N° d'ordre : .....

الجمهورية الجزائرية الديموقراطية الشعبية

People's Democratic Republic of Algeria

وزارة التعليم العالي و البحث العلمي

Ministry of Higher Education and Scientific Research

Institute of veterinary science -Blida University Saad Dahlab-Blida1



Defense of an end-of-studies dissertation to obtain a veterinary doctor's degree

Bibliographic study on the main tumors in ruminants

Presented by LARBI Nour el Houda Sustained the 4<sup>th</sup> july 2023

In front of the jury:

President :LOUNAS.AMCAISV Blida 1Examiner:AOURAGH.HMAAISV Blida 1Promoter:METREF AKMCBISV Blida 1

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To our jury president,

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To our examiner jury,

Miss the Doctor,

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#### ABSTRACT

Tumors in ruminants are abnormal growths of cells that can occur in any part of the body. They can be benign or malignant but certain tissues develop only malignant forms (lymphoma, glioma, etc...), and can cause various clinical signs depending on their location and size . The most common tumors in ruminants are lymphoma, leukemia, squamous cell carcinoma, and melanoma.

Tumor or also called neoplasm refers to new cell growth. It is popularly known as tumor (swelling), but not all swelling is considered as a neoplasm. This neoplasm study is called oncology, oncos - tumors, logy- study.. whereas all tissues and organs may be impacted, at different frequencies and preferred locations wich depends on species, race, age, gender, exposure to potentially carcinogenic substances.

A few of the most common tumors, such as lymphoma and spinocellular carcinoma have better documentation.. So on the other hand, ocular squamous cell carcinoma manifests as an infiltrating palpebral mass in adult cattle with low periocular pigmentation.in the similar way, juvenile and dermal forms of LBS affect young dairy cattle with polyadenomegaly or skin nodules. Nevertheless other tumor processes, that are related to the organ involved in the primary tumour or metastases.

Histology examination is the microscopic examination of tissues to study the appearance of cells and tissues in order to diagnose tumors such as another diseases . It is an important tool for the diagnosis of cancer. Hence it is the confirmatory exam of tumors ,. Usually the immunohistochemistry is the most frequent histological examination

Necropsy can be used to diagnose tumors , It is a postmortem examination of an animal to determine the cause of death or to evaluate pathological conditions. it is the ultimate diagnostic destiny of most of the experimental animals.

The diagnosis by necropsy can still be used to implement prevention at the flock level whenever possible due to the impact of tumors which can result in reduced production and trade restrictions.

Finally even if all animal species can develop neoplasia and all organs can be affected, The economic and medical consequences of tumours in ruminants are also often underestimated.

#### **RESUME**

Les tumeurs chez les ruminants sont des croissances anormales de cellules qui peuvent se produire dans n'importe quelle partie du corps. Ils peuvent être bénins ou malins mais certains tissus ne développent que des formes malignes (lymphome, gliome, etc...), et peuvent provoquer divers signes cliniques selon leur localisation et leur taille .

Les tumeurs les plus courantes chez les ruminants sont le lymphome, la leucémie, le carcinome spinocellulaire et le mélanome.

Tumeur ou également appelé néoplasme se réfère à la croissance de nouvelles cellules. Il est populairement connu comme tumeur (gonflement), mais pas tout gonflement est considéré comme un néoplasme. Cette étude de néoplasme est appelée oncologie, oncos - tumeurs, logy- study.. alors que tous les tissus et organes peuvent être affectés, à des fréquences et des emplacements différents qui dépendent de l'espèce, de la race, de l'âge, du sexe, de l'exposition à des substances potentiellement cancérigènes.

Quelques-unes des tumeurs les plus courantes, comme le lymphome et le carcinome spinocellulaire ont une meilleure documentation.. Par contre, le carcinome spinocellulaire oculaire se manifeste sous forme de masse palpébrale infiltrante chez les bovins adultes dont la pigmentation périoculaire est faible.De la même façon, les formes juvéniles et cutanées d'AFB affectent les jeunes bovins laitiers atteints de polyadénomégalie ou de nodules cutanés. Néanmoins d'autres processus tumoraux, qui sont liés à l'organe impliqué dans la tumeur primaire ou des métastases.

L'examen histologique est l'examen microscopique des tissus pour étudier l'apparence des cellules et des tissus afin de diagnostiquer des tumeurs telles qu'une autre maladie . C'est un outil important pour le diagnostic du cancer. Par conséquent, il est l'examen de confirmation des tumeurs , Habituellement, l'immunohistochimie est l'examen histologique le plus fréquent .

L'autopsie peut être utilisée pour diagnostiquer les tumeurs , Il s'agit d'un examen postmortem d'un animal pour déterminer la cause du décès ou pour évaluer les conditions pathologiques. c'est le destin diagnostique ultime de la plupart des animaux expérimentaux.

Le diagnostic nécropsique peut encore être utilisé pour mettre en œuvre la prévention au niveau du troupeau chaque fois que possible en raison de l'impact des tumeurs qui peuvent entraîner une réduction de la production et des restrictions commerciales.

Enfin, même si toutes les espèces animales peuvent développer une néoplasie et que tous les organes peuvent être affectés, les conséquences économiques et médicales des tumeurs chez les ruminants sont souvent sous-estimées.

#### الملخص

الأورام في المجترات هي نمو غير طبيعي للخلايا يمكن أن يحدث في أي جزء من الجسم. يمكن أن تكون حميدة أو خبيثة ولكن بعض الأنسجة تتطور فقط إلى أشكال خبيثة (سرطان الغدد الليمفاوية ، الورم الدبقي ، إلخ ...) ، ويمكن أن تسبب علامات سريرية مختلفة اعتمادا على موقعها وحجمها .

الأورام الأكثر شيوعا في المجترات هي سرطان الغدد الليمفاوية وسرطان الدم وسرطان الخلايا الحرشفية وسرطان الجلد. الورم أو يسمى أيضا السرطان يشير إلى نمو خلايا جديدة. ومن المعروف شعبيا باسم الورم (تورم) ، ولكن لا يعتبر أي انتفاخ تورم، في حين أن جميع الأنسجة والأعضاء يمكن أن تصاب ، على ترددات ومواقع مختلفة تعتمد على الأنواع والعرق والعمر والجنس والتعرض للمواد التي يحتمل أن تكون مسرطنة. بعض الأورام الأكثر شيوعا ، مثل سرطان الغدد الليمفاوية وسرطان الخلايا الحرشفية لديها توثيق أفضل. في المقابل ، يحدث سرطان الخلايا الحرشفية العينية ككتلة جفنية على أبقار LBS غازية في الماشية البالغة ذات التصبغ المنخفض حول العين وبالمثل ، تؤثر أشكال الأحداث والجلد من الألبان الصغيرة المصابة بتضخم الغدة أو عقيدات الجلد. ومع ذلك ، فإن عمليات الورم الأخرى ، والتي ترتبط بالعضو

الفحص النسيجي هو الفحص المجهري للأنسجة لدراسة مظهر الخلايا والأنسجة من أجل تشخيص الأورام مثل مرض آخر. إنها أداة مهمة لتشخيص السرطان. لذلك ، هو الفحص التأكيدي للأورام ، عادة ما تكون الكيمياء الهستولوجية المناعية هي الفحص النسيجي الأكثر شيوعا يمكن استخدام تشريح الجثة لتشخيص الأورام ، وهذا هو فحص ما بعد الوفاة للحيوان لتحديد سبب الوفاة أو لتقييم الحالات المرضية، لا يزال من الممكن استخدام التشخيص التشريحي لتنفيذ الوقاية على مستوى القطيع كلما أمكن ذلك بسبب تأثير الأورام التي يمكن أن تؤدي إلى انخفاض الإنتاج والقيود التجارية.

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#### LIST OF ABBREVIATIONS

**SCC**:Squamoss cell carcinoma. **BPV:** Bovine papilloma virus . **OPC:** ovine pulmonary adenocarcinoma. **BCA:** Broncho-alveolar cancer. **JSRV:** jaagsiekte sheep retrovirus **LTR:**Long terminal repeat . HYAL2:Hyalorunidase2. PCR: polymerase chain reaction . **ENAG:** Enzootic nasal adenocarcinoma in goats. **ENAS:** Enzootic nasal adenocarcinoma in sheep. **ENT:** Enzootic nasal tumor **ENTV:** Enzootic nasal tumor virus. **PHT:** Primary hepatobilliary tumor **HCT:** Hepato-cellular tumor. **HCC:** Hepatocellular carcinoma. HCA: Hepatocellular adenoma. **CCA:** Cholongio-adenocarcinoma. **EBL:** Enzootic bovine leukosis. **SBL:** Sporadic bovine leukosis . BLV: Bovine leukemia virus. **TNF:**Tumor necrosis factor. LN: Lymphoid nodules . **CNS:** Central nervous system. **SNP:** Peripheric nervous system . **PNST:** Peripheral nervous sheath tumor.

# INTRODUICTION

#### **INTRODUCTION**

A tumor is a mass of neoformed tissue, except leukemia. It results from a disorder of proliferation and cell differentiation that is irreversible, with the exception of certain neoplasms such as papillomas (1). The tumor has a biological autonomy that results in a lack of response to control mechanisms. Unlike hyperplasia, it persists and increases even in the absence of the stimulus. Key genes are involved in the development of many cancers.

There are relatively few reports of tumors in ruminants compared to other domestic animals like dogs, cats. One propable reason is that most ruminants are not young enough to predispose them to tumour development.they are distinguished in two types ; benign tumor qualified as an organoid, malignant tumor determined as an infiltrating growth. Despite the lack of resources and interst about this topic wich refers to the age factor their rare incidence in trhis species (2). but even if all this we should focus on this domain because they can cause many complications on human health since their meat is edible, this consequences are not immediately appeared but over the time the human health will be influncef by a cumulative effect (3).

In this bibliographic review, current knowledge on major tumors in ruminants will be summarized.

We will focus on the macroscopic aspect as well as on the microscopic aspect also on their pathogenesis and their methods of diagnosis. For that we are interested on this topic in order to develop our knowledge about tumors occurring in ruminants and go deeper in this domain, for the propose of helping futur research and to show the elements that are most important for the diagnosis of a ruminant tumour, so what are the most common tumor that can affect the ruminants?

## **I.Cutaneous tumor:**

#### I.Cutaneous tumor:

#### **1.Definition**

Tumors of skin are not only dangerous to humans, but also a major issue in animal populations.cattle,horse,camel;sheep;goats all suffer from cancer (1). According to the studies, they make up 8-34% of bovine tumours, making the skin one of the main organs affected, . The impact appears to be in 8-year-olds( (2)),the most common cutaneous neoplasms are the squamos cell carcinoma and papilloma, Other rarer cutaneous tumours are described as melanomas, mastocytomas, histiocytomas, lipomas and liposarcomas, fibromas and fibrosarcomas, myxomas and myxosarcomas, and tumors of the sweat glands (3).this kind of tumors are seldom responsible for mortality and the resulting production losses are primarily a depriciation of leather( (2).

In sheep, the tumors of the various integrations account for 3.7% of the total tumors( (4)

**Squamous cell carcinoma:** It is a malignant tumour of epidermic cells and keratinocytes, they are classed as actinocancerous thus, known in numerous mammalian species; including man. it is locally invasive, but has little metastasization of local lymph nodes or other organs. the majority of squamos cell carcinoma have a low degree of malignancy. in particular those associated with sun dermatitis but some are malignant.hence the site of the tumor is almost always unique. they can be found in all skin areas however in cattle squamous cell carcinoma occurs preferentially at the level of the three areas:

**the eye and its annexes:** it includes malignant lesion caused by the epithelial cells of the occular globe, the palms or the periorbital skin, as well as the begnin lesions preceding the onset of cancer.

**the vulva :** Squamous cell carcinoma exacerbates the muco-cutaneous junction of the vulvar lips and can extend to the anus and perineal area.

**the horns :**it originates from the frontal sinus epithelium ,the tumour progressively invades the centre of the horn causing its fall (2).



Figure 1: SCC lesion involving the lower eyelid, nictitating membrane, and conjunctiva in a Holstein cow with pink skin (3).



Figure 2:Bovine limbal SCC (3)



Figure 3:Coroneal limbal SCC (3)

**Papilloma:**Papillomas are benign and exotic proliferations of epithelial revetements most often localized on the skin revetement where they are later called warts, they may also exist on the genital and digestive mucosa.Bovinepapillomas are tumours which usually regress spontaneously, but may also persist in some cases, as well as malignant transformation is a rarity (2).

Outbreaks of papillomatosis have been reported in ovine and porcine animals, but remain rare. In goats, papillomas are mostly localized on the head and ears, and primarily affect poorly pigmented skin (5).

#### 2.Etiology

When it corcens the squamos cell carcinoma the cause still poorly understood; however, the influence of various factors is recognised in carcinogenesis: exposure to ultraviolet rays, lack of epidermal pigmentation, and probable viral damage (6).

For papilloma the agents responsible are bovine papillomavirus, also known as BPV (Bovine PapillomaVirus).

#### 3.Macroscopic appearence

The coarseness of the lesions depends on their placement.

**Papilloma:** The papillomas have a verrucous or granular aspect and are pediculate (6). Finally if malignant progression in squamous cell carcinoma occurs, the lesion is more granular, hemorrhagic or ulcerated. Rather, a round white warty lesion is observed in the cornea.

**Squamos cell carcinoma:** at first we observe Sun dermatitis or keratosis at the junction of the mucous membrane or skin, It is characterized by swelling or erythema. This is followed by a thickening of the epidermis with ulceration. the surface of the lesion is granular hemrragic or ulcerous. The tumour then invades the dermis and becomes more indurated. Peritumoral tissue inflammation can often be seen (2).

The lesions on the eyelids are more diffuse and invasive, and may resemble an inflammatory ulcer. Blood clots, necrotic tissue and pus are all possible. Purulent conjunctivitis is often related to squamous cell carcinoma in the eye (2).

In cases of vulvar location; The clinical apppearence of the cancerous tissue was ulcerative masses, usually with bleeding surfaces at the pattern distribution of the vulvar lip.while the

tumor may still be palpated deeply into the tissues. where the majority of a tumor was a deep fistula discharge of fetal pus was commonly present (7).

When horns are affected, in majority the left horne is attacked.there is then a clear line of separation between the horn and the skin. At times, a greyish, thick and felted material emanates from this slot. Later, the release of the horn increases and, by moderate pull, it can be removed, leaving the impaired core exposed.

#### 4. Microscopic appearance

**squamos cell carcinoma**: there is severe hyperplasia of the epidermis with hyperkeratosis or parakeratosis. Cornea globes made up of concentric layers of keratin are characteristic, the cellular shape is variable. they can be cubic or cylindrical or at the periphery of the tumor or flattened at the centre with differentiation of the corneocytes.we observe a voluminous hyperchromatic nucleus with large nuclei and mitotic patterns (2).

in well differentiated types, cells are arranged in clusters or cords with often keratinized centers. Intercell bridges are readily observable. on the other hand, types that are not widely differentiated are more difficult to identify. keratinisation is often restricted and related to caryorrhexia(the destructive fragmentation of the nucleus of a dying cell, its chromatin being distributed irregularly in the cytoplasm); (2).

**papilloma:** it presents hyperplasia of the different layers of the epidermis, accompanied by acanthose and hyperkeratosis (9) as well as irregular papillary protrusions of the epithelium in the dermis (10). The tumor epithelium is ongoing with the normal epidermis (11).

#### **5.Pathogenesis**

**Squamos cell carcinoma**:Occular squamous cell carcinomas metastasize only after a prolonged period of growth.localmetastases;when the nictitant membrane or eyelids are affected by invasion of the orbital bone cartilage and nasal cavity.the lymph node (parotidal) is invaded only at the advanced stages of the disease.metastases may be found in other lymph nodes as well as in the heart; in the liver; in the lungs; in the pleura and kidneys.Hematologicaldesissimination has not been reported (2).

Bovine horn cancer has the biological features of an epidermoid carcinoma in humans.

It seeps into the adjacent soft tissues of the dermis and occasionally metastasises to other parts of the body. The metastasis found in our study in the parotid gland of an animal is a sure evidence that H.C. is a malignant growth.

As for the vulvar location, the lesions appear at the cutaneous-mucosal junction and can extend to the perineal and perianal regions; usually a mass tending to grow infection.hence spinocellular carcinoma in the anal and perineal area has been described in an elderly bull (12).

The sequence of lesions is similar to the one observed at the level of the eye note corneal lesions the Malpighian cells indeed have the ability to produce corneal tissue.

**Papilloma:** the pathogenicity of the virus is limited to minor mucous membranes.and it seems to be strongly linked to the process of differentiation of epithelial cells.so the virus comes into the body most often by contact and then persists in a variable manner depending on the lindividu and its immunity.the virus infects the keratinocytes in the basal layer and then expresses part of its genome in the basal and superbasal layers of the epidermis.Genome replication occurs in the spinous and granular layers, and then the structural genes are expressed in the corneal layer.In this way, new infective viral particles are obtained in the keratin scales eliminated during skin desquamation;This allows for further infection (2)

# **II.TUMORS OF INTERNAL ORGANS**

#### **II.TUMORS OF INTERNAL ORGANS**

#### 1. Tumors of the respiratory system

#### 1.1.ovine pulmonary adenocarcinoma

#### 1.1.1.definition

ovine pulmoary adenocarcinoma (OPA) is contagious tumor of the respiratory epitheluim affecting small ruminants for wich a viral etiology has been prooved ;this animal cancer is simillar to a human bronchioloalveolar cancer (BCA); (13) .

#### **1.1.2.** Macroscopic appearence

OPA is recongnized by two pathological forms are classical and atypical. In the classical forms; When the chest is opened the lungs do not collapse and they appear enlarged; the neoplastic lesions may be involved in any part of the lungs but the cranioventrical parts are particulary involved with a grey or purple color also an increased consistency.

At an early stage the neoplastic zones are small discret nodules then vary to diffuse extensive lesions wich are usually bordered by small satelitte nodules(Fig. 1a)The cut surface of the tumor lesions presents a granular aspect ,exudes a foamy liquid and it's moist(Fig.1b).

Mediastinal and traqueobronchial lymph nodes may also be enlarged even contain metastasis, occasionally an extrathoracic spread of tumors has been reported. Atypical forms are usually subclinical and used to be found incidentally at necropsy or abbatoir studies, the nodules are mainly located in diaphragmatic lobes in solitaire or multiple aspects with hard coherence and pearly white color (Fig. 2a); the incision surface of the nodules is dry with a very well delineated from the surrouding areas (14); (Fig. 2b).



Figure 4:Gross pathology of classical OPA. a. The black arrows indicate diffuse extensive tumour lesions, bordered by small satellite nodules. b. The cut surface of the tumour lesion is moist and frothy fluid is pouring from the bronchioles (14).



Figure 5:Gross pathology of atypical OPA. a. The black arrows indicate a well-demarcated white tumour nodule. b. Transverse section of a nodule showing a dry surface (15).

#### 1.1.3.Microscopic appearence

The natural cases of OPA are histologically characterised by a mixed multifocal ;papillary and/or acinar adenocarcinoma in alveolar(Fig. 3a) an bronchiolar regions(Fig. 3b) ;wihout vascular or pleural invasion (13).variable amounts of lymphocytes may infiltrate into the tumoral stroma ; the neoplastic alveoli and affected bronchioles are found bounded by plasma cells and connective tissues fibres and macrophages .in the case of a secondary bacterial infection a neutrophils can also be found (14).the atypical forms present essentially the same appearence but the epethilial neoplasia is more often acinar and the stroma is over-infiltrited by inflammatory cells and connective fibres .



Figure 6:Histological observation of an OPA lung section stained with haemotoxylin and eosin. a. Neoplastic proliferation of epithelial cells with cuboidal or prismatic morphology in an alveolar region. b. Bronchiole showing epithelial cells growing in a papillary pattern (16).

#### 1.1.4.Etiology

Ovine pulmonary adenocarcinoma is caused by jaagsiekte sheep retrovirus (JSRV) ; wich induces the transformation of epithelial cells of bronchioli and alveoli. JSRV genome is simple and the oncogene is unknown but it is well reported that the expression of the envelope glycoprotein is oncogenic through itself .in small ruminant JSRV presents an interaction with the cells via the Hyal2 receptor . the tumoarldevelopement and the telomerase activation are associated to each other (13) .

it is envelopped RNA virus ,dependent for its replication of the reverse transcriptase and a RNA dependent DNA-polymerase .during early phases of the virus cycle the provirus is definetely integrated into the cellular genome and will persist in DNA-host for the rest of life (15).

#### 1.1.5.Pathogenesis

The infection occurs in wide way ;by oncogenic reterovirus (JSRV) thus the glycoprotein of surface and the viral particle present at the surface of viral envloppe and LTR(long terminal repeat) regions interacting specifically with a cellular receptors allowing entry of the virus into the cell.

Therefore it has been established that the cellular receptor of the JSRV is Hyal2(hyalorunidase) inducing the transformation of the pneumocytes of type II And clara cells by JSRV wich replicates actively only in these epithelial differenciated pulmonary cells transformed . it has a broad cellular tropisme but despite this the viral expression is restricted to bronchoiolar and alveolar epithelial cells (13), as a result from coalescing smaller masses a one large tumor is formed; in naturals circmustances, the transmission of JSRV happens most commonly via the aerosol route.affected animals produce a lung fluid wich is contagious and more effective in spreading the disease therefore apparently the virus is able to spread even before the appearence of clinacl signs.

The close contact between susceptibles animals is a major risk factor, in an other side the lambs could be infected after birth from JSRV-infected dam ;by suckling the milk and colustrumwich contain the virus.in other study by PCR it has shown that vertical transmission is possible from OPA-affected ewes to fetuses .

The outcome of JSRV infection is potentially influenced by secondary infections or genetic resistance ,in the case of an infection the absence of a detectable immmune response to the virus (16).

Diagnostic:in lung tumors cells or inlung secretions wich accumulates inthe airways of the most animals with clinical signs, JSRV antigens are readily detectebale by immunohistochemistry or ELISA only . it was revealed occasionally the lymphoid cells contains JSRV antigens by immunohischemistry in mediastinal lymph nodes draining lungtumors (17).

#### 1.2.Enzootic nasal tumor

#### 1.2.1.Defenition

Enzootic nasal adenocarcinoma (ENAG) wich affects goats ;but also known as (ENAS) when it affects sheeps ; this contagious respiratory tumor present a neoplastic disease wich results from ethmoidal turbinate nasal mucosa ,it is an adenocarcinoma of the secretory epithelial cells (18).

wich cause several cranialdeformation and respiratory blockage due to the evetuall progress of tumors and it ends up with the death (19).

OPA and ENT are independent disease but it has been noted before the co-infection of the sheep by JSRV and ENTV-1 (16).

#### 1.2.2.Macroscopic aspect

At necropsy,we found tumors in the nasal cavity, either unilaterally or bilaterally originating from the ethmoidal mucosa, thus the normal architecture of the ethmoidal conchae is altered. they consist of soft, grey or reddish-white in color with a mucus covering the fine granular suurface an inflammation of necrosis or purulent type could be seen (18), frequently, in the nasal adjacent cavity inflammatory polyps accompanied the tumors (20).

#### 1.2.3.Microscopic aspect

The tumors are usually presented in law-rate adenocarcinomas, adenomas or adenopapillomas, the neoplastic tissue is moist and invase locally but the metastasis is rare (20).

Epithelial secretory cells proliferate into an acinar,tubular,papillary or solid patterns are revealed by microscopy light, external zones have a clear papillary patterns whereas

internal regions of the tumors are more acinar or tubular . the stroma is infiltrated by scattred or gourped lymphocytes/plasmocytes cells in spite of it itscanty .it's been proven by electron microscopy and histologically studies that neoplastic cells corresponds serous ,mucos or mixed glands and seem to arise either in olfactory or respiratory mucosal glands (18).



Figure 7:Gross pathology and histopathology of enzootic nasal adenocarcinoma of sheep. A: Skull section showing tumor originated in the ethmoidal mucosa. Etmoidal nasal turbinates have been replaced by the tumor growing pressing dorsal and ventral conchae and causing obstruction of the nasal passages. B: Histopathology of the tumor. Nasal glands proliferate in an acinar and tubular pattern (asterisks). Nasal gland epithelia proliferates in tubulopapillary pattern (star). Lympho-plasmocytic cells infiltrate the interstitium(3).

#### 1.2.4.Etiology

ENT is associated with two different retroviruses ;ovine nasal tumor virus ENTV-1 in sheep also( enzootic nasal tumor virus type-1) and type-2 (caprine nasal tumor virus)ENTV-2 in goats ; although they cause the same disease in the two host species .

ENTV-1 ;ENTV-2 and JSRV present a simillarity with each other in their genomes ; rated more then 92% but there is a differences squences between them (16).

Whereas ENTV-2 establishes a deployed lymphoid infection ;ENTV-1 is mainly bonded in the tumor (14).

#### 1.2.5.Pathogenisis

In addition to the similarities presented by these three retroviruses (ENTV-1;ENTV-2;JSRV); ENTV-1 uses Hyal2 receptor like JSRV to interact with mammalian cells in order to assure attachement virus and entry and finally can infect a wide range of cells.

so the epithelial nasal cavity show a viral LTRS (long terminal repeat) where the ENTV-1 active replication is mostly limited on it the oncogenic properities are mainly in envloppe

proteins wich an importance to this active replication (18).however, ENTV-1 env and JSRV env own the same transforming activity, also it seems that they act through an identical transduction steps (16).

#### 1.2.6.Diagnostic

Currently for ENTV-1infected sheep a diagnostic test is not available to detect it ; but sheep with small tumors and some of them clinacally blind can be detected using a specific PCR methods (18).

In sheep, respiratory tumours account for 12% of all tumours. Almost all (96%) are adenomas (21).

#### 2.2.Tumors of the liver and galbladder

#### 2.2.1.primary hepatic tumors

#### 2.2.1.1.Definition

Primary hepatic tumors are the tumor of liver pranchyma and biliary tract ; thus expecting the cholangiocarcinomas they may be found in immature and adults (22);they are quite frequent in animals according to Kelly (1985) probably they are classified after lymphomas as the most common visceral tumors in cats ,cattle , sheep and dogs. Among primary hepatobiliary tumors(PHT) ;hepatocellular tumors(HCT) are listed as the most common tumor in the cattle as in other animals and man (23); as it is been established that there is no significant correlation between the primary hepatic tumors and the presence of any pre-exsiting disease process (22).

**Hepatocellular carcinoma :** (HCC) is a malignant neoplasmof hepatocytes with three forms of exhibitation :massive,nodular and diffuse with rare occurrence in farm animals with ruminants being the most affected species (24); and they present the majority of HCT (80 %); (25).

**Hepatocellular adenoma :**(HCA) present the minority of hepatocellular tumors ;usually they affect certainly the immature ones ,as well known the tumor is formed with well-deffirenciated hepatocytes (26).

#### 2.2.1.2 Macroscopic appearance

There were no noticable macroscopical differences between hepatocellular carcinomas (HCC) and adenomas (HCA) ; (23); .at necropsy the liver appeared hypertrophied,non-luster with a dull edges ;deposition of fibrin on the surface and generally protruded above

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its surface (fig5-A) by hepatocellular tumorsexhibitied as a distinct multiple pale to white foci , forming a well-delineated masses variable in sizes ,rounded ;fairly soft and spongy nodules ;mostly solitary (solitar nodules form)and in some cases multiple (multinodular form) ; those two last forms have a relative predilection for the right lobe,sometimes replacing the entire liver (diffuse form).on the crackling cut surface the nodules (fig5-C-D)present a sharply circumscribed borders and a connective tissue wich divided them into thin lobules ,and for the tumor parenchyma was friable and had a mottled appearence with a various range of colours from greyish-white to red ;brown ;yellow and green refering to the presence of necrotic ,heamorragic and cystic areas ,cholestasis and lipid infiltration ; in other few cases of HCC metastasis was observed in portohepatic lymph nodes ;in the kidney cortex ; and diffusely in the parenchyma of the lung (27), (23); (24) .



Figure 8: Macroscopic examination of the liver of a cow with CHC. A- Area of adhesion between the border of the liver and the abdominal wall. B- Liver with multiple nodules of varying sizes and irregular surface C- liver at the cut evidencing nodules that deepened and evidenced crackling. D- Cutting surface of liver tumor mass with irregular white - yellowed areas interspersed with fibrous tissue and areas with necrosis and hemorrhage (14).

#### 2.2.1.3. Microscopical appearance

Through the histolopathological examination of nodules showed the neoplastic masses that consisted of hepatocytes cells-like cells but larger then the normal ones with discret to moderate cytoplasm and eosinophilic to pale; thus round centrale nuclei, fragmanted chromatin and evident nucleolus. with the addition of the considerable varied histological appearence of HCC according to the degree of deffirentitaion and histological arrangement of hepatocytes. hence HCC are

classified into four groups :pseudoglandular ;compact ;scirrhous and trabecular wich present the most common pattern (23); (27).

Adenomas are compound from a uniforme proliferation of two or three cells in thickness; arranged mainly in tubules or cords and they are simillar to normal hepatocytes. sinosuidalcapilaries surrounded them and supported by a still intact reticulum; usually liver cells-adenomas are well-demarctaed and solitary also the portal triads is absent, and no tumoral-invasion to the adjacent tissue (23).

#### 2.2. 1.4. Etiology

Hepatocellular carcinoma has a spontaneous occurrence, through its etiology is unknown but chronic infections ( parasites, viruses and bacteria) hereditary ; dietary and hormonal factors thus chemical ingestion (aflatoxins ; pyrrolozidines and nitrosamines) may be a promoting agents in tumor development (27).

#### 2.2.1.5.Pathogenesis

Although little is known about the mechanisms of hepatocarcinogenesis, some signalling routes are frequently deregulated.Hepatitis viruses have a direct oncogenic role through interaction between viral proteins and cellular proteins,which control cellular homeostasis, or by integrating the genome of the hepatitis B virus into the host genome (28).

#### 2.2.1.6.Diagnostic

The diagnosis of HCC is based on clinical (lean, active, with mucupurulent secretion in nostrils; ocular conjunctiva edema; and edema of the dewlap); and it is carried out postmortem .

Although histopathology is the definitive diagnosis of this neoplasm, such as a complementary test like hemogram(neutrophilia, trombocytopenia); bio-chimestry(hypofibrinogemia, hypoproteinemia), ultrasongraphy, urinalysis (24).

#### 2.2.2.Neuroendocrine carcinoma of the liver and the gallbladder:

#### 2.2.2.1.Definition

Neuroendocrine carcinoma is a tumor wich originates from the scattered neuroendocrine system. They are uncommon in men and rarely seen in pets (29).

#### 2.2.2.2Macroscopic appearance

Restricted examination of other viscera revealed an enlarged liver, with all lobes containing pale, circumscribed,non encapsulated foci depressed ,1\_4 cm in size.the gallbladder has been expanded to nearly double its size and the surface of the mucosa presented diffuse villiform outcrops(fig2), pedunculate, 3-4.5 cm and 2-3 cm long (30).

#### 2.2.2.3.Microscopic appearence

Histology showed that hepatic parenchyma was infiltrated by trabecular neoplastic cells, acini and rosettes divided by bands of variable size of connective tissue fbre. The projected masses of the gall bladder mucosa were composed of a loosely arranged matrix stem of edematous connective tissue(fig2.B), bordered by ciliated columnar epithelium and with zones of glandular hyperplasia represented by numerous cystic submucosal glands filled with mucus(fig2;A).

A mild lymphoplasmocytic inflammation was associated with these areas of glandular hyperplasia. The lining of the gall bladder was more extensively infiltrated by neoplastics described in the liver, Theyspread from serosis to the mucous surface. The gall bladder neoplastic cells frequently formed dense cell leaves and trabeculae separated by fibrovascular stroma. Tumor cells were observed in the lumine of medium-sized blood and lymphatic vessels in the bladder wall (30).



Figure 9: Opened gallbladder showing mucosal villiform masses projecting into the lumen (30).



Figure 10:A/ Section of gallbladder showing infiltration of neuroendocrine carcinoma to the mucosal surface, often intimately associated with the submucosal glands.B/ Section of liver showing rosettes and trabeculae of neoplastic cells surrounded by a loose collagen matrix (14).

#### 2.2.2.4Diagnosis

То confirm the provisional microscopic diagnosis of hepatobiliary neuroendocrine been :Histochemical carcinoma :it has used stains and immunohistochemical labelling (30).

#### 2.2.3. The tumor of biliary tract :

#### 2.2..3.1.Definition

The gallbladder ;the intrahepatic and the extrahepatic bile ducts may be invloved in primary heaptictumors ; often are carcinomas and rarely adenomas (3), the yong animals are more affected by the galbladder's adenomas .

The galbladder carcinoma is aggresive ;by direct extension ; the liver parenchyma can be invaded by it and metastasise to regional (hepatic)lymphatic nodes but also to more distant ones and for the cholongiocarcinoma (CCA) is the most frequent (31);but it's occasionally founded in sheeps (32).

#### 2.2.3.2.Macroscopical appearence

Adenomas present as multinodular or papillary masses wich emerge from the mucosal surface (31) ; a significant cholestasis is caused by papillary adenocarcinoma wich block the extrahepatic bile ducts while the lesions are developped in the the inner wall of it ; as yellowish ,friable and cauliflower masses-like about15 cm in diameter (33).

#### 2.2.3.3.Etiology

In humans; it has been proven that the chronic infestation by the hepatic fluke is a triggering factor in cholangiocarcinogenisis (34), the fluke infestation has a carcinogenic role wich seems transposable to animals. the combination of CCA and large fluke is also suspected in cattle (3).

#### 2.2.3.4.Pathogenesis

The infestationbyo.veverrini is directly correlated by the risk of the development of this cancer ; while the parasite migrates is going to provoke a mechanical trauma associated to the secretion of some metabolic compounds and an inflammatory response of the host wich promotes the development of CCA (34).

#### 2.2.4.The tumor of the kidney

#### 2.2.4.1.Definition

Kidney tumours have been reported infrequently, with the exception of nephroloblastoma in pork, which is a relatively common neoplasm in this species and has been well described (35).

They are mainly nephroloblastomas and carcinomas.Metastatic tumors are relatively common, especially for EBL, but they generally do not cause clinical signs of kidney damage (36).

**Nephroloblastoma:**it is an embryonic tumour of nephrotoblasticcells. The disease primarily affects young animals (calves and fetuses); (3) This tumour is commonly found in pigs. Thus the second type of tumor depicted in slaughterhouses after lymphosarcoma, with 23.4% of porcine tumors. It develops in youth, around the age of six months. Typically bilateral, it may weigh as much as 34 kg (5).

**Renal carcinoma:**Kidney carcinoma occurs in adult bovines.Tumor growth is slow and is often found in slaughterhouses.

#### 2.2.4.2.Etiology

Chemical, physical and virological agents have been associated with renal cell tumours in animals and humans. Chemical carcinogens known to cause kidney cell tumors include nitrosamines, aromatic amines (dyes, rubber, coal, gas industry), nitrosurated, triphosphates, cadmium, aflatoxins and lead Etiology (37). The importance of each of these compounds has not been studied in ruminants. A viral cause is added to this list: the bovine or ovine leukosis virus (38), which can cause, among other things, kidney lymphoma. It is important to note that enzootic bovine leukosis (EBL) is a legally contagious disease.

#### 2.2.4.3.Macroscopic appearance

**Nephroblastoma**: The primary, yellowish, encapsulated tumor, approximately 30 cm in diameter, substituted for the right kidney. In the case of nephroloblastoma with transcoelomic metastases was however described in a 3-year-old bull; The initial, yellowish, encapsulated tumor, about 30 cm across, replaced the right kidney. Hiscenter was necrotic-bleeding. The rare still identifiable kidney structures were enlarged. The metastases, multiple pinkish-white nodules, 1-5 cm in diameter, have been disseminated in the serous and in the lungs (40).

**Renal carcinoma:**Renal lesion may be single, multifocal and bilateral, or more rarely multifocal and one-sided. The lesion is a cortical, yellow-orange, proliferative, well-circumscribed lesion that invades the renal capsule .Remote metastasis is quite rare (41).But metastases can extend into the liver, lung, retroperitoneal lymph nodes, peritoneum and for abdominal and peritoneal lymph nodes were observed (42).

#### 2.2.4.4.Microscopic appearance

**Nephroblastoma:**This tumor consisted primarily of ovoid and polygonal cells arranged in an ill-defined frondosis pattern with a delicate fibrous stroma. Rosettes have formed locally, sometimes with papillary invasions, but no well-defined glomerular bodies have been found. Cells frequently exhibited clear or weakly eosinophilic cytoplasm and indistinct cell borders, with hyperchromatic nuclei containing one or more nucleoli.It had a high mitotic frequency and focal necrosis.The scattered fronds consisted of many large multinucleate cells with abundant eosinophilic cytoplasm(Fig.11).Myofibrils in the cytoplasm confirmed to be rhabdomyoblasts.

Some elongated, belt-shaped rhabdomyoblasts were also noted. There were no additional metalasticelements (35).


Figure 11:Malignant nephroblastoma. The field shown contains nu- merous multinucleated rhabdomyoblasts, with one elongated strap-shaped form; their cytoplasm contains myofibrils (42).

**Renal carcinoma:**Microscopically, the architecture of primary renal carcinomas and cellular composition. They have been classified according to the histological standard as tubular, solid, tubulopapilifer, papillary, tubular and solid.

The papillary profile was observed in combination with the tubular type and was composed of fibropapillary structures covered by one or two layers of well differentiated cells. In terms of cell type, eosinophil cells were predominant.One case consisted essentially of bright air cells ranjadas in a solid pattern interspersed by delicate fibrous stroma with numerous thin-walled blood vessels(Fig.12.A.B). (43).



Figure 12:Clear renal cellcarcinoma.A/The tumor is characterized by cells with abundant cytoplasmclear, with generally central and uniform nucleus. The neplastic cells are arranged in small lobes separated bydelicate bundles of connective tissue.B/ demonstrating the typical network of small vessels thin wall (small lakes of blood) (25). Tumours were usually restricted, but there were areas of invasion of adjacent tissues. The renal parenchyma adjacent to the tumour masses was compressed, atrophied and in most cases with variable degrees of fibrosis. Not all cases have a tumor capsule. Pleomorphism and mitoses were observed with areas with a solid model and in al Neoplastic tubule guns(Fig.13).In all cases, the metastases were confirmed to be similar to the original primary kidney tumours (44).



Figure 13:Renal tubulopapiliferous carcinoma, demonstrating strong nuclear pleomorphism. Some nuclei are large (39).

#### 2.2.4.5.Pathogenisis

Secondary tumors are generally more common than primary tumors, regardless of the species. They occur in association with bronchial, cholangiohepatic, ovarian or uterine carcinomas, or with fibrosarcomas (10) (35).

#### 2.2.2.6.Diagnosis

The diagnosis of nephroblastoma is based on tumour distribution, neoplastic epithelium layout, and the presence of rhabdomyoblasts in the undifferentiated component (35).

The diagnosis of renal carcinoma is enhanced by the distribution of tumours and the presence of acidophilic inclusions in neoplastic cells, a feature observed in some human parenchymal cancers. The anti-CD10 is a useful marker in the diagnosis of primary renal cell carcinoma in cattle (35).

# **III.MAMMARY TUMORS**

#### **III.MAMMARY TUMORS**

#### **1.Definition**

The rate of mammary neoplasm varies tremendously according to the species ;this kind of tumors is rare in cows,goats,ewes as the literature hase reported only few cases.they exhibit a sporadic appearing in domestic animals contrariwise are very frequent in dogs and cats.It exisit a similarity in morphological patterns between bovine mammary gland in humans and cows; wich explains the common latter used for cancerogenic studies.

**Sheeps:**It is interesting to note that the sheep reports mention benign breast adenomas (45) and fibroadenomas (46).and low-grade carcinomas known to have existed for some time, suggesting slow clinical progress (47).

**Cows:**In contrast, metastatic mammary carcinomas to draining lymph nodes were recorded and reviewed in cows and, in some cases, further metastatic spread was also observed (48).

Therefore, it cannot be assumed that primary breast epithelial tumors in sheep and cows have the same clinical behavior.

#### 2.Etiology

Because of the rarity of mammary tumours in professional lactators, risk factors and biological behaviour for mammary carcinomas are unknown. There are many factors that could affect the high rate of tumor development in women and reduce the development of tumors in ruminants. Apart from eating, lifestyle, history of reproduction, stress load, Overall physiology and metabolism can influence (49).

#### **3.Pathogenesis**

It's Given that 8 years of cattle life equals 40 years of human life (50), many cows are allowed to live well past their "cancer age" of about 8 years (51).

The mammary tissues undergo continual changes throughout the life of the active reproductive females; The morphogenesis of the mammary glands implies the regulation function of several signalling routes, i.e. growth factors, hormones...During the tumorigene process, the signaling is deregulated, allowing the mammary epithelium to expand, proliferate and invade neighbouring tissues (hyperplasia); (52).

Estrogenic ovary hormones and progesterone are essential for the development of the mammary gland and are involved in breast cancer (53). Estrogen is crucial for the growth of epithelials, while progesterone promotes lobuloalveolar differentiation during pregnancy and breastfeeding.

There is substantial evidence that lactation reduces the risk of breast cancer in premenopausal women (54). The low rate of mammary tumours in cattle can be attributed to the high rate of pregnancies as enhanced parity reduces estrogen exposure and high lactation requirements provide protection against breast carcinoma. But the mechanisms responsible for this protective effect are still unclear. Henceit has been proposed that stem cells be the cells that cause breast cancer.

#### 4.Diagnosis

Immunohistochemistry (55).

# IV.TUMORS OF LLYMPHOPOEITIC SYSTEM

## **IV.TUMORS OF LLYMPHOPOEITIC SYSTEM**

#### **1.Definition**

Lymphosarcoma bovine is the most common neoplastic disease among bovine animals(Onuma.,1979).it is a bovine lymphoproliferative disorder that is split into two separate entities based on the underlying etiology. Whereas enzootic bovine leukosis (EBL) is caused by the bovine leukemia virus (BLV), it is regarded as an infectious disease (56).

#### 2.Enzootic bovine leukosis(EBL)

#### 2.1.Definition

Enzootic bovine leucosis (EBL) is a complex disease of cattle associated with retrovirus lymphocytotrope B, bovine leukaemia virus (BLV), (57); It is a chronic disease that develops over a long period of time and can be broadly divided into three phases:

- (1) from birth until infection (certain animals are already infected at birth).
- (2) from virus infection to tumour transformation (several infected animals do not develop tumours prior to slaughter).
- (3) from tumour processing to death (rare cases of tumour regression have been reported); (58).

#### 2.2.Etiology

The etiological agent of enzootic bovine leukosis is bovine leukemia virus, wich demands a latent long periode to induce EBL (59). A recent study on the relationship between tumor necrosis factor (TNF) and BLV infection suggests that TNF is a key factor in the progress of dysplasia (60).

#### 2.3.Macroscopic appearance

Upon autopsy, the tumor lymph nodes are remarkably conspicuous; Tumorisation is not symmetrical and varies in size and position. Typical tumor tissue appears white pink on the section; necrosis and hemorrhage are common. The lymph nodes of the pelvic area are often affected intensively, more than those of the cardiopulmonary area. Apart from lymph node damage, which can be absent or very discrete, tumors of varying size, shape and appearance are present. Tumours in the spinal duct and behind the eyes are typical of EBL. Splenomegaly is observed, but not frequently; it usually happens with terminal leukemias. The infiltration of the organs induces hypertrophy and a whitish overall appearance and lumps (61).

#### 2.4. Microscopic appearance

Normal tissue structures disappear due to invasion by tumor lymphoid cells that are polymorphs, with multiple mitoses. In affected organs like the liver and kidneys, widespread infiltration is the rule. The total destruction of normal histologic structures is the final phase. Histopathological lesions are typically mixed type, characteristic for lymphoreticulosarcoma (58), Certain cells had atypical nuclei and prominent nucleolae.

#### 2.5.Pathogenesis

After inoculation with BLV, the infection starts with a transient viremia followed by an asymptomatic incubation period that lasts several years. The provirus built into the host genome remains quiet and the viral load is low.

Most born cattle remain only seropositive, but about 30% develop persistent lymphocytosis (62), which appears to be related to genetic sensitivity (5). Only a minority (1-10%) of infected cattle show clinical signs in tumour form, most of which transform into multi-centre lymphosarcoma (63) Animals that have persistent lymphocytosis are predisposed to the disease (62).

BLV is transmitted horizontally by arthropods such as taon or to calves through an in utero infection and colostrum ingestion from a cow infected with BLV, Iatrogenic transmission may occur through surgical instruments or sleeves contaminated with infected blood when palpating rectally. Cases of in utero infection may lead to immune tolerance to BLV, as is the case with a viral infection with the bovine diarrhea virus (64), None of this has been flagged. It has been suggested that vertical transmission of the human T-lymphotrope I virus, which is closely related to the BLV virus, is a risk factor for the development of adult T-lymphocyte leukemia (65).Although the link between transmission pathway and EBL pathogenesis is unclear in this case. immune status of the host, timing of infection with the virus, and proviral loading may be important factors in the pathogenesis of EBL at a young age (64).

#### 2.6.Diagnosis

The iPCR determined the diagnosis of EBL because the BLV had identical integration sites in anatomically different tumours (64).

Only the detection of antibodies in the serum is carried out in practice. The baseline test is agar immunodiffusion (GBI), carried out with a specific antigen (p24 or gp 51). Enzymemediated immune responses (ELISA) are more sensitive and can also be used on milk (63). Other techniques, such as immunological radiation tests, can also be used.

Experimentally, the virus may be isolated through culture of infected lymphocytes, followed by virus identification by electron microscopy or antigen detection. Proviral DNA may be detected in blood or tumors through polymerase chain reaction (PCR); (66).

#### 3.Sporadic bovine leucosis(SBL)

#### **3.1.Definition**

Sporadic bovine leukosis (SBL) is rare, but the disease occurs most commonly in single cases.SBL is treated as non-contagious (67). SBL was subdivided into juvenile, thymic and cutaneous forms. Juvenile form is present in calves under six months of age, but it has sometimes been reported in animals under two years of age;typical signs are rapid and multicentre lymphlymphadenopathy progression, leading to rapid disappearance and death. (68). The thymic form mainly affects bovine animals aged 6 to 24 months and is characterised by massive lymphoproliferation of thymic tissue, often involving other organs. . Skin LBS was observed in cattle aged 1-3 years It is characterized by multifaceted cutaneous lymphoproliferation with or without organ damage (69).

#### 3.2.Etiology

Different forms of sporadic leucosis have been confirmed to be generally not associated with BLV (70).However, in rare instances, a monoclonal integration virus is reported (71). The precise etiology is still unknown, but a genetic trace has been revealed by the presence of protooncogene c-myb in tumor cells. Expression of this gene seems strongly related to their differentiation (72).

## 3.3.Macroscopic aspect

**the juvenile form:** Macroscopically, besides polyadenomegaly, tumor infiltrations of the spleen, liver and bone marrow are very frequent (73)Lesions have also been reported in thymus, kidneys (Figure14), tonsils and intestinal lymphoid tissues (74). The heart, clot and uterus are less commonly affected than EBL (68), but cases are always described.

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Figure 14:Bovine kidney with sporadic leucosis, showing cortical lymphomatous infiltration (66).

**The thymic form:** The main lesion is the significant hypertrophy of the thymus (75);a single mass is observed at the cranial mediastinum or at the entrance of the thorax, with possibility of NL damage to the front chest and head. In rare cases, the muscles of the head, mandible and jaw can infiltrate (71). Adenomegaly and spinal cord infiltration may also be present (76).

**The cutaneous form**: In addition to skin lesions, the LN is enlarged and certain organs (heart, kidney, liver, spleen) are infiltrated in approximately 50% of cases (76).

#### 3.4.Microscopic aspect

60% of sporadic lymphomas are lymphomas that have large cells and small non-clivate cells. Mitotic scores are lower than those of enzootic lymphomas (71). The juvenile lymphocytes concerned are either LB or LT. Under both thymic and dermal forms, they are LT (78).

**the juvenile form:** The microscopy shows the infiltration and proliferation of immature B cells (74).

**the cutaneous form:** This clinical entity is divided into two subsets: epitheliotrope (LT) and not epitheliotrope (LB) as a function of the degree of epidermal involvement (76). Early forms of Pautrier microabscesses may be observed (71).

# 3.5.Pathogenisis

The tumour phase of SBL appears between four months and one year of age, However, the tumours develop exceptionally late in SBL.

It should be noted that the geographic distribution of the SBL is consistent within a country and contrasts sharply with the SBL in this respect. with EBL. On top of that, SBL is untransmissible (58).

# **3.6.Differential diagnosis**

Differentiation between multicentre lymphadenopathies in EBL and SBL cases require testing for a virus, Both cases have identical clinical and pathohistological presentation (68).

# 4.0ther lymphomas.

Their etiology is not known and their incidence is sporadic, like multicentre lymphoma in adult cattle. Sporadic multicentre lymphoma has been described in sheep, but its incidence appears to be very low and its etiology is unknown (78).

A study conducted in Scotland for 35 years (4); shows that lymphosarcomas, localized or generalised, account for almost all tumors of the hematological system in sheep, or 13.2% of the total tumors. The distribution appears global and the frequently affected organs are NL, spleen, heart, liver, kidneys, intestine, bone marrow, skin and, more seldom, thymus (3).

# **5.OTHER TUMORS IN THE HAEMATOPOIETIC SYSTEM.**

Hematopoietic tumours are anecdotal in cattle, so we don't develop them. Sporadic cases of myeloid leukemia with massive seepage of the skin and mediastinum have been reported (80).

Leukemias are malignant neoplasia, where normal leukocytes are replaced with large numbers of lymphocytes, monocytes, or myelocytes (4). A case of myeloma was reported in Canadian slaughter facilities on 1,370 tumours observed.

# V.TUMORS OF THE REPRODUCTIVE SYSTEM

# **V.TUMORS OF THE REPRODUCTIVE SYSTEM**

### **1.Definition**

Male and female bovine animals can be affected by genital neoplasms. However, due to the very strong "feminization" of the bovine population, tumours affecting the female reproductive system are the most described and have a significant impact on the entire population.

## 2.Female genital tract

## 2.1.Definition

Tumors of the reproductive system are classified in the following categories: ovary, fallopian tube, uterus, cervical, vagnal (81).

**Vaginal and vulvary tumors**: they include leiomyos leiomyo-sarcoma, fibroma, fibrosarcoma, fibro-leiomyosarcoma and squamous cell cancers (82).



# Figure 15:Vaginal tumour measuring 18 × 11 × 7 cm (80).

**Ovarian tumors:** in their turns they ;are primarily divided into epithelial, stromal gonad and germ cells. The granular cell tumor is the most common ovary tumor in cattle and is usually unilateral (82).

# 2.2.Macroscopic aspect

Uterine adenocarcinoma:the lesion is usually a single stiff and rough mass. It is usually circumscribed, but may sometimes spread all over the wall and be perforating. Metastasis of NL and lungs is possible, more rarely on abdominal serum, ovaries and mediastinum (83).

**Lymphosarcoma :** it can develop on a localised, multifocal or diffuse basis. The lesions are generally firm, pediculate masses in the uterine wall, resembling caroncules (3).

**Cervical tumors:**they take the form of a firm, encapsulated, pinkish-white mass, which may exceed 20 cm in diameter. Lesions can cause ulceration, abscess and metastasis. According to size (84).

**Granulosa cell theca tumors:** the lesion is unilateral and can reach up to 50cm in diameter, for 32kg. It is a solid, multi-slobulated mass containing cystic structures, reddish brown, haemorrhagic(Fig.16and 17). The contralateral ovary is usually quiet and atrophic.



Figure 16:Granulosa cell tumour, ovary, cow. Solid white tumour (73),



Figure 17:Granulosa cell tumour, ovary, cow. Cystic/solid tumour (45).



Figure 18:Right ovary measuring 35 × 20 × 25 cm exteriorised during ovariectomy in a 5year-old German Holstein cow. Prominent enlarged functional ovarian stages can be seen (3).

#### 2.3.Pathogenesis

Uterine adenocarcinoma occurs mainly in a uterine horn from the endometrial glands, rarely in the body or cervix (4).Lymphosarcoma are more seldom diffused, causing thickening. body or horns and can affect the cervical, vaginal and even oviducts. NL and other organs are generally implicated. The infected animal usually dies within six months.

#### 3.Male genital tract

#### **3.1.Definition**

Male genital tumors are poorly described because they occur sporadically. In contrast, there are few males in the mature cattle population (3).

**The testicules:** Testicular tumours arise primarily in older bulls, less frequently in calves (85)). Rare instances of semiinoma and Sertoli cell tumours have been described.

**The penis:** Primitive tumors are usually fibropapilloma, associated with BPV1 or 2 infection. They develop on the glans and penis, and can ulcerate and become necrotic.

Melanoma and lymphosarcoma metastases can affect the penis and foreskin (86).

#### 3.2.Macroscopic aspect

Serotonin cell tumours (serotonins) are generally unilateral, firm, greyish-white to reddish. Foci of calcification, bleeding and necrosis are present. Regional LN metastases are rare, but they may be spread to blood and lymphatic vessels. Hyper-estrogenism is occasionally associated (85).testicular tumors are well-defined sphere tumors (86).

# **VI. Bone tumors**

# **VI. Bone tumors**

#### **1.Osteosarcomas (in cattle)**

#### **1.1.Definition**

Ostesarcomas are malignant neoplasms of the skeletal tissue. This is the primary bone tumor most commonly found in pets such as dogs and cats (3). Cases of osteosarcoma of the mandible have been documented in bovine animals (5).

#### **1.2.Macroscopic aspect**

Neoplastic masses were estimated in the mandibular rostral region. The masses were macroscopically large, firm, ulcerated, infiltrative, whitish and solid, and resulted in tooth displacement and loss (87).

#### 1.3.Microscopic aspect

Histologically, well differentiated and uncapped mesenchymal neoplastic proliferation replaced the mandibular bone and spread to the buccal mucous membrane. neoplastic cells had few cytoplasms and fusiform or oval hyperchromatic nuclei with free chromatin, and were arranged in clusters in different directions.

In the neoplastic tissue, there were mineralized bony trabeculae and non-mineralized osteoids, doubled by a layer of osteoblasts and osteocytes in the lacunae (87)

#### 1.4.Diagnosis

radiography reveals that the neoplastic masses were intrabone and radioclear with radiation protection foci (87).

#### 2.Ossifying fibroma (in sheep)

#### **2.1.Definition**

Ossific fibroma is a disfiguring benign tumor of the jaw of young adults of various animal species. This tumour is most frequently reported in young horses (88). Ruminants have been recognized anecdotally as the second most frequently hit group (89).

#### 2.2.Macroscopic aspect

A firm, gravelly mass extended beyond the rostral mandible(Fig.19). a portion of the skin was ulcerated and covered with a dark crust on the rostrodorsale margin.

The mass was well contained across the mandibular symphysis. with bilateral breakdown of the bones and roots of the lower incisors (90).



Figure 19:Sheep mandible with multifocal ossifying fibroma, sagittal section. The larger, lobulated mass(large arrow) protrudes from theeffaced rostral mandibular margin. The caudal, less distinct mass(small arrow) abuts the roots of two molar teeth, which have dark necrotic centers (90).

#### 2.3.Microscopic aspect

On the histological plane, the masses of the rostral mandible and the left caudal mandible were identical, with the exception of a focal area of superficial skin ulceration accompanied by suppu rative inflammation in the rostral mass. The masses were well bounded but not condensed. A leaf of isomorphic fibroblasts and disorganized fibrocytes formed most of the masses. Mitotic figures were rarely found (90). On the periphery, the masses were bordered by discontinuous, irregularly shaped, mineralised woven bones bordered by osteoblasts and a thin edge of osteoids(Figs 20 and 21). Bone trabecules were less frequent near the center of the masses. Different individual osteocyte cells in the lacunas were found in most bone spiculae. No haematopoietic cells or areas of lamellae bone were present in the masses. Scattered throughout the masses were single multinucleate cell osteoclasts that were most common near bone trabeculae(Fig21).

The outer margins of the masses were largely confined to a dense fibrous connective tissue that formed a clear demarcation with the adjacent normal bone. In the masses, no normal tissue was present, except for teeth that were occasionally trapped without identifying periodontal structures (90).



Figure 20:Photomicrograph of ossifying fibroma, low magnification. The leading edge of the tumor is rimmed by discontinuous spicules of woven bone (smaller arrow, lower left). Residual lamellar bone of the jaw is much denser and organized in concentric whorls( larger arrow upper middle). Note the increased density of the fibrocollagenous matrix of the tumor, below, with residual loose areolar connective tissue (52).



Figure 21:Photomicrograph of ossifying fibroma, higher magnification. A small bony spicule is lined by osteoblasts( broad arrow, upper middle). Nearby is a multinucleate osteoclast( thin arrow, lower left),( 3).

#### **3.1.Definition**

Chondrosarcomas are malignant tumours in cartilaginous tissue. They are common in great breed dogs, in which they most often grow in the nasal cavity. These are sporadic in cattle and involve bones more often short, extra-skeletal location is rare. Cartilage tumours develop by matrix synthesis, with a moderate growth rate. Metastases may occur, but they're late. A case of nasal chondrosarcoma was documented in a five-year Simmentale (91).

# 3.2.Macroscopic aspect

The tumor blocked the entire nasal cavity. The lesion was firm, milky, cartilage and contained mineralizing pockets (91).

# **VII. TUMORS OF NERVOUS SYSTEM**

# **VII. TUMORS OF NERVOUS SYSTEM**

# **1.Definition**

Tumors of nervous tissues can touch the central nervous system (CNS) aswell as the peripheral nervous system (SNP). Schwannomas and neuro-fibromas are the most common (92).

**1.1.Tumors of the central nervous system:** CNS tumors are not common in cattle. They may be glial or meningeal and consist primarily of lymphosarcoma and intracranial SCC (Hayes et al., 1975).

**1.2.Tumors of the peripheric system:** SNP neoplasia is common in cattle, especially those in the envelope of peripheral nerves (93). **2.TUMORS OF THE PERIPHERIC NERVE SHELL** 

# 2.1.Definition

Neoplasms currently reported in the literature are schwannoma and neurofibromas. The first term is a tumor made entirely from Schwann cells (68). and the second has a tumour consisting of Schwann and other peripheral nervous components (perineural cells,fibroblasts, collagen), (94).

Peripheral nerve envelope neoplasms are commonly discovered in cattle slaughterhouses ;(Bundza et al., 1986).and Peripheral nerve sheath tumors (PNST) occur as slow growth tumors which can be located anywhere within the neural system peripheral (92).

# 3.1.Etiology

In animals, the exact etiology has not yet been determined. However, a number of avenues are being explored at this time.

A genetic background also needs to be considered. A genetic background also needs to be considered. A mutation of neu oncogene has been reported in malignant forms of tumors of the peripheral nervous sheath. It seems to be a specific genetic marker found in various animal species (95).

Viral damage appears probable in some cases. Bovine syncytial virus and oncovirinae have been implicated because similar particles were detected in affected animals (91).

Retroviral particle-like structures have also been observed in successive cases of malignant schwannome (96).

#### 4.1.Macroscopic aspect

Upon removal of the head, spinal cord tissue protruding from the foramen magnum was observed on the right side. It was firm, lobed and cream-coloured, and when the brain was removed the "tumor" was seen to stretch along the brain stem from the spinal cord to just posterior to the acoustic tuber. The lesion had discrete edges and it dropped from the meninges when the brain was sliced. The right internal auditory meatus was not implicated; No relevant findings were found in other organs (97).

#### 5.1.Microscopic aspect

The tumor was made up of clusters of elongated cells laid out at random angles. The cells were long and slender and had an abundant eosinophilic cytoplasm. Chromatin was thicker in some nuclei compared to others. There was no mitotic count and there was a relatively consistent cell population. Between the beams there was a scattered collagen array, and reticuline. There were no endotheliomatous cell verticiles characteristic of meningioma, but there was a certain palisage (97).

#### 6.1.Pathogenisis

Schwannomas are often mild in cattle, and multicentre forms appear to develop through simultaneous neoplastic transformations rather than the metastasization of a primary site. However, in some cases, tumors of the external nervous envelope may metastasize to NL (91).

#### 3. Multicentric Fibromyxoid Peripheral Nerve Sheath Tumor in a Dromedary Camel

#### **3.1.Definition**

Schwannomas of animals have been more widely recognised in dogs and cattle and less commonly in cats.but This tumour (Multicentric schwanoma)has not been registered in camel all over the world (92).

#### 3.2.Macroscopic aspect

the nodules and masses were often discrete, round, smooth and white to gray, convex relative to the capsular surface. or the serous coating of the affected parts of the food tract, including prepackages(Fig.22). large intestines(Fig.23);mesentery(Fig.24);liver(Fig.24) and spleen. The sliced surfaces of the masses contained discrete tumors, round, white to grey, and relatively homogeneous, without necrotic or liquefied centres(Fig.24).

The masses in the liver were approximately 1-3 cm, but the masses on the serous surface of the bowel and mesentery were slightly smaller. No major macroscopic lesions were found in other tissues or organs of the body (92).



Figure 22: Forestomachs; camel. Numerous small nodules to large masses on the serosal surfaces of forestomachs (arrows), (92).



Figure 23: Large intestines; camel. Multiple white to gray masses are seen embedded in or bulging from serosal layers (arrows), (92).



Figure 24: Liver; camel. Multiple white to gray, round masses are seen embedded in and/or bulging from the hepatic capsule. Cut surfaces of the masses consist of white to gray, relatively homogeneous tissue without necrotic foci. Formalin fixed, (92).

#### 3.3.Microscopic aspect

Histopathological examination of the masses showed a multicentre neoplastic procedure with a common cell type and growth pattern. They were encapsulated and comprised of loose whorls of long tapered cells with indistinct cell borders. The tumour had weak to moderate cell size, including a mixture of round, spindle-shaped cells in a loose cell arrangement. There weren't any nerve fibres in the tumour tissue (92).

#### **3.4.Diagnosis**

The diagnosis is based on morphopathologic characteristics Moreover, it is supported by ultrastructural results, which confirmed the uniform presence of Schwann cells (92).

## conclusion

Neoplasia may occur in all animal species and all organs may be affected. However, the frequency and sites of choice depends on species, race, age, sex, exposure to potential carcinogens.

Basically ; our bibiliographic review about major tumors in ruminants; allowed us to collect a new informations concerning this domain as well as discovering the tumors that mostly affect the ruminants, and in order to respond to the question mentionned up in the introduction , we will quote the most common rural tumors :

1-PAPILLOMA AND SQUAMOS CELL CARCINOMA (CUTANEOUS TUMORS).

2-OVINE PULMONARY ADENOMA (RESPIRATORY SYSTEM).

3-CHOLONGIOCARCINOMA (TUMORS OF THE LIVER).

4-ENZOOTIC BOVINE LEUKOSIS (LYMPHOPOEITIC SYSTEM).

5-CHONDROSARCOMA(BONE TUMORS).

6-OVARIAN TUMORS (REPRODUCTIVE SYSTEM OF THE FEMALE).

7-SCHWANOMA( NERVOUS SYSTEM).

This review permit us to exhibit an advanced knowledge in lot of estates as; immune, origin ,appearence and pathogenesis of different types of tumors.

This bibliographic study established a groundwork in the aim of helping futur investigations and explorations due to the fact that rural tumors are still little studied due to the lack of interest in these production animals. Even if they are moderately frequent, they should not be overlooked in the future.

Finally ; we advice at the end of this work the veterinary practitioners to take into consideration the macroscopic aspect and basically in the state immune also the age and the essentials predisposing factors in their professional diagnosis in rural oncology.

# Index

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# Annexes

#### Abstract

A tumor is a mass of neoformed tissue, except leukemia. It results from a disorder of proliferation and cell differentiation that is irreversible, with the exception of certain neoplasms such as papillomas (1). The tumor has a biological autonomy that results in a lack of response to control mechanisms. Unlike hyperplasia, it persists and increases even in the absence of the stimulus. Key genes are involved in the development of many cancers.

There are relatively few reports of tumors in ruminants compared to other domestic animals like dogs, cats. One propable reason is that most ruminants are not young enough to predispose them to tumour development.they are distinguished in two types ; benign tumor qualified as an organoid, malignant tumor determined as an infiltrating growth. Despite the lack of resources and interst about this topic wich refers to the age factor their rare incidence in trhis species (2). but even if all this we should focus on this domain because they can cause many complications on human health since their meat is edible, this consequences are not immediately appeared but over the time the human health will be influncef by a cumulative effect (3).

Tumors in ruminants are abnormal growths of cells that can occur in any part of the body. They can be benign or malignant but certain tissues develop only malignant forms (lymphoma, glioma, etc...), and can cause various clinical signs depending on their location and size . The most common tumors in ruminants are lymphoma, leukemia, squamous cell carcinoma, and melanoma.

Tumor or also called neoplasm refers to new cell growth. It is popularly known as tumor (swelling), but not all swelling is considered as a neoplasm. This neoplasm study is called oncology, oncos - tumors, logy- study.. whereas all tissues and organs may be impacted, at different frequencies and preferred locations wich depends on species, race, age, gender, exposure to potentially carcinogenic substances.

A few of the most common tumors, such as lymphoma and spinocellular carcinoma have better documentation.. So on the other hand, ocular squamous cell carcinoma manifests as an infiltrating palpebral mass in adult cattle with low periocular pigmentation. Tumors of skin are not only dangerous to humans, but also a major issue in animal populations.cattle,horse,camel;sheep;goats all suffer from cancer (1). According to the studies, they make up 8-34% of bovine tumours, making the skin one of the main organs affected, . The impact appears to be in 8-year-olds( (2)),the most common cutaneous neoplasms are the squamos cell carcinoma and papilloma, Other rarer cutaneous tumours are described as melanomas, mastocytomas, histiocytomas, lipomas and liposarcomas, fibromas and fibrosarcomas, myxomas and myxosarcomas, and tumors of the sweat glands (3).this kind of tumors are seldom responsible for mortality and the resulting production losses are primarily a depriciation of leather( (2).In sheep, the tumors of the various integrations account for 3.7% of the total tumors( (4). in the similar way, juvenile and dermal forms of LBS affect young dairy cattle with polyadenomegaly or skin nodules. Lymphosarcoma bovine is the most common neoplastic disease among bovine animals(Onuma.,1979).it is a bovine lymphoproliferative disorder that is split into two separate entities based on the underlying etiology. Whereas enzootic bovine leukosis (EBL) is caused by the bovine leukemia virus (BLV), it is regarded as an infectious disease (56)

As we have also tumors of internal organs ,in first degree the tumors of repiratory system ,as well as ovine pulmoary adenocarcinoma (OPA) is contagious tumor of the respiratory epitheluim affecting small ruminants for wich a viral etiology has been prooved ;this animal cancer is simillar to a human bronchioloalveolar cancer (BCA); (13).

In the second degree we mention the tumors of the liver and gallbladder.

Primary hepatic tumors are the tumor of liver pranchyma and biliary tract ; thus expecting the cholangiocarcinomas they may be found in immature and adults (22);they are quite frequent in animals according to Kelly (1985) probably they are classified after lymphomas as the most common visceral tumors in cats ,cattle , sheep and dogs. Among primary hepatobiliary tumors(PHT) ;hepatocellular tumors(HCT) are listed as the most common tumor in the cattle as in other animals and man (23); as it is been established that there is no significant correlation between the primary hepatic tumors and the presence of any pre-exsiting disease process (22).

In the other hand The gallbladder ;the intrahepatic and the extrahepatic bile ducts may be invloved in primary heaptictumors ; often are carcinomas and rarely adenomas (3), the yong animals are more affected by the galbladder's adenomas .

The galbladder carcinoma is aggresive ;by direct extension ; the liver parenchyma can be invaded by it and metastasise to regional (hepatic)lymphatic nodes but also to more distant ones and for the cholongiocarcinoma (CCA) is the most frequent (31);but it's occasionally founded in sheeps (32).
In the last position referring to tumors of internal tumors we have renal tumors. Kidney tumours have been reported infrequently, with the exception of nephroloblastoma in pork, which is a relatively common neoplasm in this species and has been well described (35).

They are mainly nephroloblastomas and carcinomas.Metastatic tumors are relatively common, especially for EBL, but they generally do not cause clinical signs of kidney damage (36).

In the third degree; mammary tumors , The rate of mammary neoplasm varies tremendously according to the species ; this kind of tumors is rare in cows, goats, ewes as the literature hase reported only few cases. they exhibit a sporadic appearing in domestic animals contrariwise are very frequent in dogs and cats. It exisit a similarity in morphological patterns between bovine mammary gland in humans and cows; wich explains the common latter used for cancerogenic studies.

Hence for the tumors of reproductive system, Male and female bovine animals can be affected by genital neoplasms. However, due to the very strong "feminization" of the bovine population, tumours affecting the female reproductive system are the most described and have a significant impact on the entire population.

In the other hand bone tumors present a rarity but we mention chondrosarcomas as the most common . chondrosarcomas are malignant tumours in cartilaginous tissue. They are common in great breed dogs, in which they most often grow in the nasal cavity. These are sporadic in cattle and involve bones more often short, extra-skeletal location is rare. Cartilage tumours develop by matrix synthesis, with a moderate growth rate.

Metastases may occur, but they're late. A case of nasal chondrosarcoma was documented in a five-year Simmentale (91).

In the last position, Tumors of nervous tissues can touch the central nervous system (CNS) aswell as the peripheral nervous system (SNP). Schwannomas and neuro-fibromas are the most common (92). Schwannomas of animals have been more widely recognised in dogs and cattle and less commonly in cats.but This tumour (Multicentric schwanoma)has not been registered in camel all over the world (92)

In order to diagnose tumors such as another diseases, histology examination is the microscopic examination of tissues to study the appearance of cells and tissues. It is an

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important tool for the diagnosis of cancer. Hence it is the confirmatory exam of tumors ,. Usually the immunohistochemistry is the most frequent histological examination

Necropsy can be used to diagnose tumors, It is a postmortem examination of an animal to determine the cause of death or to evaluate pathological conditions. it is the ultimate diagnostic destiny of most of the experimental animals.

The diagnosis by necropsy can still be used to implement prevention at the flock level whenever possible due to the impact of tumors which can result in reduced production and trade restrictions.

Neoplasia may occur in all animal species and all organs may be affected. However, the frequency and sites of choice depends on species, race, age, sex, exposure to potential carcinogens.

Basically ; our bibiliographic review about major tumors in ruminants; allowed us to collect a new informations concerning this domain as well as discovering the tumors that mostly affect the ruminants, and in order to respond to the question mentionned up in the introduction , we will quote the most common rural tumors :

1-PAPILLOMA AND SQUAMOS CELL CARCINOMA (CUTANEOUS TUMORS).

2-OVINE PULMONARY ADENOMA (RESPIRATORY SYSTEM).

3-CHOLONGIOCARCINOMA (TUMORS OF THE LIVER).

4-ENZOOTIC BOVINE LEUKOSIS (LYMPHOPOEITIC SYSTEM).

5-CHONDROSARCOMA(BONE TUMORS).

6-OVARIAN TUMORS (REPRODUCTIVE SYSTEM OF THE FEMALE).

7-SCHWANOMA( NERVOUS SYSTEM).

This review permit us to exhibit an advanced knowledge in lot of estates as; immune, origin ,appearence and pathogenesis of different types of tumors.

This bibliographic study established a groundwork in the aim of helping futur investigations and explorations due to the fact that rural tumors are still little studied due to the lack of interest in these production animals. Even if they are moderately frequent, they should not be overlooked in the future.

Even if all animal species can develop neoplasia and all organs can be affected, The economic and medical consequences of tumours in ruminants are also often underestimated.

Finally ; we advice at the end of this work the veterinary practitioners to take into consideration the macroscopic aspect and basically in the state immune also the age and the essentials predisposing factors in their professional diagnosis in rural oncology.

2022/2023

Mémoire PFE

## LARBI NOUR EL HOUDA

University of Blida- 1 / Institute of veterinary Promoter : Dr METREF AHMED .Kh

## Theme

Abstarct : Tumors in ruminants are abnormal growths of cells that can occur in any part of the body. They can be benign or malignant but certain tissues develop only malignant forms (lymphoma, glioma, etc...), and can cause various clinical signs depending on their location and size . The most common tumors in ruminants are lymphoma, leukemia, squamous cell carcinoma, and melanoma.

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Histology examination is the microscopic examination of tissues to study the appearance of cells and tissues in order to diagnose tumors such as another diseases . It is an important tool for the diagnosis of cancer. Hence it is the confirmatory exam of tumors ,. Usually the immunohistochemistry is the most frequent histological examination

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Key words : Tumors , neoplasm , metastasis, neoplasia, ruminants