Enzootic Bovine Leukosis

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SUMMARY

The author emphasizes the significance of enzootic bovine leukosis in Canada. He describes in detail diagnostic methods, various types of the disease and methods of transmission.

Various aspects of the disease in Canada are compared with those in other countries. Prevention and control are discussed in a Canadian context and include the current policies of the Government of Canada in relationship to this disease. The possibility of developing a certification program for herds free of the disease is also discussed. The paper includes incidence in various parts of Canada.

RÉSUMÉ

Leucose bovine enzootique

L'auteur insiste sur la signification de la leucose bovine enzootique, au Canada. Il décrit en détails les méthodes de diagnostic de la maladie, ses diverses formes et ses modes de transmission. Il compare les différents aspects que prend la maladie au Canada, avec ceux qu'elle revêt dans d'autres pays. Il discute aussi de la prévention et du contrôle de la maladie, dans un contexte canadien, en donnant la position actuelle du gouvernement du Canada à l'égard de cette maladie. Il commente également de possibilité de développer un programme de certification des troupeaux exempts de leucose enzootique. L'article donne un aperçu de l'incidence de la maladie, dans les dix provinces du Canada.

Enzootic bovine leukosis (EBL) has been one of the most talked about disease entities in Canada over the past couple of years.

We have been surprised to find that cattle shipped from Canada have reacted to enzootic bovine leukosis when tested in other countries. This was particularly true in cattle tested prior to export using the hematological keys rather than the agar gel-immunodiffusion test. Our industry and the veterinary profession, particularly those in regulatory work or those involved in export certification are becoming increasingly concerned with the potential loss of export markets. The industry is also puzzled that a disease condition that they have not recognized to be a problem in the vast majority of herds is regarded so seriously by a number of the countries to which we export.

This discussion should raise a number of the relevant issues as we consider this disease, its impact and the possibility of applying control or eradication programs. It presents for your consideration many of the factors relevant to this disease and its potential control.

Infection Versus Disease

In discussing the etiology of EBL (Tables I and II), it is important to review briefly one important principle of disease itself. We must recognize a significant difference between an animal harbouring a virus and an animal harbouring a tumour associated with a virus. Some factor other than the virus is necessary for the tumour to appear. It has been widely recognized for many years that virtually all species of animals are infected with viruses that may or may not induce disease in their hosts. It is important, particularly with EBL, to realize that as in all other animals and with most viruses, infection does not mean disease. In fact, disease develops only very rarely in cattle infected with bovine leukosis virus (BLV).

If we are anticipating an eradication program for a particular disease, the above becomes strictly academic because it is generally understood that the eradication of a disease from a given population implies the eradication of the causative agent as well. The control of the disease, on the other hand, can involve the use of many techniques not necessarily involving the removal of the causative agent. Such factors could be vaccination, selection for genetic resistance, drug or antibiotic therapy and management control.

A very basic principle of both disease control and disease eradication programs is that the cost must in the long run at least be less than the disease itself. It is very difficult to support programs that are very costly to an industry and to the general public unless it can be shown that a definite cost: benefit exists.

Sporadic Bovine Leukosis (SBL) (Table II)

The thymic form occurs most com-

TABLE I
DEFINITIONS

Leukemia: A usually fatal disease of the blood-forming tissues, characterized by a marked increase in the number of leukocytes in the blood, together with enlargement and proliferation of lymphoid tissue
Leukosis: A proliferation of leukocyte-forming material
Lymphocytosis: Excess numbers of lymphocytes in the blood. A benign lymphoproliferative response
Lymphoma: Any tumour made up of lymphatic tissue
Lymphosarcoma: A malignant tumour arising in lymphatic tissues from the proliferation of atypical lymphocytes
Enzootic Disease: A disease that is constantly present in a given population or in a particular district or region

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TABLE II
COMPARATIVE FACTORS-EBL/SBL

BOVINE LEUKOSIS	
ENZOOTIC (EBL)	SPORADIC (SBL)
Caused by Virus (BLV)	Cause(s) not known
Leukemia Leukosis Lymphoma Lymphosarcoma	Leukemia (rare) Leukosis Lymphoma Lymphosarcoma
No Clinical Signs (common)	
Persistent Lymphocytosis	Thymic Form Juvenile Form Skin Form
Serology	No serology

monly in calves from one to two years of age. Thymus is primarily involved, but some nodes may also be involved. Clinical signs are primarily enlargement of the thymus of the lower cervical and anterior thoracic area, respiratory distress, loss of weight and decreased appetite.

The juvenile form is most common in calves of three to six months of age. Disease is primarily characterized by generalized bilateral lymphodenopathy, depression and weight loss. Leukemic blood picture is sometimes present and anemia due to bone marrow involvement may be found.

The skin form is very rare, but occurs in cattle one to three years of age. Local skin lesions are seen as neoplastic lymphocytic cells but are rather benign and regression has been observed.

The above conditions happen at random in cattle populations and there is no evidence that they are caused by an infectious etiological agent. Further study is required to establish whether or not some of the leukotic conditions currently classified as EBL should be included with the SBL group.

Virology and Molecular Biology of BLV

The causative agent of EBL is classified as an oncornavirus "C" of the retrovirus family. The retrovirus family comprises viruses involved in tumour production in chickens, mice, some primates and other animals. It also contains some nontumour forming viruses of importance including maedi-visna of sheep and equine infectious anemia. The tumour forming viruses of this family are known as oncornaviruses.

BLV Replication (Exogenous)

1) The virus enters the host cell and is broken down to release RNA and reverse transciptase enzyme (RT).
2) Viral RNA under the influence of the RT enzyme produces a DNA copy of itself.
3) The new DNA enters the cell nucleus and is inserted into the cellular DNA as part of the cell genome.
4) As the infected cell replicates, the viral DNA is replicated as well as the virogene or provirus.
5) The viral DNA may replicate itself within a cell by leaving the nucleus and synthesizing new viral proteins.
6) The new viruses are released from the cell by "budding", taking a portion of the cell with them as a virus coat.
7) It is the presence of the transcribed viral DNA in the cell genome that eventually can transform the cell from normal to a tumour cell.

Some retroviruses have their replicative gene as part of the genome of the host gamete and the virus is passed from parent to child of each generation. Exogenous viruses such as BLV do not infect gamete cells, but are transmitted from host to host through external means.

Natural Modes of Transmission of Disease Prenatal (Congenital):

1) Transmission of the genome via the gametes is genetic or chromosomal transmission as part of the genetic material of the sperm or the ovum. There is no evidence to date that this is the case in EBL. All evidence, to the contrary, indicates that the gamete is incapable of transmitting the virus as an inherent part of the germ tissue. The embryo would, therefore, be free of EBL virus but would be susceptible to infection.
2) Transmission of complete virus to the embryo or fetus is known to occur by epigenetic or extrachromosomal transmission. The infected lymphocyte probably moves through the placenta from the dam to the fetus.

Vertical:

Transmission from one generation to the next via prenatal transmission and postnatal contact transmission from parent to offspring.

Horizontal:

Transmission between animals of the same generation via milk, secretions, excretions, fomites, insect vectors, hypodermic syringes, surgical instruments (mass dehorning and castrations) and blood transfusions.

Natural Modes:

There is conclusive evidence that BLV is transmitted by contact. Inasmuch as BLV particles are seldom produced *in vivo* it is probably logical to conclude that cattle become infected by exposure to infected lymphocytes.

1) Role of vectors: some researchers are of the firm opinion that blood-sucking insects are involved in the transmission of infected lymphocytes from one animal to another; this role is strongly supported by the observation that cattle become infected by contact much more efficiently during the summer months; BLV-infected lymphocytes have been recovered from horseflies allowed to feed on an infected cow; only a very small quantity of blood is required to infect a cow (0.005 mL).

2) Syringes and transfusions; blood-contaminated syringes, needles and instruments are a potential means of transmitting BLV.
3) Natural secretions; BLV has not been demonstrated in saliva and nasal secretions.

Milk-Borne

It has now quite widely been accepted that BLV can be experimentally transmitted by innoculating milk from infected cows into noninfected cows. It is generally accepted that the virus particles in milk exist only within infected lymphocytes. Natural transmission by milk is not believed to occur under natural conditions. It is believed that BLV-infected cells cannot pass through the intestinal mucosa after the first few days of life.

Semen:

There is data available to show that cattle may be infected by placing infected lymphocytes into the uterus under experimental conditions. Bovine leukosis virus has not been detected in the semen of infected bulls. In repeated studies no differences were observed in the frequency of BLV infection among the progeny of BLV-positive and BLV-negative bulls. One recent study in Great Britain has reported successfully infecting three of 11 sheep by intraperitoneal innoculation of semen samples, containing large volumes of seminal fluid, from an infected bull.

Milk Versus Contact Spread

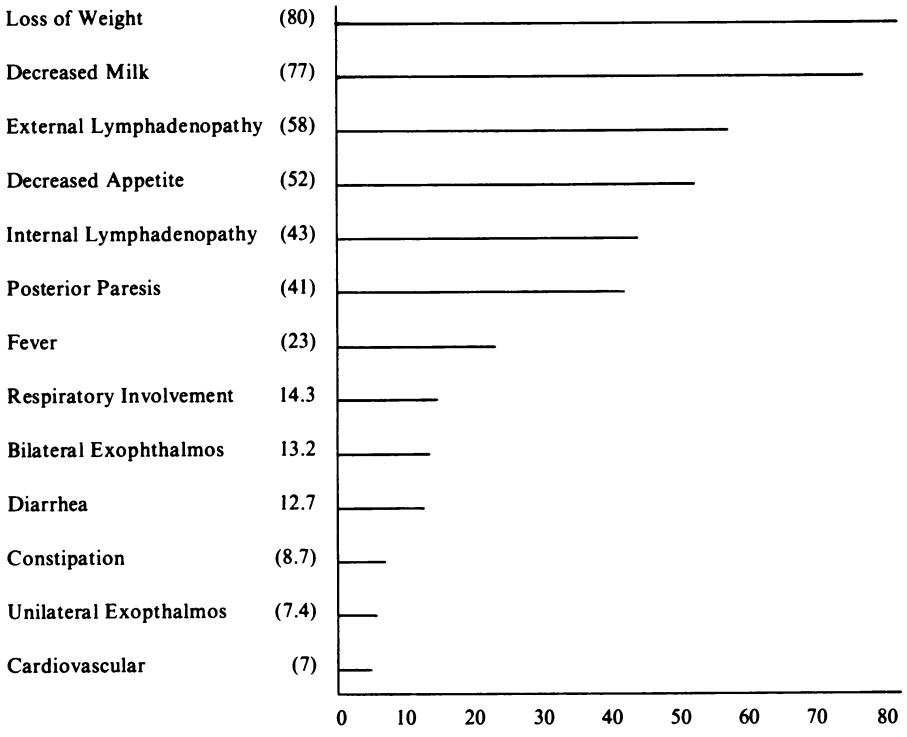
Thirty four BLV-free calves were nursed on infected dams for five to six weeks. Seventeen were raised in strict isolation for 27 to 29 months and three became infected. Seventeen calves were raised in contact with infected cattle for 27 to 29 months and 17 became infected.

While there continues to be much speculation on the natural modes of transmission of EBL at the present time, it is accepted that infection is transmitted by contact but the mechanism of the transmission has not been proven.

The clinical signs in EBL are presented in Table III.

TABLE III

CLINICAL DIAGNOSIS: FREQUENCY OF PREDOMINANT SIGNS OF BOVINE LEUKEMIA — 1 100 FIELD CASES



The Serological Diagnosis of EBL

All of the following tests may be used in the diagnosis of enzootic bovine leukosis. Only those considered to be major importance in the diagnosis of EBL are discussed.

Serological Tests:

1) The Agar Immunodiffusion
2) The Radioimmunoprecipitation Assay
3) Complement-Fixation
4) Synctiasm Inhibition
5) Immunofluorescent
6) Anti-Complement Immunofluorescent
7) Indirect Immunoperoxidase

The Bovine Leukosis Virus Antigens

The P24 antigen has the following characteristics: molecular weight 21 000-25 000 dalton, characterized biochemically as a protein, prepared by treating purified BLV with ether (ether resistant), represents the inner core of the virus particle.

The GP antigen has the following characteristics: molecular weight 51 000 dalton, contains both protein and carbohydrate, is ether soluble and is a component of the virus envelope.

The above are not the only antigenic components of the BL virus; they are mentioned only to demonstrate the need to prepare specific antigens to be used in the development of sensitive and specific test procedures.

The Agar Gel-Immunodiffusion Test (AGID)

This test is based on the established principle that an attraction exists between an antigen and its specific antibody. The most common test in which this principle is employed is the tube agglutination test in which the antibody:antigen attraction in the test tube results in a precipitate that can be observed. In the AGID test, the antigen and the antibody are placed in wells in plastic Petri dishes, the antigen and the antibody migrate through the agar towards each other, unite and precipitate, forming a precipitation line that may be observed.

The AGID test for BLV antibodies is conducted using the following procedure:

1) melted agar is poured into plastic Petri dishes and cooled in the refrigerator.

2) holes are cut in the agar with a specially designed agar gel punch. Each set consists of seven wells, 7 mm in diameter, placed at 3 mm from each other and from the central well.
3) the central well is filled with antigen and wells 1 and 4 with the positive reference serum. Wells numbered 2, 3, 5, and 6 are filled with the sera under test.
4) the plates are placed in a humidified chamber at room temperature (25° C).
5) the plates are examined with the help of a strong, indirect light source at 24 and 48 hours. A magnifying glass may be used to assist in observing the reaction.

Precipitation lines usually begin to appear within 24 hours and are read at 48 hours. The reference precipitation lines should be sharp and formed midway between the antigen and the serum wells.

The quality and standardization of the prepared antigen are very important to the success of this test.

Radioimmunoprecipitation Assay (RIA)

After the demonstration of RNA tumour virus particles in tissues of leukemic animals, BLV was successfully propagated in cell cultures. The virus has been biochemically characterized and the major structural proteins of the virus have been isolated. The P24 protein has been used to develop a specific and sensitive immunoprecipitation test for the detection of BLV antibodies in infected animals. In this procedure, the purified protein is labelled with radioactive iodine ^{125}I to form the antigen for the test. The addition of the antigen to the serum results in the precipitation of the antigen/antibody fraction. The radioactivity of the precipitate is measured using a gamma counter.

The advantages of the RIA test are:
1) the data obtained from the test is quantitative.
2) the test appears to be more sensitive than the other serological tests.
3) rapid, lends itself to automation.
4) results are automatically recorded on a printout, reducing the opportunity for clerical error and subject bias.

Summary of Serological Diagnosis

While there is not complete agreement on the comparative values of the various serological tests for BLV antibody detection, my overall impression of the comparative efficiency of the different serological tests is that:
1) The radioimmuoassay test is highly specific and sensitive. Almost all workers agree that the RIA test is considerably more sensitive than the other serological tests in identifying serum samples having relatively low antibody titres.
2) The RGID test and the RIA test agree quite well, except in cases where the antibody titre is relatively low.
3) The RGID test and the CF test are quite specific with 80% agreement. The RGID test is relatively more sensitive than the CF test.

Diagnosis

Virus Isolation

Bovine leukosis virus can be isolated by culturing leukocytes from an infected cow with cell cultures from the spleen of lamb fetuses. The virus from the leukocytes of an infected animal cause the lamb spleen cells to fuse into large cells. known as syncytia, containing a number of nuclei (multinucleated cells).

Because other viruses do affect bovine lymphocytes, procedures are required to identify the virus present:
1) *Electron Microscopy* — the techniques involved are too time-consuming and costly to be used routinely.
2) *Fluorescent Antibody Staining* — a) The direct method requires a staining reagent composed of purified gammaglobulin antibodies to BLV that have been chemically linked to a fluorescent dye. When cultures containing BLV-infected cells are exposed to the staining reagent, the fluorescein-linked gammaglobulin attaches to the parts of the cells containing viruses and these become visible when viewed under ultraviolet light. b) The indirect method is similar to the direct method except that it permits a culture to be tested for more than one kind of virus. It is more sensitive and selective but under some circumstances is less specific.
3) *Radioimmunoassay* — this method involves the binding of radioactive iodine labelled viral antibody to the virus antigen of EBL.
4) *Enzyme Linked Immunosorbent Assay* — The ELISA test uses an enzyme in a type of staining reaction that can be observed using an ordinary light microscope. The procedure is similar to that used in the FAT.

Hematological Testing

Hematology is of only very limited value in the diagnosis of EBL (Table IV). It can be useful in confirming clinical diagnosis by the identification of leukemic cells in peripheral blood smears. Bendixen, in his work in Denmark, has reported persistent lymphocytosis in 90% of tumour cases. American workers report that hematology is of some value in providing a clear diagnosis in about 50% of clinical cases.

An experienced clinical pathologist or hematologist is necessary to make a positive diagnosis on hematological examination.

The Hematological Keys

The hematological keys have been used for the diagnosis of EBL but they have some very grave limitations. Based on a single lymphocyte count, they have very little value as lymphyocytosis is a very natural and common phenomenon. In order for the keys to have any significant reliability they should be conducted on a herd basis and with multiple testing. Persistent lymphocytosis (PL) has been reported as an indicator of animals in the preclinical stages of leukosis. The issue remains very controversial, but PL is

TABLE IV
ABNORMAL RANGE OF LYMPHOCYTE COUNTS IN CATTLE

Age — Years	Abnormal Range 10^3 Lymphocytes/μL
< 1	> 11
1-2	> 10
2-3	> 8.5
3-4	> 7.5
4-5	> 6.5
5-6	> 6
6+	> 5.5

one parameter that may be used to identify animals in the latent period. The vast majority of BLV-infected cattle, however, that do develop PL do not develop into tumour cases during their lifetimes. The hematological keys have no real practical value in control and eradication programs.

Summary of Diagnosis

1) The identification of animals infected with BLV can be made accurately with the available serological tests.
2) Positive diagnosis of a tumour cannot be made by serology. Biopsy or pathological examination is necessary, or in some cases, hematological examination may confirm a diagnosis.
3) Many cattle with other diseases that mimic leukosis may be infected with BLV.
4) A negative serological test would be reason to rule out EBL.

EBL and Artificial Insemination

The animal disease and protection regulations require that all bulls entering a semen production centre be tested negative for leukosis. For some time the test used for this purpose has been the AGID test. The regulations also state that "if an animal proves positive to any test it shall be immediately segregated from other animals in the centre or removed from the centre." Section 117(1) of the regulations prohibits the distribution of "any animal semen that is affected or has been exposed to a communicable disease that is capable of being transmitted in semen." Some semen is still sold in Canada by semen production centres that was collected from AGID-positive bulls. This semen is primarily from bulls that have proven to be excellent sires and for which there is a strong demand. We, at the present time, take the position that EBL virus is not transmitted through semen by artificial insemination. The possibility remains, however, that should the semen contain infected lymphocytes, infection could be transmitted in this manner. At present there is no legislative requirement that semen sold in Canada be collected from EBL-negative bulls. The artificial insemination industry can expect, however, increased pressure to discontinue the sale of semen from BLV-infected bulls. It must be stressed that there is no evidence that EBL virus is spread in bovine semen by artificial insemination, but there is much evidence supporting the position that infection is not transmitted by artificial insemination.

Prevalence and Economics of Bovine Leukosis in Other Countries

The bovine leukosis situation and its development in Europe was well presented by Bendixen in his "leukosis enzootic bovis." Early veterinary literature reported the occurrence of leukosis in many countries but impressions were that the disease was relatively rare (Norway, Holland, Switzerland, Austria, Bulgaria, France and Great Britain). In north eastern Europe the disease was recognized to have wide incidence and it was considered to be the dominant tumour disease of cattle (North Germany, Estonia and Sweden). Extensive descriptions of leukotic cases in cattle were published in Germany as early as 1978. Study indicates that, prior to World War II, the disease was widespread in central Europe and Clinical cases were observed with increasing frequency, particularly in those areas east of Elbe River. In some areas of Germany, practising veterinarians reported cases from 100 to 380/100 000/year. Extensive investigations of bovine leukosis were started in Germany in 1953. The reason for this work was the observation of a large increase in leukosis tumour cases after World War II in parts of the country where the disease previously had been virtually unknown.

Sweden had relatively high incidences of the disease reported after World War II. Up to 100/100 000 head of cattle were reported to have died or been discarded because of the disease. An increased incidence of leukosis was demonstrated among animals in herds in which piroplasmosis vaccines had been used. Material for the production of the vaccine originated mainly from leukotic areas.

Reports indicate that leukosis has spread all over the USSR. The disease is considered a serious problem.

In Great Britain, infection levels are very low, believed to have been recently introduced by imported cattle.

In Denmark, a questionnaire mailed to all veterinary practitioners in the country in 1953-54 indicated a disease incidence of 4.1 cases per 100 000 head of cattle for the whole country.

Significant levels of infection have been reported in France, Czechoslovakia, Ireland, Venezuela and Japan.

United States authorities write that no reliable data exist on the prevalence of EBL and its economic impact in that country. They consider it extremely difficult to accurately relate tumour frequency data in slaughter cattle to prevalence in any given area. Many tumour animals are not slaughtered at federally inspected plants and many are disposed of by means other than slaughter (Table V). It is estimated that the BLV infection in the United States is similar to that in Canada (Table VI).

The figures given in Table V are interesting in that while there appears over the years to have been an increasing prevalence of malignant lymphoma in the United States, the total tumour incidence has remained relatively unchanged. Overall assessment of these figures would appear to indicate no significant increase in tumour frequency, but rather, an increased expertise in diagnosing malignant lymphoma.

The prevalence of bovine leukosis varies markedly in different countries and even within geographic areas of each country. It was only with the

TABLE V
UNITED STATES —
TUMOUR FREQUENCY RATES IN CATTLE
SLAUGHTERED UNDER FEDERAL INSPECTION

	Malignant Lymphoma	Total Tumour
	Per 100 000	
1952	30	178
1954	34	109
1956	47	104
1958	59	118
1960	78	143
1962	95	275
1964	89	165
1966	71	130
1968	88	154
1970	100	168
1972	97	152
1974	82	147
1976[a]	54	92
1978	100	156

[a]High number of beef cows sent for slaughter

advent of serological testing that more accurate information on prevalence was obtainable. It is known, however, that this disease is widespread throughout the world.

The Prevalence and Economics of EBL in Canada

In Canada, condemnations for lymphoid leukosis for the fiscal year 1978-79 were: 36 lymphoid leukosis, out of 13 170 total condemned, out of 3 183 772 total cattle slaughtered (not including calves).

The Canadian statistics (Table VI and VII) with respect to EBL have no relationship to the prevalence of virus infection. They do show, however, that very few cattle are condemned at the time of slaughter because of this condition.

There is little doubt that Canada has a relatively high herd prevalence of EBL. It is also apparent that more that 50% of our dairy herds are free of infection and more than 85% of our beef herds are free of infection. The clinical impact of the disease is apparently quite small. There is no doubt that a requirement that a herd be negative to EBL to qualify for export would greatly increase our difficulty in exporting cattle.

Possible Association Between Bovine Leukosis and Human Disease

Investigations into the cause of human leukemia started well before the discovery of bovine leukemia virus in 1969, and the subsequent development of serological tests. The earlier studies relied upon epidemiological methods and, since some were the first to suggest the possible link between cattle and human leukemia, reference is made to them in this discussion.

Some of the earlier epidemiological studies on human leukemia investigated the possible relationship between this disease and general environmental factors. Analysis of the data collected in these studies showed that human leukemia was not more common in rural inhabitants. In fact, three of the studies found a significantly higher frequency of cases in urban areas rather than rural areas. These reports showed that human leukemia was, in general, more common in an urban environment, giving no evidence for an association between the disease and bovine leukosis.

TABLE VI
CONDEMNATIONS AND NUMBERS AND PERCENTAGES OF TOTAL SLAUGHTER CATTLE IN CANADA FOR THE FISCAL YEAR 1975-1976

	Number	Percent
Arthritis	371	2.2
Bruises	786	4.7
Emaciation and mucoid degeneration	4 723	28.6
Imperfect bleeding	22	0.1
Leukemia	23	0.1
Mammitis	188	1.1
Metritis	337	2.0
Nephritis	225	1.4
Pericarditis	473	2.9
Peritonitis	1 681	10.2
Pneumonia and pleurisy	1 481	9.0
Septicemia and pyemia	1 502	9.1
Pyrexia	10	0.1
Other causes	4 709	28.5
Total slaughter	3 412 431	
Total condemnations	16 531	
Total leukemia	23	

TABLE VII
A SURVEY OF THE PREVALENCE OF EBL IN CANADA

	Total Tested		Reactor Herds[a]	
	Dairy	Beef	Dairy	Beef
Newfoundland	0	0	0	0
Prince Edward Island	6	5	0	0
Nova Scotia	2	10	0	0
New Brunswick	5	6	2	0
Quebec	121	30	40	7
Ontario	74	112	41	23
Manitoba	12	82	5	27
Saskatchewan	8	136	2	7
Alberta	6	128	2	1
British Columbia	9	26	0	1
Total	244	535	92	66
Percent			45	14

[a]One or more reactors to the AGID test

Reports from time to time have suggested a possible link between cattle and human cancer. Many investigations have been made into these reports. It is interesting to report a few of them.

1) A study considered an adult cluster of leukemia cases around a village in Wisconsin over a four-year period. That cluster represented a greater than twentyfold increase in the expected frequency of the disease for that population. The author speculated that the cases might have been related to bovine leukosis because the village was located in a dairy farming county and some of the patients had either worked in or near the local creamery. The sera from two surviving patients, twenty three relatives and the twenty creamery employees were tested for antibodies to bovine leukemia virus and were negative. Unusual clusters of leukemia in rural populations are, apparently, uncommon and none has been shown to be associated with bovine leukosis.
2) A number of statistical studies have investigated the possible association of farming or exposure to cattle with human disease. Studies in California examined the mortality risk for various diseases in veterinarians and farm residents, and found no significantly increased risk of death from leukemia in either group.
3) A case controlled study in Oregon and Washington demonstrated a significant association between farming and death from leukemia, with poultry farmers showing a particularly high frequency of the disease. There have been other studies that suggested a relationship between human leukemia and exposure to animals but scrutiny of the procedures followed reveals serious bias.
4) Scandinavian reports have compared the geographical distribution of human leukemia and bovine leukosis on a national level in Denmark and Sweden. No relationship was found between these distributions.

No human serum has ever been found to contain anti-BLV antibodies.

The degree of contact with BLV-

positive animals seems so close that if BLV could be transmitted to humans, ample opportunity for it to do so had occurred by a variety of routes. Persons handling raw milk, animal wastes, and animal carcasses have all been negative for BLV antibody. If BLV could be transmitted to humans, one likely route would be through the ingestion of raw milk because virus-like particles have been found in such milk. Despie fairly extensive use of raw milk by farm families with BLV-positive herds, all sera had been universally negative even if milk consumption began in infancy and continued throughout life.

Investigators have attempted to transmit BLV to chimpanzees through parenteral injection. These animals developed anti-BLV antibodies but repeated attempts to reisolate BLV have failed. Because BLV virus is transmitted naturally there will continue to be a concern of the possibility of spread to humans. Bovine leukosis virus can replicate in human cells in tissue cultures.

In summary, BLV is a naturally transmitted oncornavirus which can be transmitted in cattle herds across species barriers to sheep, and questionably, to subhuman primates. Adequate serolocial tests which are sensitive and specific have failed to demonstrate infection in humans despite close contact or raw milk ingestion from BLV-infected herds. Consequently, BLV does not appear to represent a public health hazard.

The Prevention of EBL

For most commercial dairy herds in Canada, the prevention of EBL would simply be best accomplished by not purchasing additions or by not permitting contact with other herds.

Prevention for persons buying replacement stock may be difficult. The isolation and testing of imported animals has practical limitations as well as the limited availability of the diagnostic tests. False negative results from cattle in the early stages of infection also pose a problem.

For the owner producing breeding stock, the necessary precautions to prevent the introduction of infection are strongly advised, including as much knowledge as possible of the source herd.

There would appear to be uniform agreement by world authorities that EBL is transmitted from herd to herd and from one area to another by the movement of infected cattle.

The Control of Enzootic Bovine Leukosis

Feasibility:

It is generally accepted that EBL can be eradicated from infected herds using a combination of good management and the serological tests. The fact that EBL spreads very slowly in infected herds lends this disease to control by good management.

Current Options:

Enzootic bovine leukosis is not a reportable disease in Canada. Tests are conducted at the federal laboratories for export and for entry into artificial insemination centres. We do, on occasion, approve the testing of animals and herds when special requests are made by veterinarians and owners.

The Department is very reluctant to undertake the testing of all cattle, on demand, for EBL. The cost would be very high and we are reluctant to participate in a program that would identify infected animals, thus permitting owners to sell unmarked reactor animals. There is a probability that this would increase the spread of infection within Canada.

The question has arisen as to the ethics of veterinary practitioners' testing a client's cattle for EBL. Veterinarians in Canada practise veterinary medicine under licence and legislation administered by provincial authorities. The question of ethics with respect to EBL has no greater relevance to EBL than it has to any other disease or condition. It is perfectly normal for a client to seek the assistance of his veterinarian in identifying any EBL problem in his herd and to deal with that problem in the confidence of the normal veterinary/client relationship. The Food Production and Inspection Branch licenses the importation of approval diagnostic agents and takes no exception to diagnostic services for EBL being provided by veterinary practitioners or veterinary laboratories.

It would appear that in those herds not having a large percentage of reactor animals, the disease could be reduced or eliminated by longer term good management, including the serological identification of infected animals.

Eradication:

Since EBL is transmitted primarily by contact, the accurate identification and prompt removal of all infected cattle are essential considerations in the design of an eradication program.

A herd cannot be considered free of BLV infection until all animals in the herd are seronegative in a series of tests. The number of tests required would depend upon the number and sensitivity of the tests used. Tests should be conducted from three to six months apart.

The probability of eradicating infection from an infected herd is directly related to the level of infection in the herd. It has been shown that the AGID test will reduce the level of infection to a very low level after two to three tests. Some workers, however, have doubts that the AGID test is sufficiently sensitive to be used in a herd eradication program. Most workers, however, feel that all factors considered, it is the best test available at the present time.

The possible role of wild animals as natural reservoirs of EBL remains to be investigated.

Canada is not considering a national eradication program. The economic losses caused by the disease would not appear to warrant any such action.

Vaccination:

Some apparent facts of consideration:

1) Calves born with maternal antibodies may be protected for a short period from postnatal infection. This theory is by no means proven and would not appear to be consistent with other infomation, nor with other viruses in this group.
2) The EBL vaccine-produced antibody will not prevent later infection after exposure to the EBL virus. This is consistent with the finding in Marek's disease in chickens in which vaccination does reduce the level of clinical infection but does not significantly reduce the level of virus.
3) There is speculation that a vaccine antigen prepared from the tumour

might prevent the development of lymphosarcoma. The antigen in this case is not the virus or a part thereof, but a purified extract of the tumour cell.

The development of a vaccine, at least at the present time, is of great scientific and academic interest. From a practical viewpoint however, the apparent losses with this disease would not warrant the vaccination program even if a suitable vaccine were developed. To date in Canada, our major concern with EBL is with respect to our export markets. It is almost certain that the serological tests will remain the criteria for deciding the eligibility of our cattle for export. A vaccine that might possibly prevent the development of lymphosarcoma and not prevent infection by the virus would not help us in qualifying our cattle for export, at least at the present time. An additional problem could be the production of antibody by the vaccine that could cause problems in any subsequent serological testing.

The Preservation of Valuable Genetic Seed Stock

It is believed that, by calf selection, at least 80% of calves born from BLV-infected dams will be free of BLV at the time of birth. Young calves not infected with the virus may, however, have received passive antibodies and may test positive up to six months. The point is, however, that calves raised in isolation will remain free of BLV if they are free of the virus at the time of birth.

The genetic material from the sire or the dam and, therefore, the embryo, is not infected with BLV. There is a possibility that virus could be transmitted in uterine fluids surrounding the embryo but the techniques used in collecting and identifying the embryos would seem to make this possibility highly improbable. The cost of the embryo transfer procedure make this procedure less practical than the selection and isolation of the calves.

CONCLUSIONS

Enzootic bovine leukosis is not a reportable disease in Canada and it would appear to be very difficult to support a move to this end as being in the public interest. It is expected that the livestock industry will demand some program to permit herds to be certified free of EBL. This could be a program similar to our brucellosis-free tested herd program.

It is highly unlikely that the government would, at least in the near future, approve a compensation policy for cattle infected with EBL.

As increased numbers of cattle and herds are tested for EBL we will have at least a moral responsibility to identify reactor animals.

BOOK REVIEW

Antidiuretic Hormone, Volume 4. Mary L. Forsling. Published by Eden Press, Annual Research Reviews, Montreal. 1980. 165 pages. Price $26.00.

The development and application of radioimmunoassays for hormone measurement have resulted in a burgeoning of published papers in the last decade. So extensive has the yearly output of endocrinological literature become that it is now impossible for any one person to follow all aspects. Fortunately, individuals such as Mary Forsling exist who define a particular area of interest and are able to summarize recent findings in this area in a pertinent and lucid style.

Antidiuretic hormone (ADH), or vasopressin as it is often referred to, has received intense scrutiny in the past few years. This volume covers about 550 references, mostly from 1978, and reviews the latest understanding and applications of this hormone. Good coverage is given to the osmometer control versus sodium sensor control of ADH as well as to the blood pressure versus blood volume regulation of ADH production in response to severe hemorrhage. An interesting effect of ADH pertains to memory. Learned behaviour is impaired in rats with diabetes insipidus and restored with injections of ADH. Is a similar finding true in the dog?

Of most interest to the practicing veterinarian are the summaries of recent work in central diabetes insipidus, the syndrome of inappropriate secretion of ADH (SIADH) and the therapeutic uses of ADH in hemorrhagic conditions. Newer analogues of ADH have been examined and desamino-8-arginine vasopressin (DDAVP) shows much promise with its enhanced antidiuretic activity. To this reviewer's knowledge, SIADH has not been reported for the dog or other domestic species. It is a condition believed to exist however and E.T. Siegel, in his text Endocrine Diseases of the Dog, confesses to probably having observed the condition without recognizing it. He devotes some space to the likely signs that would be exhibited.

With the inexorable pressure towards semispecialization and specialization in veterinary medicine a book of this type will appeal greatly to practitioners with an interest in conditions involving body water balance, electrolyte balance and hemorrhage. Despite a number of typographical errors (15 noted) this offset printed text will serve well to refresh and update practitioners on information pertaining to antidiuretic hormone. Forsling has a gift for exposition and summary. Her style is clear, flows easily, is interesting and is recommended. To quote one of her favourite authors, Samuel Johnson — "A man will turn over half a library to make one book". *R.M. Liptrap.*