THE HISTORY OF THE USE OF GLYOXYLIDE IN DAIRY ANIMAL EXPERIMENTATION

In presenting data on the experimental use of Glyoxylide in the treatment of bovine diseases, I shall give a brief history of the work from the beginning.

Dr. D. H. Arnott, H. D., a general practioner in the City of London, Ontario, Canada, for almost fifty years, has long been active in the advancement of the Koch Therapy. I doubt whether there is another individual who has contributed as much to advancement of the Therapy, except Dr. Koch, himself. Dr. Arnott's work brought the first official recognition of Koch Therapy in North America. It was in 1940 Dr. Arnott used Glyoxylide in treating a patient suffering from Undulant Fever. His patient responded so quickly and. completely that he was prompted to investigate the possibilities for Glyoxylide in the treatment of Bang's Disease, or contagions abortion, in dairy animals.

For several years Dr. Arnott and T. S. Campbell, both veterinarians, carried on an investigation in the Province of Ontario, near London, using Glyoxylide in the treatment of mastitis, acute and chronic and Bang's Disease. The results of their work are recorded in five pamphlets printed by Dr. Arnott. They Are:

1. "*The Successful Treatment of Acute Infectious Mastitis in Cows*."

2. "*Clinical Notes Which Illustrate the Successful Treatment of Acute Mastitis in Cows,*" presented before the Annual Meeting of the Middlesex Holstien Association in London, January 20, 1943.

3. "*The Koch Treatment Used for the Control of Mastitis in Cows; Prevention of and Recovery from Acute and Chronic Mastitis Promoted through the use of this Method*."

4. "*The Cure and Prevention of Mastitis and Contagious Abortion. New Light Derived from Prompt Successful Results Obtained Through the Use of The Koch Treatment*."

5. "*Good Progress Against Bang's Disease*."

Ontario Officials of the Department of Agriculture were silent to appeals made by Dairymen for an investigation of the Koch Therapy.

Dairymen in the Province of British Columbia were receiving Treatments during 1943 and early 1944 through Dr. Arnott's agent, Mr. W. A. Gooder of Vancouver. Reports of successful treatment of Mastitis and other seriously destructive

diseases of Dairy Animals in British Columbia were being placed before the then Minister of Agriculture, with the request that the Department investigate the merits of this new method of Treatment. .

Dr. K. C. Mc Donald, The Minister, realizing the great need, of the Dairymen, wrote Dr. Arnott for information, and the doctor complied by mailing all available literature, together with a full statement, revealing opposition to this Therapy and the morbid attitude of Ontario Officials.

Dr. Mc Donald, after careful study of the Literature, decided that an entirely new approach to the study and treatment of bovine diseases had been disclosed and invited Dr. Arnott to confer with him in British Columbia.

Two meetings were scheduled for members of his staff, together with Representatives of University of British Columbia, The Breeds Associations, The Veterinary Association, Dairymen and. others. During the second meeting it was agreed that an investigation of the merits of Glyoxylide be conducted, starting with mastitis and sterility and it was understood that all pathological conditions revealed during the examination, or treatment of animals selected for investigation, would be recorded and progress accurately noted.

The Department of Agriculture reported highly successful results were obtained in the treatment of both mastitis and sterility and also made note of fifteen pathological conditions that responded equally well to one administration of Glyoxylide. Full information is available from reprints of the *Annual Report* for 1944 — 45 — 46 — 47 and 49, which can be obtained here at the Convention, through the courtesy of Koch Cattle Shots, Inc.

It was in 1946 I learned that Glyoxylide had been used successfully in the treatment of mastitis. The information was contained in a letter received from the late Dr. Willard H. Dow, then President of Dow Chemical Company of Midland, Michigan. **Dr. Dow stated, "This type of treatment has been used with outstanding success in the case of cattle and other animals. The record of mastitis cures is of the order of better than 90 percent."** Located, as we are, in the very heart of the best dairy in section in Michigan, and because the prosperity of local business and professional men are largely dependent upon farm income, directly or indirectly, we are always seeking means by which we can help to increase farm income.

A brief investigation revealed the serious losses farmers were experiencing from mastitis, sterility and other diseases. Dr. Koch was contacted and. agreed to furnish Treatments, gratis, to farmers in the area for investigational purposes and a score or more farmers made use of Glyoxylide during the next few months. The results were good, and in some instances, startlingly so.

When more farmers became interested, the Imlay City Chamber of Commerce and Imlay City Rotary Club called a public meeting of all interested parties and. Dr. D. H. Arnott was asked to address the meeting, which was held in the Imlay City High School Gymnasium, March 9, 1948. About 300 farmers, business and professional men were present. The meeting was lively from the start. Dr. Arnott's address was presented in such an interesting way that the audience was reluctant to permit the doctor to conclude his address, even after more than one hour and thirty minutes had passed. An additional hour was consumed in answering questions put to him from the floor.

At this meeting the dairymen appointed a committee composed of five farmers and two businessmen, with myself as chairman (L. B. Thatcher), which was later called the KOCH THERAPY EVALUATION COMMITTEE.

The Committee agreed that Michigan State College officials in East Lansing, should be approached and their cooperation solicited. This was done with the Committee meeting the Deputy Commissioner of Agriculture, Dr. Clark, the state veterinarian, members of the Agricultural Committee of the House of Representatives and several members of the Senate. These representatives were in agreement that our cause was worthy of their support and agreed to give us financial help through legislative appropriation, if such was desired. Dr. Clark said the matter was one that should be presented to the Research Director at Michigan State College and he proceeded to make an appointment for our Committee for that very afternoon.

The Committee met with Mr. Gardner, Research Director, and Dr. Claude S. Bryan, Dean of the College of Veterinarian Medicine; Bryan being the one who would conduct all research, if any was forth-coming. Dr. Bryan evidenced great interest and asked for all of the British Columbian literature currently in our possession. We assumed he had no knowledge of the British Columbia reports, but afterward found the college library had copies of all the literature and so there was little doubt that Dr. Bryan was well versed on the subject long before our meeting.

A second meeting was scheduled for our Committee and Dr. Arnott to meet with Dr. Bryan and members of his staff, for the purpose of setting up a demonstration or evaluation program at Michigan State College. The officials were very cordial but the tenor of the meeting was such that we readily realized they were diplomatically avoiding any program, which would truthfully and properly evaluate Glyoxylide' s efficiency. Dr. Bryan stated that for him it was almost impossible to diagnose mastitis and he had 'no expert' who could do the simple test for Acetonemia, which is a condition for which Glyoxylide is a specific

Treatment, and a condition that responds quickly and completely to the Koch Treatment, and for which there is no other specific treatment.

The Committee left East Lansing somewhat bewildered by the official action, but jointly decided to initiate research and evaluations, if sufficient support could be found. The Imlay City Chamber of Commerce offered financial support, as did Dr. Willard H. Dow. Dr. Arnott offered his help and Dr. Koch agreed to provide the needed Glyoxylide and to also reimburse the veterinarians for their services.

Farmers in the area offered herds and the work was started in April, 1948 with the first animals being treated May 8th, and the second May 16, 1948. Before animals were treated, complete physical examination was made, also blood samples were drawn and milk specimen taken from each quarter. Laboratory tests were made of both blood and milk samples. Animals were checked monthly for a period of thirteen months.

The Committee followed a plan similar to the one used in British Columbia. We hoped to demonstrate Glyoxylide's beneficial effects in the treatment of mastitis, especially fibrosis, since this condition causes the premature slaughter of a very important percentage of our best dairy animals annually. It is generally agreed, by veterinary authorities, that fibrosis does not respond to know udder infusion treatments and therefore recommend that animals thus affected be slaughtered. The British Columbia Department of Agriculture had reported in l944—45, "a consistent result was a definite softening of the udder after Treatment. The disappearance of fibrous tissue was noticed in a considerable number of cases! In no case was any other treatment used."

Our Committee therefore decided upon this one demonstration as being of utmost importance to dairymen. The Committee also undertook to demonstrate Glyoxylide's value in the treatment of sterility and Acetonemia (Ketosis) and to record and report all other pathological conditions observed during the demonstration, which responded to Glyoxylide.

In addition to the two original herds selected for treatment, an additional seven hundred dairy animals were treated during the demonstration from May 1948 through June 1949. Also, over two thousand dairy animals have been treated since the Christian Medical Research League began in December 1948; research is currently being conducted in sixteen states in addition to Michigan. Several State Colleges have indicated an interest in Glyoxylide and some are following our work closely.

Our research and evaluations to date have provided a wealth of sound information. We have been able to confirm and corroborate the outstanding

clinical results reported by: Dr. Arnott, officials of the Department of Agriculture of British Columbia, along with published reports by W. Bruce Richardson, Dr. S. N. Wood B.S.A., D.V.M., Professor and Animal Pathologist at the University of British Columbia, Dr. G. P. R. Barton, B.V.Sc., of Chilliwack and others. We are pleased to report that our work in the treatment of fibrosis revealed 85.5% recovery in the Koning herd of forty-five Jerseys of which twenty-nine cows were affected and of the twenty-nine, fourteen of the most severe cases were treated, leaving the others as controls. Within twenty-eight weeks, 85.5% of the treated animals were clear of fibrosis. The extent of fibrosis was classified as slight, moderate, marked and severe, or 25, 50, 75 and 100%. The method used to provide easy comparison between treated and control animals, was the number of teats in each class multiplied by the percentage in each classification and then the totals were added. For example: ten teats in the 25% class equals 250% and two teats in the 50% class equals 100%, two teats in the 75% class equals 150%, making a grand total of 500%.

Koning Herd
Fibrosis, 85.5% Recovery,
Average number of Treatments 1.35

	1948							1949	
	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.
Treated	1250	800	325	550	400	374	nr	300	200
Control	725	975	750	725	800	625	nr	950	925
	525	175	425	175	400	250	nr	650	725

Milk production in this herd increased, subsequent to the Koch Treatment, from 11 to 14 cans per day or from 880 lbs. to 1120 lbs. This was the highest production in history of the herd had been 11 cans.

In the Max Graybiel herd of eighteen Holstein animals, the fibrosis recovery rate was 64.5% within twenty-eight weeks. The average number of Treatments used was 1.8 per animal.

The experience gained from this demonstration indicates that more liberal use of Glyoxylide can bring about a higher recovery percentage and that recovery will take place more quickly.

	1948 May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	1949 Jan.
Treated	1300	900	875	925	1025	575	525	nr	450
Controls	375	400	275	600	400	275	225	nr	325
	-925	500	600	325	625	300	300	nr	-125

In contrast to the Koning herd, with an average of 1.35 Treatments used per animal and a recovery percentage of 85.5%, The Graybiel herd recovery percentage was 64.5%, and the number of Treatments averaged 1.8% per animal. It must be remembered that the Koning herd was considered an average herd with a history of very little serious trouble from mastitis and other diseases, while the Graybiel herd has a history of several years of mastitis in the herd, with veterinary fees averaging about $450.00 annually and with no permanent relief until Glyoxylide was used in May 1948. Since then veterinary bills have averaged less than $50.00 annually, with little or no disease problem. Injuries are now Mr. Graybiel's main reason for veterinary service. Several of the Gabriel cows were to have been sold because of fibrosis. With one exception, all animals are still in the herd and producing satisfactorily. Needless to say, Mr. Gabriel is very well satisfied with the results obtained from Glyoxylide.

Records obtained in the Treatment of more than 1500 dairy animals affected with chronic or acute mastitis, show that Glyoxylide is over 80% effective.

Acute mastitis responds quickly to one injection of Glyoxylide. The pathological trend is completely reversed in many instances within a few hours, with complete recovery anywhere from a few hours to a few days. When response is not immediate a second injection within three days has proven beneficial.

Chronic Mastitis…Good results follow use of one Treatment, but recovery requires a longer period (usually one to four weeks), except where the condition has been chronic for a period of one or more years, or where the underlying damage (scar tissue) is extensive. In this instance recovery may not be complete in less than sixty to ninety days. In such cases, we recommend retreating in seven or twenty-one day intervals until three Treatments have been given. We found this procedure very highly successful. Recovery very definitely can be promoted and sustained by this method. Where tissue changes are necessary, it is doubtful whether much can be gained by repeating the Treatment in less than weekly intervals.

We found Glyoxylide to be a specific treatment for Acetonemia. The number of animals treated for this condition is less than 200, with recovery approximately

94%. Most animals respond within 24 to 48 hours to one injection... others were given two... and some were given three Treatments. On several occasions when an animal was down with a commanding degree of the affection we administered Glyoxylide and glucose. I think it hastened recovery somewhat, however, more work will be needed to determine its worth.

Two hundred or more Bang's positive cows have been treated with Glyoxylide within the past sixteen months, however, we lack complete reports on some of the herds. The following will give an indication of what may be expected:

In treating Bang's positive cows in order to correct sterility and. prevent further abortion one Treatment was used. This method proved successful in Michigan in over 100 Bang's positive animals treated. All cows conceived, there were no abortions... all calves were healthy... as were the cows. Milk production was also very satisfactory.

Where it was considered important to change the blood test from positive to negative, three successive Treatments, at weekly intervals, were recommended and used. Our records are complete on several herds, however the numbers are limited. The picture we now have is very encouraging. In one herd, six cows were treated and five responded, all blood tests becoming negative. Two are still negative and three have been retreated… no test since. In another herd two were treated and both are negative. We have had several instances with only one positive animal in the herd. Three Treatments were administered and in each instance the blood tests were negative. We hope to run tests on several hundred Bang's positive animals within the next year, which will permit more comprehensive conclusions to be drawn and reported upon.

We have used several of the well known udder infusion treatments as well as other forms of medication in conjunction with Glyoxylide in the treatment of mastitis and other pathological conditions, and although this work is very limited, there has been no evidence that any of the drugs used have inhibited Glyoxylide's beneficial action. On the contrary, there is evidence that the combined use of such drugs should be investigated thoroughly. We are currently making plans to continue this investigation.

In addition to mastitis, sterility, Acetonemia and Bang's Disease, Glyoxylide was applied successfully to many pathological conditions... such as, septic conditions associated with retained placenta, difficult labor with possible infection, milk fever relapses, Pneumonia, shipping fever, hoof rot, ring worm, edema of the udder…to mention only a few... Scovers, pink eye, cancer, and other systemic conditions.

We consider a cow cured of mastitis by Glyoxylide when the udder became soft and pliable, the flaky, stringy milk became normal and the causative organism was eliminated from the milk samples as shown by laboratory tests or when the blotter test showed clear. Streptococcus was found present in about ninety percent of the animals before being treated.

We consider the use of the Glyoxylide Treatment in a cow suffering from Acetonemia as being used successfully, when she soon regains her strength and her appetite 'when her milk is again saleable, when her production of saleable milk equals or exceeds in amount that which had been obtained previously, and when the chemical test for Acetone in the urine has proven to be negative.'

In summary...We have drawn the following conclusions from our evaluation and research program:

1. We have been able to confirm and collaborate results reported by Dr. D. H. Arnott and others based on the thorough research done in Canada.

2. We have been able to confirm British Columbia reports of Glyoxylide's efficacy in treatment of fibrosis and have established records indicating the Treatment to be successful up to 85.5%.

3. Our results of recovery in sterility are above the 70% reported in British Columbia.

4. Complete clinical control of Bang's Disease or Contagious Abortion resulted in all animals being treated in Michigan. In many cases where only one Treatment was administered, the blood test changed from positive to negative. A much higher percentage of negative blood changes occurred in animals that were given three consecutive injections at weekly intervals.

5. Glyoxylide was found a specific treatment for Acetonemia (Ketosis) with a very high percent recovery.

6. We have established records of the fact that most acute conditions are quickly controlled by one injection of Glyoxylide and that chronic conditions such as mastitis responds well to frequent injections. We have used weekly injections and find we can maintain and promote recovery by this method. In no case have we found any inhibitory action resulting from repeating the Treatment.

Where tissue changes are necessary in the recovery process, we doubt whether anything can be gained by repeating the dose in less than seven days. In some

acute conditions it appears that Treatment may be repeated in less than seven days with satisfactory results.

These conclusions were drawn from the observations and correlation of the results obtained in treating over three thousand dairy animals with Glyoxylide during the past two years. We do not wish anyone to infer that disappointment has not followed the use of Glyoxylide in the treatment of individual animals, or that all herds responded equally well, but on the whole there has been general satisfaction obtained by those who have used the method of Treatment to cure, control and prevent common seriously destructive diseases of dairy animals.

Twenty-eight projects are now being carried out in 18 states. It will take many more years of extensive research to determine the possibilities for Glyoxylide in the treatment of bovine diseases. Our work to date has provided a pattern for the future. We look to the future with great hope for sound progress.