The Clinical Picture of the Enzootic and Sporadic Forms of Bovine Leukosis

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Before entering into the subject of bovine leukosis, let me first express my heartiest thanks for the honorable and kind MASUA invitation: It gives me the pleasure and opportunity to gather a lot of new practical, scientific and social experiences. I am bringing the greetings of the Hannover Veterinary School to all of you, and I do hope to meet many of you there some time.

Definition

Let us begin with a short definition of 'Leukosis': The fully developed diseases of this complex are characterized by malignant tissue growth in the production centers of the white blood cells, for example in the lymph nodes, in the spleen, or in the bone marrow, but also, and sometimes only, in other organs. Before, or simultaneously with, the appearance of these tumors, the proliferation rate of cells of the type concerned entering into the blood stream may - but will not obligatorily, increase thus leading to 'leukemic' blood findings.

The term 'leukosis' was first proposed by Dobberstein (Berlin) in 1934. Though coming from a pathologist, this term used together with appropriate adjectives also serves clinically best to denominate or differentiate:
- the various types of the disease complex: as for example lymphocytic (lymphatic), monocytic, neutrophil/ granulocytic (myelogenous) leukosis, etc.; - the occurrence of the disease: namely sporadic or enzootic leukosis;
- the age group concerned: juvenile, adolescent or adult leukosis;
- the course of affection: acute, subacute or chronic leukosis;
- the involvement or not of the white blood picture: that is, aleukemic or leukemic leukosis;
- the stage of the disease: it may be pre-tumorous (with positive findings in serum or blood only) or tumorous (and then affect certain organs such as the abomasum, heart, lymph nodes, spleen, thymus, skin, etc. - and finally impair vital functions of the organism.

In cattle, most of the various forms of leukosis are of the lymphatic type. This means that the proliferating cells are lymphocytes or lymphoblasts. When just speaking of "bovine leukosis' veterinarians and farmers usually refer to the most important form of the complex, that is enzootic lymphatic leukosis of adult cattle. It is caused by a virus detected by Miller and her co-workers in the U.S. Department of Agriculture National Animal Disease Center, Ames, Iowa in 1969 and belonging to the C-particle/oncornavirus/retraviruses. This BL-virus is transmissible under usual management conditions, and experimentally.

As enzootic lymphatic leukosis of adult cattle has been the most frequent tumorous ailment in large ruminants in our country. It became notifiable in 1965 and an official program was elaborated to eradicate it in the Federal Republic of Germany (and in other European countries). Contrary to the other forms of bovine leukosis, animals infected by the BL-virus develop (within 2 weeks to 3 months) specific antibodies in their serum; these antibodies serve to detect the carriers of the virus at an early state, when all the other symptoms enumerated here are still lacking. Since the introduction of the serological control campaign in 1978 which uses the agar-gel immuno-diffusion-test (gp 69) and gradually superceded the former control by counting the number of circulation lymphocytes to find the animals affected with persistent lymphocytosis, we only very rarely get cases of tumorous enzootic leukosis in our clinic; therefore, the following report is based on an earlier
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situation and these animals were, at that time, not been tested serologically:

We had a total of 470 cases of tumorous leukosis of all types as indoor patients during the 15 years from 1960 to 1974. Among them, 439 were of the enzootic lymphatic adult type; 27 concerned calves with juvenile or adolescent (thymic) lymphatic leukosis, one animal suffered from lymphatic leukosis of the skin (and we saw two more cases of this kind in the meantime); two patients showed monocytic leukosis and one animal was diagnosed as mastocytic reticulosis with tissue mast-cells in the blood, so we may classify it as mastocytic leukosis.

Clinical Signs

Based on the observations gathered in this material and on those contained in veterinary literature, I will try to describe the more important symptoms of enzootic lymphatic leukosis in adult cattle, first. After that, we will have a comparative look into the characteristics of the sporadic forms of bovine leukosis. As the pretumorous stages of all forms of the bovine leukosis complex are clinically 'silent', their tumourous stages will be discussed here only. (Some Scientists such as Ferrer from New Bolton Center/Pennsylvania, stress that a positive serologic reaction towards BL-virus antigen or a persistent lymphocytosis per se should not be considered as 'leukosis', because there is no disease involved yet; my personal opinion is that we may leave things together, if we clearly define the states we are dealing with).

In enzootic lymphatic leukosis of adult cattle, the tumorous state affects animals of more than 2, and preferentially between 5 and 6 years of age. As a rule, the tumors in the lymph nodes and/or in the organs develop rather slowly (that is chronically) and may remain undetected for several weeks or some months, if they do not cause disturbances of vital functions; once these disturbances occur, the general state of the animal often worsens suddenly, simulating an acute course of the disease. Based on the observations gathered in this material and on those contained in veterinary literature, I will try to describe the more important symptoms of enzootic lymphatic leukosis in adult cattle, first. After that, we will have a comparative look into the characteristics of the sporadic forms of bovine leukosis. As the pretumorous stages of all forms of the bovine leukosis complex are clinically 'silent', their tumourous stages will be discussed here only. (Some Scientists such as Ferrer from New Bolton Center/Pennsylvania, stress that a positive serologic reaction towards BL-virus antigen or a persistent lymphocytosis per se should not be considered as 'leukosis', because there is no disease involved yet; my personal opinion is that we may leave things together, if we clearly define the states we are dealing with).

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In an unselected sample of 296 cows with enzootic leukosis, we found a seasonal increase of the functional disturbances caused by the tumors: Only 124 of these cases came to the clinic during the 6 "pasture" months (May to October), whereas 172 of them were obtained during the stabulation period, that is from November to April; the difference is statistically valid.

The same sample of cows was also analyzed as to the state of pregnancy of the animals: We found that 190 of them were between 4 months before, to 2 months after calving, whereas only 106 had calved more than 2 months before or were up to 5 months pregnant. This difference is statistically valid, too. Thus, advanced pregnancy seems to enhance the growth of the tumors or weaken the resistance of the organism.

The white blood findings of this group of 296 leukotic cows were checked for correlations with season or state of pregnancy; we found that the number of lymphocytes per cubic millimeter of blood is unrelated to these two factors in adult cattle with tumorous enzootic leukosis.

In the individual animal, a clinical diagnosis of tumorous leukosis is based first of all on the findings obtained by a thorough palpation of the lymphnodes; this includes all lymphnodes which are externally accessible (Fig. 1) and those to be reached by rectal exploration: (Fig. 2)

To do this, the mandibular lymph nodes (Fig. one, No. 1) are examined together with the mandibular salivary glands, using thumb and index of both hands introduced bilaterally and deeply into the intermandibular space (at the angle of the mandibles), trying thereby to ‘grasp’ both structures which are then felt ‘slipping’ through the fingertips; normally, the mandibular lymph node is too small and too soft to be felt individually (that is apart from the adjacent salivary gland). The same is true for the parotid and the retropharyngeal lymph nodes, (Fig. one, Nos. 2 and 3 respectively). They are the size of a hazelnut or a walnut in normal cows. The parotid lymph node is palpated by grasping - between the thumb and index - the upper end of the parotid gland which covers it. The retropharyngeal lymph node is examined by introducing the tips of the extended fingers of both hands simultaneously from the right and the left into the ‘soft’ space between the posterior border of the mandible, the spine (wings of the atlas), and the larynx; when moving the pressing fingertips of both hands alternatingly to and fro, normally no lymph node is to be felt ‘slipping through’ the manipulation and it does not cause respiratory distress. The prescapular and the subiliac lymph nodes (Fig one, nos. 4 and 5) are about finger-size when unaltered. The mammary lymph nodes (Fig. one, No. 6) should be palpated after milking the animal, then, the examiner crouches behind the cow and lifts the left hind quarter with the palm of his left hand, while the tips of the extended fingers of his right hand are introduced into the intermammary rim from behind, using the thumb to grasp the posterior border of the left mammary lymph node; afterwards, the procedure is repeated accordingly on the right side.(Fig. three) Normal udder lymph nodes are about the size of a watch and feel more smooth than the adjacent granulated udder parenchyma.

The ileofemoral lymphnodes (Fig. two, No. 8) are half the size of a hen's egg when normal; they are to be found following the anterior border of the ilium from above, that is beginning at the promontorium, and are situated at about one third the way down.

There are some small sublumbar lymphnodes located in the bifurcation of the abdominal aorta (Fig. two, No. 7), which usually are too small, that is pea or bean sized, to be felt; if they reach the size of a hazelnut, they are easily found.

If more than one of the lymph nodes are enlarged to more than twice or triple normal size, and if there are no signs of an inflammatory process (as for example: tenderness, heat,
The findings have to be considered as a tumorous lesion. If the increase in size is less than that, it should only be rated as a suspicious sign. In enzootic leukosis of adult cattle, the tumors of the lymph nodes are, as a rule, asymmetrical and often not generalized. Leukotic lymph nodes show moderate tightness or firmness (instead of the normal soft-elastic consistency), they are insensitive to the touch and, in most cases, freely movable within their neighborhood; sometimes, accessory lymph glands are found next to them, which are also tumefied. The enlargement of several subcutaneous lymph nodes, on the sides of the neck or in the flank may be considered as a suspicious sign, but is, per se, no proof of tumorous leukosis.

Now let us have a look at the lymph nodes of leukotic cattle:

Figure four shows the properly grasped mandibular lymph node having the size of a hen's egg.

Figure five, the parotid lymph node, about the same size, thus also clearly tumorous. In Figure six, both mammary lymph nodes are enormously enlarged to about double fist size.

Figure seven shows the subcutaneous lymph nodes in the paralumbar fossa of a normal cow; they are the size of hazelnuts and therefore suspicious, but the animal did not show other symptoms of leukosis.

Table one underlines the value of rectal exploration for the diagnosis of tumorous enzootic leukosis. Whereas the external lymph nodes showed clear tumorous enlargement in 35% of our cases, only the lymph nodes accessible to rectal examination were found tumorous in 48% of them; considering the findings of all lymph nodes together, 58% of the cases could be diagnosed by proper palpation of the lymphatic organs enumerated (in the stage were functional disturbances impaired the general state of the animal).

Clinical examination of adult cattle suspect for tumorous leukosis is therefore insufficient if it does not include an examination of the lymph nodes to be reached from the rectum.

The mere leukosis tumourisation of lymph nodes sometimes results in marked impairment of the function of neighboring organs, and this occurs mostly in an advanced stage of the disease only, for example: Ex- and panophthalmia caused by tumors of the intra-orbital lymphollicles; difficulties in swallowing, tympany and lack of rumination with enlargement of the retropharyngeal or mediastinal lymph nodes and so on.

Next in importance for the clinical diagnosis of enzootic leukosis are the white blood findings.

Until 1976, the number of lymphocytes per cubic millimeter of blood, according to Gotze, Rosenberger and Bendixen, was used to detect cattle with persistent lymphocytosis as compared with the so-called 'leukosis-keys'. Animals with persistently high lymphocyte counts were considered to be the carriers of the BL-virus and therefore sent to slaughter. Today, we know that the time lag between infection with the BL-virus and the appearance of persistent lymphocytosis is too long (several months to more than 2 years), and that only about 30% of the carrier animals (as detected already within 2 to 4 weeks after artificial infection by serological means, for example the immunodiffusion-test) eventually develop lymphocytosis. So, as a means of herd control, the white blood count has been, in several countries of the European community (Germany, Netherlands, Denmark) superceded by serology, especially by the immunodiffusion-test.

In the individual animal, the proof of an abnormal number of lymphocytes or lymphoblasts in the blood may be of help when leukemia in the disease stage is suspected: In Figure eight, the blood smear contains more than 20,000 lymphocytes per cubic millimeter of blood and there is a lymphoblast in mitosis in the middle of the picture.

In our clinical material affected by tumorous enzootic leukosis, we had leukemic blood findings in 64% of the cases, whereas 11% of them showed suspicious lymphocyte counts and the remaining 25% had normal values. Considering the results of the palpating lymph nodes and those of the white blood picture, one or both criteria were positive in 82% of the animals, and only 6% of them remained without any clinical suspect of leukosis. (Table two.) In these cases, the leukotic tumors were detected either by explorative laparotomy or at slaughter.

We tested several cytochemical reactions in blood smears of normal cattle and compared the results to those obtained in animals with tumorous enzootic leukosis, but none of them was found of diagnostic help.

Besides the enlargement of accessible lymph nodes and persistent lymphocytosis (or leukemia), cattle in the advanced stage of tumorous enzootic leukosis often show symptoms caused by lymphatic tumors in certain organs which we will discuss next. These signs should therefore call the attention of the responsible veterinarian and induce him to take the necessary steps, that is to examine the lymphatic system including a lymphocyte count and an immunodiffusion-test, if leukemia cannot be ruled out by other means.

In more than a half of all cases, leukotic tumors of the heart, affecting the pericardium, the myocardium and/or the endocardium cause more or less marked cardiac symptoms; these may be intensified by the anemia which we often observe in tumorous enzootic leukosis, but they are, per se, not specific for this disease: Thus, we note tachycardia with the heart beats either thumping or fainter than normal and unclearly cut (or seperated) from each other. Endo- or pericardial sounds, or arrhythmias, are to be auscultated in the final state of the disease only. Then, percussion of the cardiac area shows a remarkable zone of absolute dullness. We do know, that, within the heart, the right atrium is most often, or first, affected by the leukotic tumors, but we do not know why this is so. The electrocardiogram does not contribute specific signs to support the diagnosis of heart leukosis.
Table One
Pulpatory findings in the lymph nodes of 298 adult cattle with enzootic lymphatic leukosis

<table>
<thead>
<tr>
<th></th>
<th>Tumorous</th>
<th>Suspicious</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes accessible to external examination:</td>
<td>35%</td>
<td>31%</td>
<td>34%</td>
</tr>
<tr>
<td>Lymph nodes accessible to rectal exploration:</td>
<td>48%</td>
<td>22%</td>
<td>30%</td>
</tr>
<tr>
<td>Total findings:</td>
<td>58% +</td>
<td>22% ?</td>
<td>20% -</td>
</tr>
</tbody>
</table>

Table Two
Lymph node and blood findings in 298 adult cattle with enzootic lymphatic leukosis

<table>
<thead>
<tr>
<th></th>
<th>Leukotic/Leukemic</th>
<th>Suspicious</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes (palpatory findings):</td>
<td>58%</td>
<td>22%</td>
<td>20%</td>
</tr>
<tr>
<td>Blood findings (lymphocytosis):</td>
<td>64%</td>
<td>11%</td>
<td>25%</td>
</tr>
<tr>
<td>Total findings:</td>
<td>82% +</td>
<td>12% ?</td>
<td>6% -</td>
</tr>
</tbody>
</table>

Table Three
Frequency of clinical symptoms in tumorous enzootic lymphatic leukosis of cattle

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enlargement of more than one accessible lymph node:</td>
<td>58%</td>
</tr>
<tr>
<td>Leukemic blood findings:</td>
<td>64%</td>
</tr>
<tr>
<td>Circulatory symptoms:</td>
<td>64%</td>
</tr>
<tr>
<td>Hemorrhagic anemia:</td>
<td>52%</td>
</tr>
<tr>
<td>Indigestion caused by abomasal tumors and ulcers:</td>
<td>62%</td>
</tr>
<tr>
<td>Overload and/or tympany of the rumen (with abomasal reflux):</td>
<td>19%</td>
</tr>
<tr>
<td>Exophthalmus (with secondary eye lesions):</td>
<td>9%</td>
</tr>
<tr>
<td>Tumours of uterus, vagina or perivaginal tissues:</td>
<td>33%</td>
</tr>
<tr>
<td>Paresis or paralysis of the hind quarters:</td>
<td>16%</td>
</tr>
<tr>
<td>Tumour of the spleen (percutory dullness):</td>
<td>9%</td>
</tr>
</tbody>
</table>

In advanced cases of pericardial or heart leukosis, stasis of the jugular vein and brisket edema are observed as a consequence of constriction or increasing failure of the heart muscle. If external lymph nodes are not visibly enlarged, the clinical impressions of such cases simulate traumatic pericarditis or endocarditis with stenosis of the tricuspid valve. To make a diagnosis, besides thorough auscultation and percussion of the heart and detection of localized sensitivity (as in 'hardware-disease'), a differential white blood count should be done: In endocarditis (especially during the hyperthermic stages) and in traumatic pericarditis, there will be marked neutrophilia with a 'shift to the left', but as a rule, no pronounced lymphocytosis or anemia, that is, no indication of (enzootic) leukosis.

In about 80% of the cases, the abomasum participates in the process of leukotic tumourisation. As this organ very often shows the largest tumors within the affected animal, and sometimes is the only one to be macoroscopically involved, the abomasum seems to play a special role in the pathogenesis of the disease, maybe as a site of entrance for the endogenous agents into the body.

More than a half of our patients with tumorous enzootic leukosis suffer from recurring or continuous indigestion caused by the tumors of the abomasal mucosa which lead to impairment of the ingesta transportation and finally to ulceration with more or less severe bleeding.

These animals show alternating appetite and periodical or persistent dark-brown to blackish-tarry discoloration of their feces, which have a foul smell and may be diarrheic. Because of the admixture of blood, such feces give positive reactions to hemoglobin-testpaper (Heglostix) up to dilutions of 1:3000 and more.

The mucous membranes of these patients appear anemic and their general condition is weak (recumbency, cold ears, bumping heart beats).

The nature of the anemia observed in enzootic leukosis is always hemorrhagic; bone marrow and erythropoesis are obviously not involved or impaired by the lymphatic tumors. The hemorrhage mostly ensues into the lumen of the abomasum or, but much more seldom, after rupture of the tumorized spleen, into the abdominal cavity. The red blood picture is then characterized by anisocytosis, poikilocytosis, oligochromasia, and the occurrence of erythroblasts which should not be mistaken for lymphocytes.

In one fifth of the cases of enzootic leukosis presented clinically, the transport of ingesta from the prestomachs to the intestine is more or less impaired by tumourisation of the abomasum. This ensues in the accumulation of its contents, and especially of the heavier particles, mostly sand. The condition first implies a recurring, and finally a persistent and lethal stasis of the gastrointestinal flow with reflux of abomasal contents into the prestomachs, thus upsetting their activity too.

In advanced cases of abomasal tumorization or 'silting', that is, geosedimentation, you will feel a firm counterblow, or crepitation, when pressing your fist deeply into the right
### Table Four

Cytochemical reactions of the blood cells from normal and leukotic cattle

<table>
<thead>
<tr>
<th>Cell type</th>
<th>RNA</th>
<th>Polysaccharides</th>
<th>Lipids</th>
<th>Peroxidase</th>
<th>Lactate-dehydrogenase</th>
<th>Succinate-dehydrogenase</th>
<th>Alkaline phosphatase</th>
<th>Acid phosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils:</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>-/++</td>
<td>-</td>
<td>++/+++</td>
<td>-/++</td>
<td>-/++</td>
</tr>
<tr>
<td>Eosinophils:</td>
<td>+</td>
<td>+/+</td>
<td>+++</td>
<td>-/+(+)</td>
<td>-</td>
<td>-/++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Basophils:</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
<td>-/+</td>
<td>+/++</td>
<td>-</td>
<td>-</td>
<td>-/++</td>
</tr>
<tr>
<td>Monocytes:</td>
<td>+++</td>
<td>-/+</td>
<td>-/+</td>
<td>-/+</td>
<td>-/++</td>
<td>-</td>
<td>-/++</td>
<td>-/++</td>
</tr>
<tr>
<td>Lymphocytes:</td>
<td>++</td>
<td>-/+</td>
<td>-</td>
<td>(+)/+</td>
<td>-/++</td>
<td>-/++</td>
<td>-</td>
<td>-/++</td>
</tr>
<tr>
<td>Leukemic lymphoblasts</td>
<td>+++</td>
<td>-/+</td>
<td>-</td>
<td>(+)/+</td>
<td>-/++</td>
<td>-/++</td>
<td>-</td>
<td>-/++</td>
</tr>
<tr>
<td>Leukemic mast-cells</td>
<td>+++</td>
<td>+/+</td>
<td>-</td>
<td>++</td>
<td>-/+</td>
<td>-</td>
<td>-</td>
<td>-/++</td>
</tr>
</tbody>
</table>

- = untraceable; (+) = faint; + = weak; ++ = moderate; +++ = strong reaction

### Table Five

Synopsis of the essential criteria of the various forms of (tumorous) Bovine Leukosis

<table>
<thead>
<tr>
<th>Type</th>
<th>Occurrence</th>
<th>Age group</th>
<th>Cell line</th>
<th>Frequency of leukemic blood findings</th>
<th>Character of eventual anemia</th>
<th>Tumours of the lymphnodes</th>
<th>Organs preferentially tumorized</th>
<th>Involvement of the bone marrow</th>
<th>Agargel-immuno-diffusion-Test gp69</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphatic adult:</td>
<td>enzootic</td>
<td>&gt;2 years</td>
<td>lymphatic</td>
<td>65%</td>
<td>hemorrhagic</td>
<td>(+)</td>
<td>abomasum, heart, spinal membranes</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>sporadic</td>
<td>&gt;2 years</td>
<td>monocytic</td>
<td>100%</td>
<td>(hemorrhagic)</td>
<td>(+)</td>
<td>as in enzootic leukemia</td>
<td>(+)</td>
<td>?</td>
</tr>
<tr>
<td>Lymphatic calf:</td>
<td>sporadic</td>
<td>&lt;6 months</td>
<td>lymphatic</td>
<td>~</td>
<td>50% hypoplastic</td>
<td>(+)</td>
<td>liver, spleen</td>
<td>(⁺)</td>
<td>-</td>
</tr>
<tr>
<td>Lymphatic adolescent thymic:</td>
<td>sporadic</td>
<td>½-2 years</td>
<td>lymphatic</td>
<td>~</td>
<td>50%</td>
<td>(+)</td>
<td>thymus</td>
<td>(⁻)</td>
<td>-</td>
</tr>
<tr>
<td>Lymphatic skin:</td>
<td>sporadic</td>
<td>&lt;1 year</td>
<td>lymphatic</td>
<td>~</td>
<td>33% hemorrhagic</td>
<td>(+)</td>
<td>skin</td>
<td>(⁻)</td>
<td>-</td>
</tr>
<tr>
<td>Mastocytic adult:</td>
<td>sporadic</td>
<td>&gt;2 years</td>
<td>mastocytic</td>
<td>?</td>
<td>hemorrhagic</td>
<td>+</td>
<td>skin, muscles, lung, spleen, liver</td>
<td>(⁺)</td>
<td>(⁻)</td>
</tr>
</tbody>
</table>

- = negative or lacking; (⁻) = probably negative/lacking; + = positive or present; (+) = often, but not always; ? = unknown; = about
hypochondrium of the animal; this is first done slowly (to seek for crepitation), and then by several thrusts (to provoke an eventual counterblow).

In these animals, the clinical impression, and especially the outline of the animal seen from behind, is the same as in functional or any other anatomical stenosis of the pylorus, a condition which we may call the 'abomasal reflux syndrome': We observe an enormous increase of the abdominal perimeter with distension on the whole left and ventrally also on the right side. Palpation and percussion of the rumen show an overload with unstratified (mixed or frothy) ingesta.

Rumen juice samples obtained from such animals are usually characterized by grey-olive to dark brown color (depending on the presence of blood from abomasal ulcers), watery or foamy consistency, a stale-acid smell resembling abomasal contents, or a moldy to fecoidal smell. The biochemical activity of the rumen contents sample is diminished, with a reduction time of methylene blue delayed to 5 minutes and more, loss of the infusoria, and predominance of the Gram-negative bacteria; the pH maybe lowered, and a chemical analysis will show a normal concentration of lactates (30 - 40 mg/100 ml), but marked increase in chlorides (20 - 30, and up to 100 m.Eq./l). Besides, there is hypochloremic alkalosis and hemoconcentration.

In beginning leukotic tumORIZATION of the abomasum, the symptoms just shown are lacking. In these animals, exploratory rumenotomy may be of diagnostic help. Palpating the abomasum from the anterior pouch of the ventral rumen sac, its wall will be felt thicker than normal. Then, with the left hand well covered with mucus or oil, introduced cautiously and screw-like through the reticulomasa orifice, the folds of the abomasal mucosa can be touched directly, and a biopsy sample may be taken from their free border using the fingernails to pinch it off.

In spite of the fact that the uterus, vagina or perivaginal tissues, and exceptionally the ovaries are tumorized in almost one third of the animals with advanced enzootic leukosis, the lymphatic tumors of these organs do only rarely cause disturbances of fertility or of parturition.

These genital and paragenital tumors are usually detected, incidentally, by rectal exploration, at the end of pregnancy, during calving, or at the beginning of lactation: They form circumscribed or extended firm swellings of the organs named before. Thus, we may assume that the lesions often develop during, or at the end of gestation, without disturbing the maturation of the fetus.

We had only two bulls in the material with tumorous enzootic lymphatic leukosis. We do not believe that this is due to a resistance of the male or a predisposition of the female sex: It depends certainly on the fact that bulls only rarely reach the age necessary to develop the tumors, and that they are usually raised without close contact towards older BLV-shedding animals (and not serially bled for diagnostic purposes). One of our bulls showed marked leukotic lesions of his testicles. Transmission of enzootic leukosis by artificial insemination seems improbable (Bartlett, 1979); but the BL-virus has been found in bull semen recently (Lucas et al., 1980).

One fifth of our animals with enzootic leukosis showed uni-or bilateral exophthalmus from tumourisation of the retrobulbar lymph follicles. In a more advanced stage, this causes local venous stasis, edema, and thus protrusion of the conjunctivas around the eye. When the bulbous tissue impedes the movements of the eyelids, the cornea will dry, get solid and infected, and finally necrotize. In typical cases, its yellowish-brownish surface is then surrounded by a circular bead of tumored bleeding conjunctiva, as thick as a finger. This lesion may be differentiated from inflammatory orbital phlegmosis caused by traumatization or by metastatic infection (which are rare in cattle) by examining the lymphatic system of the animal.

Finally, the necrotized cornea will break, giving rise to evil-smelling panophthalmitis. Some owners call their veterinarian at this stage of the disease only, telling him that the eye has been 'hit' recently by a horn blow of another animal. If in doubt, do not operate on such an eye before having taken a biopsy tissue sample from the bulging conjunctiva, and wait for the result of histological examination. Here, in the United States, you will have to differentiate between leukotic tumors and 'cancer eye', a condition which is rather uncomont in our country.

One sixth of our cases with enzootic leukosis had locomotory disturbances of the hind legs caused by tumourization of the meninges. The predilection site for these lesions is between the last lumbar vertebra and the sacrum.

Contrary to traumatic paresis and paralysis of the hind quarters, where symptoms always occur suddenly, the impairment of gait observed in tumorous enzootic leukosis is gradually increasing and characterized by asymmetrical paresis of the pelvic limbs with steadily worsening ataxia, abnormal fexion of the tarsi and knuckling of the fetlocks; in the beginning, the active mobility of the tail is unimpaired. Within a week or two, getting up and lying down become more and more difficult to the animal, adopting the 'dog sitting' position until it is unable to rise and may thus simulate hypocalcemia or any other recumbency. In a selected case exophthalmus was a sign of help, and diagnosis could be cleared by rectal exploration, showing an enormous enlargement of the ileofemoral lymph nodes.

In one tenth of our material we found a tumor of the spleen clinically or at slaughter. Any splenomegaly causes percussory dullness at the posterior border of the projection field of the left lung.

Leukotic tumORIZATION of the spleen is nearly always accompanied by very high lymphocyte counts (20 to more than 800 thousand per cubic millimeter of blood): the leukemic lymphocytes of these cases are generally of the blast type, and you may find mitotic figures easily. Purulent splenitis also causes percussory dullness (and sensitivity) but may be differentiated by marked neutrophilia with a 'shift to
tissue in lymphatic tumorisation; we found high lymphocyte counts in the bone marrow smears of those animals only whose blood findings were leukemic. Therefore, the myelogram will not be of diagnostic help, clinically, in enzootic leukosis of cattle.

Respiratory symptoms, for example from an extreme tumor of the mediastinal lymph nodes, or from lymphatic infiltration of the respiratory muscles, are extremely rare in enzootic leukosis. Occasionally, pressure on the esophagus caused by such a lymph node may result in impairment of swallowing, rumination, or eructation, and cause tympany.

Urological symptoms are also very rare in enzootic leukosis: This kidney was found to be enlarged and to contain tumorous nodules on rectal exploration, and thus to participate in the tumorizing process, however, it still accomplished its uropoietic functions normally. (fig. nine).

Exceptionally, a tumorous thickening of the ureters may cause urine stasis and uremia; then, at rectal palpation, you feel a flabby mass surrounding the kidneys, which is due, as in other disturbances of urine flow, to an infiltration of urine into the perirenal fat tissue.

The liver rarely participates in macroscopical tumorisation, in spite of the fact that, microscopically, lymphatic infiltrations are often found in enzootic leukosis; our records contain only one animal in which the liver was so large that it could be felt from the rectum. Therefore, the usual liver function tests will give normal values in this disease.

Other rare exceptions seen by us were marked lymphoid tumorization of the muscles of the neck (one case) with permanent torticollis, and a tumor localized in the jugular vein; it may have been caused by puncturing this vein with a cannula used previously in another animal carrying the BL-virus, at least this is a frequent way of transmitting enzootic leukosis.

In conclusion, the symptomatology of tumorous enzootic lymphatic leukosis of cattle is so manifold that there are only a few bovine diseases to compete with. The course of this disease and of all other forms of leukosis of cattle is always fatal. In countries where the disease is controlled by serological methods (for example the immuno-diffusion-test), the tumorous stage has become rather rare today.

Now let me add some comparative remarks concerning the characteristics of the sporadic forms of bovine leukosis. If the leukemic cells of the blood smear show the attributes of monocytes, that is, a large indented and lobulated nucleus with a broad cytoplasm, and if there are no transitory forms between them and the lymphocytes, which themselves appear normally, it is justified to classify the case as one of monocytic leukosis. This diagnosis, however, has been made rarely (6 cases in literature, two own observation) until now. Maybe some of the animals affected with monocytic leukosis have been included in enzootic lymphatic leukosis, because its features (for example: age group affected, participation of lymph nodes and organs) seem to be nearly the same. As far as we know, monocytic leukosis of cattle occurs sporadically and serologically (for antibodies against the BL-virus) have not been done in such cases until now.

Sporadic lymphatic leukosis of calves is observed in animals under 6 months of age and will only accidentally occur in a farm where enzootic leukosis is known to exist; in some cases, a clear differentiation between calf and adolescent leukosis may be difficult.

The criterion of typical calf leukosis is the generalized and symmetric tumorization of all external lymph nodes, including those in the skin fold between the root of the tail and the tuber ischium and the inguinal lymph nodes; the latter are then sometimes mistaken for a premature development of the udder in the female or for enlarged testicles or an incarcerated inguinal hernia in male calves.

The generalized tumorization involves also all the internal lymph nodes. Perhaps, calf leukosis is already 'beginning' during the intrauterine development of the young animal; in any case, its frequency is rapidly decreasing with advancing age.

Another fact is that twin calves, if affected by calf leukosis, usually fall sick both and about the same time. The blood serum of leukotic calves is negative in the agar-gel-immunodiffusion test using the BLV-antigen.

In contrast to enzootic adult leukosis the liver and spleen are found macroscopically tumorized more often in calf leukosis.

The white blood picture is leukemic in about half of the cases, showing predominance of immature cells.

The nature of the anemia occurring in advanced sporadic lymphatic leukosis of calves seems to be hypoplastic and caused by leukotic infiltration of the bone marrow.

Sporadic lymphatic leukosis of the adolescent or thymic type is observed in young cattle of 6 months up to 2 years of age. It is characterized by marked tumorization of the thymus with irregular involvement of lymph nodes, especially the prescapular and mediastinal ones. When presented, the patient usually already shows a marked painless swelling ventrally at the entrance of the chest, about the size of a loaf of bread. The consistency of the thymic tumor itself is firm, but, in advanced cases, this may be 'masked' by an enormous collateral 'cold' edema. To detect the firmness of the central mass, the brisket should then be 'rocked' from one side to the other between the palpating fingertips of both hands.

From the brisket, the greyish-yellow tumor masses continue into the anterior part of the mediastinum thus compressing the esophagus, the heart and the roots of the large veins, and impairing the blood flow in the jugulars as
well as swallowing, rumination, and eructation. Therefore, the animal is off feed, tympanic and dull. On percussion there is a marked area of complete dullness in the ventral part of the chest wall; dorsally, this area is delineated by a horizontal border from the area of pulmonary resonance. The dullness is caused by the accumulation of thoracic fluid which contributes further to the compression of the heart and finally also impairs respiration. Therefore, animals affected by thymic leukosis usually die from circulatory failure or from suffocation. The white blood picture is leukemic in about half of the cases; the immunofluorescence test using the antigens of the BL-virus gives negative results.

Regional differentiation of thymic leukosis has to consider pericarditis (where there is brisket edema without central liver tumor, and pericardial murmurs are to be heard), nephrosis/amyloidosis (where there is brisket and intermandibular edema without thymic tumor, and the kidney is found larger than normal; proteinuria, low specific gravity of the urine), and phlegmosis caused by paravenous irritation, resulting in dark crusts which have an evil smell when decaying. Besides the skin lesions, there are nearly always tumors in some lymph nodes and/or in the same organs which are usually involved in enzootic leukosis. The white blood picture is found leukemic in one third of the cases of skin leukosis; serologically, there are no antibodies (AGIDT) against the BL-virus.

Now we come to sporadic lymphatic skin leukosis (fig. ten). It nearly exclusively affects adult animals and has until now not been observed in herds with enzootic leukosis. The characteristic lesions of the skin initially appear and later form up to the size of a hand's palm and up to half a finger's thickness; they are hairless and bleed easily after mechanical irritation, resulting in dark crusts which have an evil smell when decaying. Besides the skin lesions, there are nearly always tumors in some lymph nodes and/or in the same organs which are usually involved in enzootic leukosis. The white blood picture is found leukemic in one third of the cases of skin leukosis; serologically, there are no antibodies (AGIDT) against the BL-virus.

A particularity of lymphatic skin leukosis mentioned in the literature is the observation that the tumors may disappear completely for some time; later, they usually recur. Concerning differential diagnosis, skin leukosis of cattle should be distinguished from dermatophilosis (thick crusts, skin scrapings), urticaria (rapid onset, soft consistency of the skin swellings, involvement of eyelids, muzzle and vulva, respiratory distress), papillomatosis (site and form of the tumors), and from mast cell tumors. Curiously, cattle never suffer from myeloid leukosis, that is from tumors of the granulocytic series. In veterinary literature, some odd cases of so-called 'eosinophilic leukosis' have been described, which were partly denominated 'chloroleukosis' because of the greenish color of the tumors. After having thoroughly examined such an animal along with our Pathology Department we are convinced that these cases were malignant mast cell tumors. These invade all the skin, forming firm nodules, which may show a tendency to bleed.

Other organs found involved are lymph nodes, muscles, lungs, spleen, liver, abomasum, and intestine. The surface of cut mast cell tumors is greenish-yellowish and feels soaplike to the touch. With the usual histological stain, the microscopic impression is that of a tumor consisting of eosinophil granulocytes. The actual structure of the malignant growths is recognizable after metachromatic staining only (blue toluidine blue, cresylviolet), showing the mastocytes.

In our observation, these tissue mast-cells were also found in smears of the bone marrow and in blood smears also. Therefore, the case was classified as mastocytic leukosis. As far as we know about this rare form of the bovine leukosis complex, it has no connection whatsoever with enzootic leukosis; serologic controls (using BLV-antigen) have so far not been done. In cattle with skin tumors, especially bleeding ones, mast-cell leukosis should be considered as a differential diagnosis, besides lymphatic skin leukosis.

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**ADDENDUM**

"Diseases of the Ruminant Stomachs and Intestines of Cattle," by Dr. Otto Radostits. Proceedings of the 13th Annual Convention, American Association of Bovine Practitioners (pp. 63-97).

The editor regrets that the following bibliography was omitted from the Proceedings.

4. Whitlock, R.H. & Becht, J Bovine Gastrointestinal System: A Re-

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**Selected Reference**


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NOVEMBER, 1981