Cocker Spaniel	4	M	NR	NR	NR	NR
	7	6 months	Australian Terrier	8.5	M	0	0	14 (4 weeks)	14 (4 weeks)
	8	4 months	Australian Terrier	7	M	NR	NR	NR	NR
	9	5 months	Australian Terrier	13.5	M	NR	NR	NR	NR
	10	6 months	Corgi	4	M	1	4	0 (16 weeks)	0 (16 weeks)
	11	5 months	Corgi	7.5	F	NR	NR	NR	NR
	12	4 months	Corgi	4.5	F	NR	NR	NR	NR
	13	7.5 months	Corgi/Pug	10	M	NR	NR	NR	NR
	14	3 months	Crossbred	4	M	NR	NR	NR	NR

* *Salazopyrin®* — *Pharmacia Pty. Ltd., North Ryde, New South Wales.*
† *Tribrissen®* — *Burroughs Wellcome & Co. (Aust) Ltd., Kewdale, Western Australia.*
‡ *Debenal®* — *Bayer Pharmaceutical Co., Botany, New South Wales.*

Abbreviations

OS : Left eye
OD : Right eye
NA : Not applicable as drug not withdrawn
NR : Not recorded

KCS in dogs include — sulphadiazine, phenazopyridine, and salicylazosulphapyridine. The formula of each is shown (Figure 1). Sulphadiazine and salicylazosulphaypyridine in common with most sulphonomides have nitrogen-containing rings attached to the sulphonamide nucleus. Phenazopyridine also has a nitrogen containing ring in its structure. It is hypothesied that the pyrimidine and pyridine rings are associated with the toxic action of these drugs on canine lacrimal and nictitans glands.

The authors thank Drs J. Anderson, R. Bradley, E. Groom, R. Hemming, H. Jones. A. Pearson and W. Porges for referring some of the affected cases and Drs D. Baggott and M. Nairn for valuable counsel.

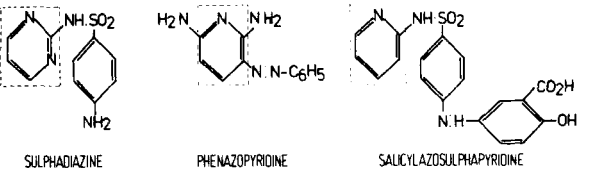

Figure 1. Formulae of sulphadiazine, phenazopyridine and salicylazosulphapyridine

References

Aquirre, G.D. (1973) — *J. Am vet. med. Ass.* **162:** 8.
Bryan, G.M. and Slatter, D.H. (1973) — *Arch. Ophthal.* **90:** 310.

Lorenz, M.D. (1975) — in *Textbook of Veterinary Internal Medicine* Vol 2, Ed. S. Ettinger, W.B. Saunders Co., Philadelphia.
Slatter, D.H. and Bryan, G.M. (1973) — *J. Am. vet. med. Ass.* **162: 426.**
Slatter, D.H. (1973) — J. small Anim. Pract. **14:** 749.
Slatter, D.H. and Davis, W.C. (1974) — *Arch. Ophthal.* **91:** 484
Todenhofer, H. (1969) — *Deut. tier. Wchnschr.* **76:** 14

(Received for publication 24 October 1977)

BOOK REVIEW

THE BIG BANG

This is how the Universe is supposed to have begun — and the eradication of Bang's Disease — Brucellosis — has also begun in a big way!

The Introduction to a very useful book* begins with, 'The early stages of any large-scale brucellosis eradication scheme in a cattle population will be pre-occupied with the hard work of setting-up, de-bugging, and refining routine testing and administrative procedures. As the scheme progresses, the routine procedures come to be carried out with practised ease and the bulk of untested herds are converted to a tested, accredited status. With the bulk of herds accredited, a once familiar, endemic, and lightly regarded disease will take on the entirely different and more sinister aspect of an exotic disease'.

'It is difficult to pinpoint a particular turning point at which we will have to regard brucellosis as an exotic disease. But as the scheme continues there is no doubt that the role of the state veterinarian will turn from the routine procedures to the problem herds; to recognising the herds showing persistent reactivity or continuing abortions; to explaining break-downs, controlling movements, and recognising, isolation and removing sources of infection; to reacting to and limiting abortion storms; and to watching for the first signs of a highly infectious disease that has become an exotic threat'.

This introduction sets the scene for the book, which is a quite remarkable compendium in brief. It emanates from the Ministry of Agriculture and Fisheries in New Zealand and presents a summary of the disease and its control and eradication. It presents a comprehensive cover of the relevant literature. Open it at almost any page and on the right side is an account, succinct but adequate, of some aspect or phase of the disease, while on the opposite page are the relevant literature references.

It opens with a one-page historical perspective with dates from 1861 when Marston provided the first accurate description of brucellosis as a separate disease entity (A disease syndrome consistent with brucellosis in man was mentioned by Hippocrates around 450 BC) up to 1938-40 when McEwen and Priestley developed strain 45/20 from passage through guinea pigs.

The taxonomy of the genus Brucella is described, with differential cultural characters for each of the six species, followed by notes on nine biotypes of *Br. abortus*. A section on brucellosis in cattle deals with economic loss, pathogenesis, pathology in the cow and the bull, epidemiology (with a tremendous summarising of information), the problem herd, and then several tables and diagrams which present the epidemiology in a flow-diagram form. The section on diagnosis has notes on specimens for examination, examination of direct smears, culture, guinea pig inoculation, biotyping, bovine immunoglobulins, anti-brucellae immunoglobulins, serological tests, milk tests, serological cross-reactions and non-specific anamnestic response, leptospirosis vaccination and brucellosis reactors, *Yersinia enterocolitica* cross reactivity.

Vaccination deals with Strain 19 in some detail, and Strain 45/20 vaccine.

Brucellosis in hosts other than cattle has sections on the disease in man: Brucella species transmissible to man, virulence, route of infection, risks from carcasses, occupational incidence, age susceptibility, symptoms, diagnosis, treatment, vaccination, prevention. Similarly, the disease is described in pigs, goats, sheep, horses, dogs, cats, hares, reindeer, deer, poultry, rodents, arthropods, camels, yaks, buffalo, mink, foxes, and wild animals.

Section 4 deals with bovine brucellosis: state control programs, firstly for Australia, then alphabetically, Belgium, Bulgaria, Cyprus, Czechoslovakia, Denmark, Finland, French West Africa, Iran, Ireland (Eire), Italy, Kenya, New Zealand, Nigeria, Northern Ireland, Norway, Papua-New Guinea, Portugal, Sudan, Sweden, Switzerland, Taiwan, Thailand, Tunisia, Turkey, United Kingdom, United States of America (with a table guide to federal requirements for the interstate movement of cattle with respect to brucellosis), Uruguay, West Germany, Yugoslavia.

Appendices cover abortion investigations in New Zealand, foetal development, parturition and abortion.

Every veterinarian concerned with brucellosis will need this book and it will be a boon for undergraduates, and a very useful source of references for libraries. Altogether it is the kind of admirable compilation one has come to expect from the Ministry of Agriculture in New Zealand; it will serve great purpose.

H. McL. Gordon

* *Brucellosis; A Veterinarian's Guide to the Literature.* R.E.W. Elliott and Kathryn H. Christiansen, editors. Ministry of Agriculture and Fisheries, P.O. Box 2298, Wellington, New Zealand. 1977. pp 148.