Welkom

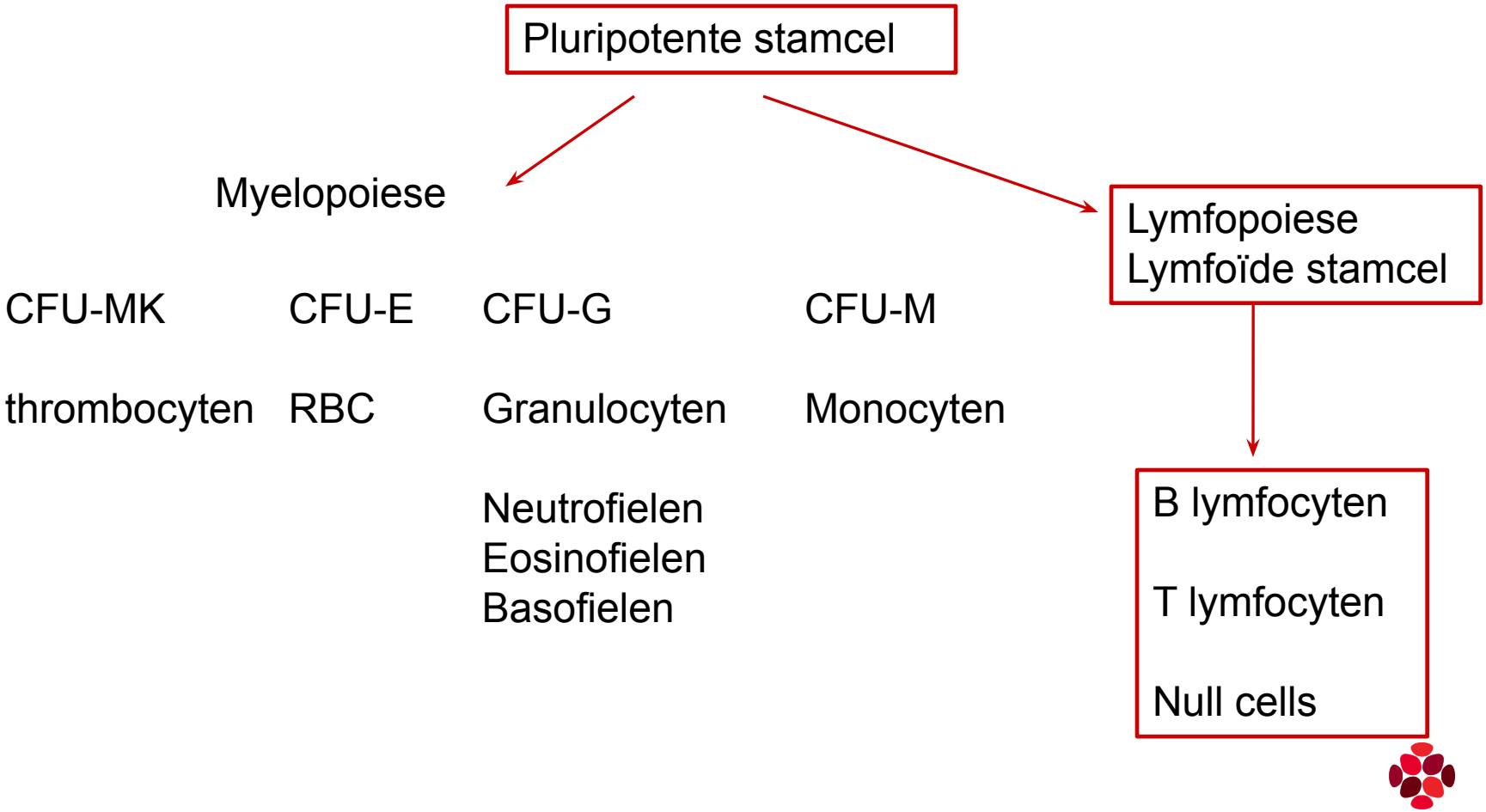
Lymfoom bij de kat

LabIntermezzo 26-03-15

Pierre Simard, Dr.

Deel 1
Lymfocyten

1. Lymfocyten

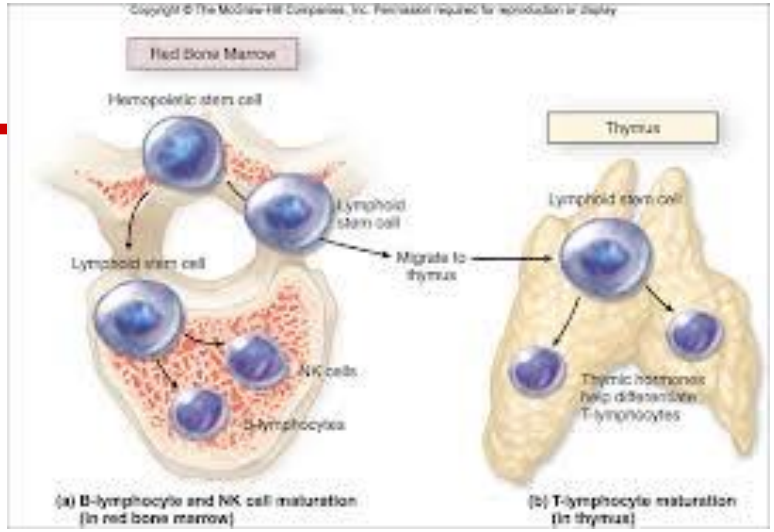


Lymfocyten

BEENMERG
Pluripotente stamcel

Beenmerg
Lymfopoiese
Lymfoïde stamcel

B- en T-cel precursor



B lymfocyten
Null cells

Beenmerg

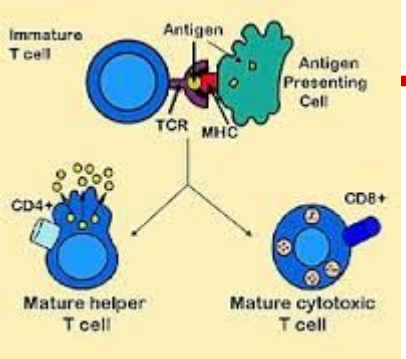
T lymfocyten

Thymus

Beenmerg vormt de imature stamcellen.
Thymus en beenmerg zijn primaire lymfoïde organen

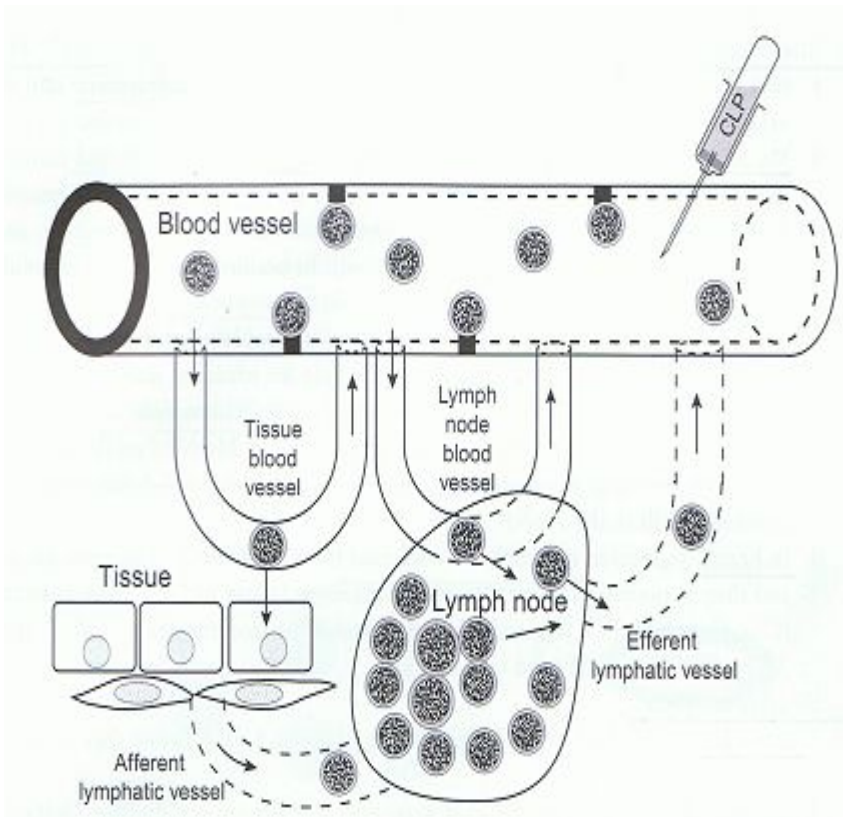
- differentiatie en rijping

Lymfocyten



- In de primaire organen: celdeling
- Tijdens de rijpingsfase
  - Membraanreceptoren TCR en BCR
  - Membraan antigenen CD (“cluster of differentiation”)
    - T: CD3
    - B: CD79
- Tijdens de multipele delingen mogelijke mutaties
  - Thymus: T-cel lymfoom
  - Beenmerg: medullair B-cel lymfoom

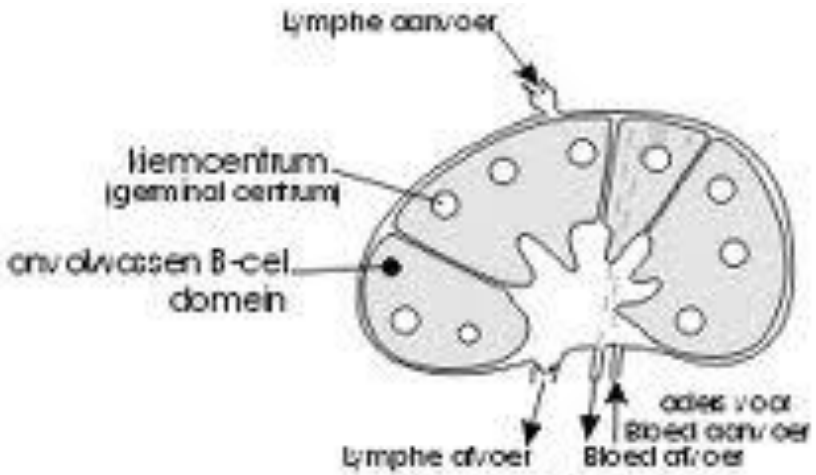
Lymfocyten



2.3. Lymphocyte kinetics in health. Lymph nodes and other primary lymphoid tissues are sites hocyte production but also potential destinations of blood lymphocytes. Blood lymphocytes are ibuted between marginal and circulating pools and may enter lymphoid organs or nonlymphoid phocytes that enter nonlymphoid tissue may remain or may enter the afferent lymphatic vessels ported to regional lymph nodes and then perhaps to blood via the thoracic duct.

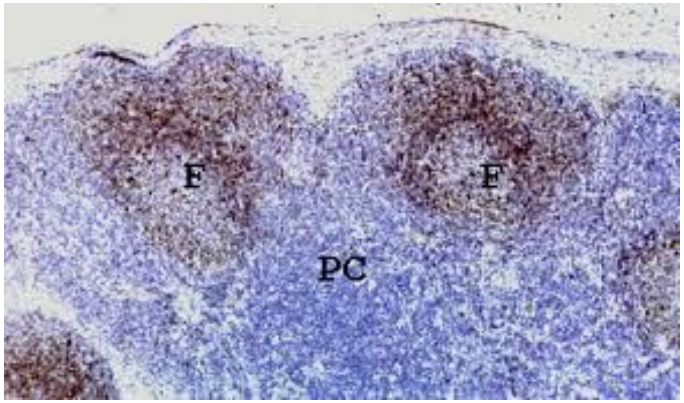
- Recirculatie en transformatie
  - Bloedbaan
  - Secundaire lymfoïde organen
    - Lymfeklieren
    - Milt
    - Mucosae
      - GALT
      - BALT

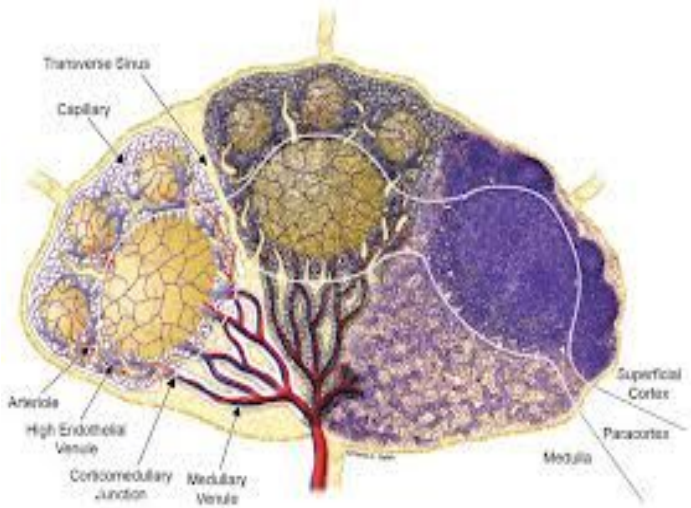
Lymfocyten



- Transformatie
  - Antigene stimulatie (in 2^{e} lymf. organen)
  - Deling en transformatie lymfocyten

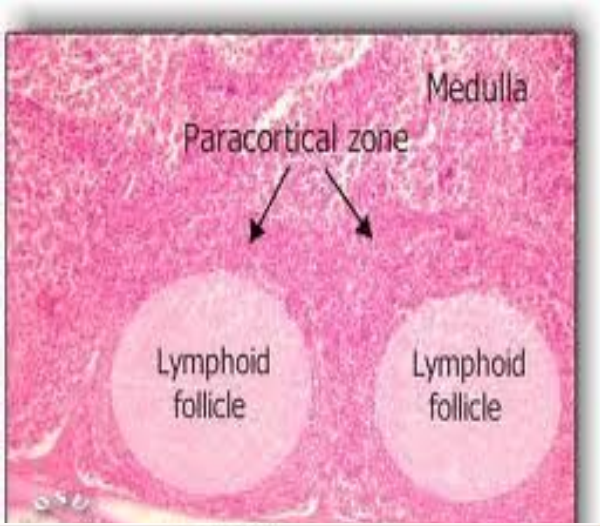
Lymfocyten

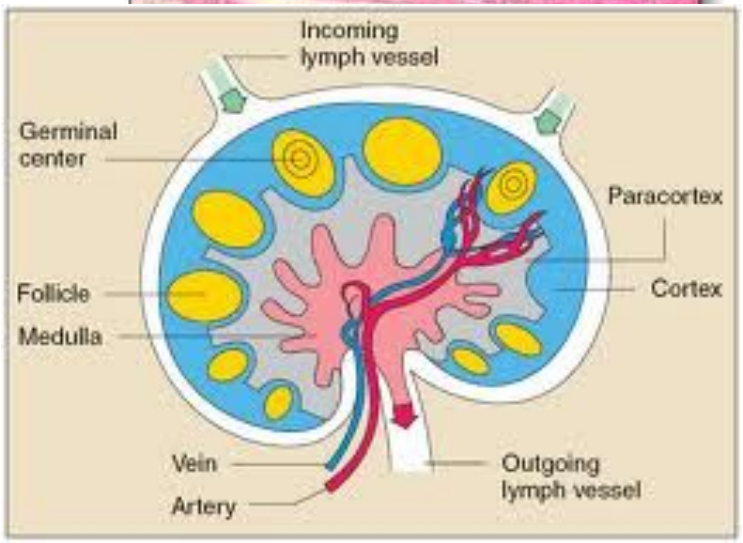




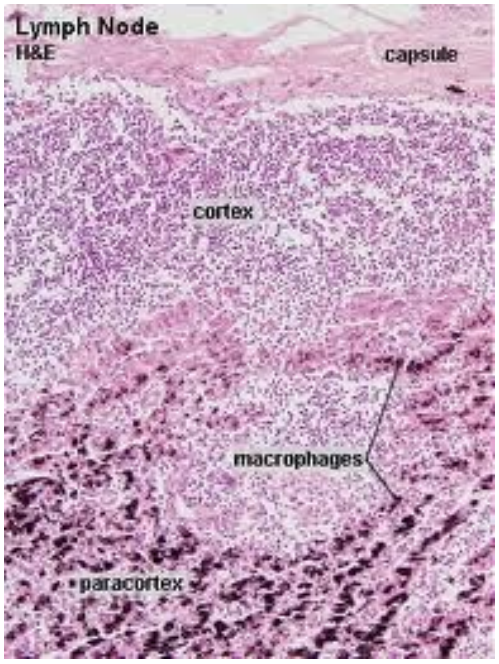
- Transformatie
  - B-lymfocyten deling+++
    - Folliculaire cortex
  - Centroblasten deling +++
    - BCR- !! (dedifferentiatie)
  - Centrocyten
    - BCR+ (differentiatie)
  - B-lymfocyten (memory cells)
  - Preplasmatocyten
  - Plasmacellen: vorming immunoglublines

Lymfocyten

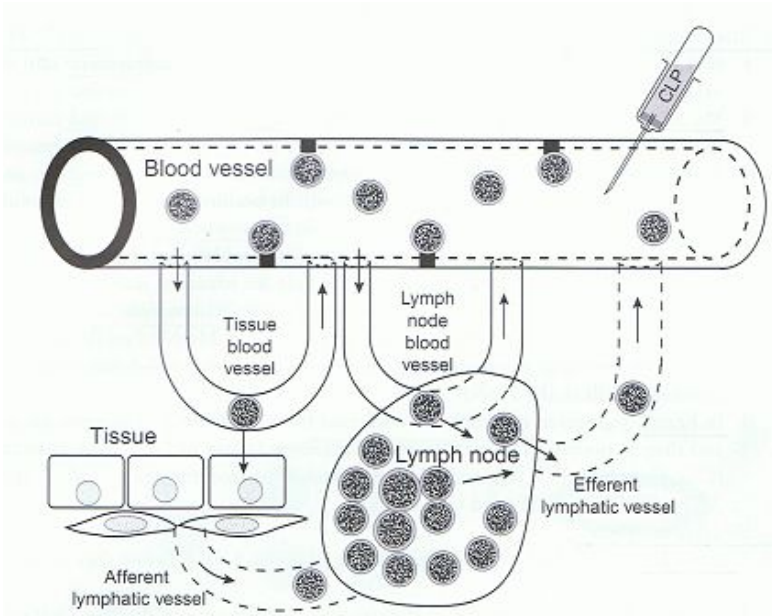




- Transformatie
  - T-lymfocyten
    - Paracortex
  - Immunoblasten



Lymfocyten



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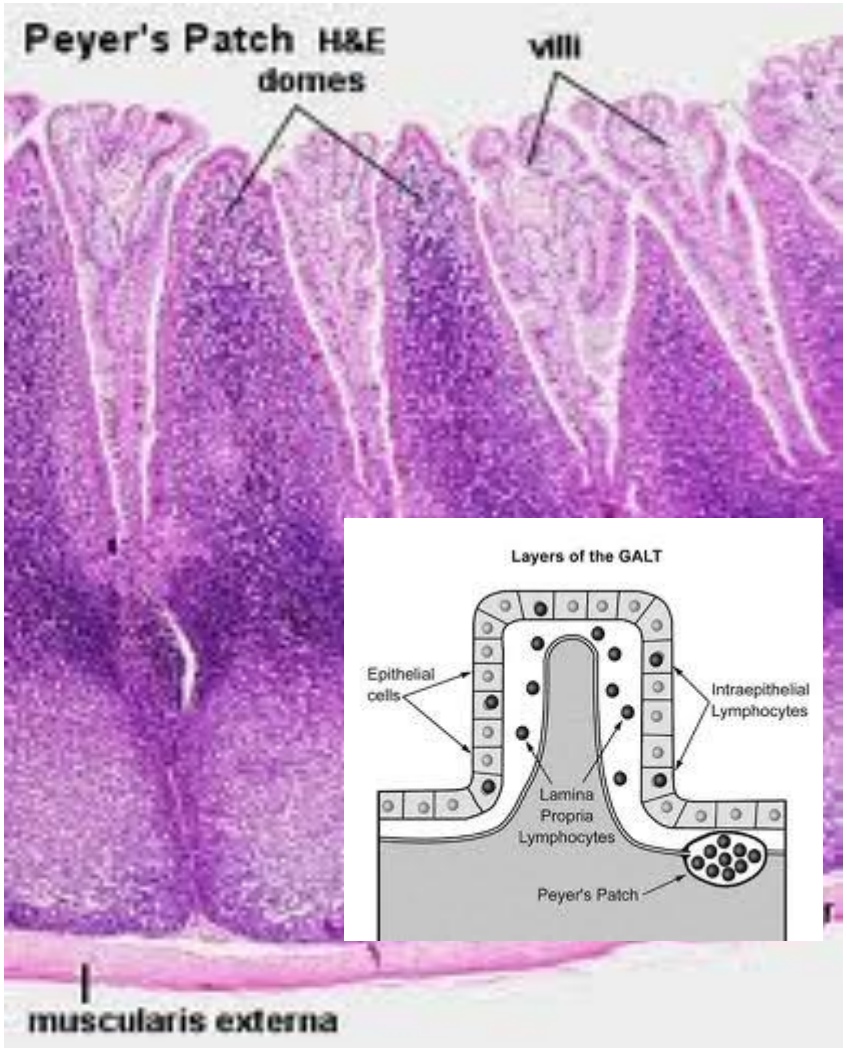
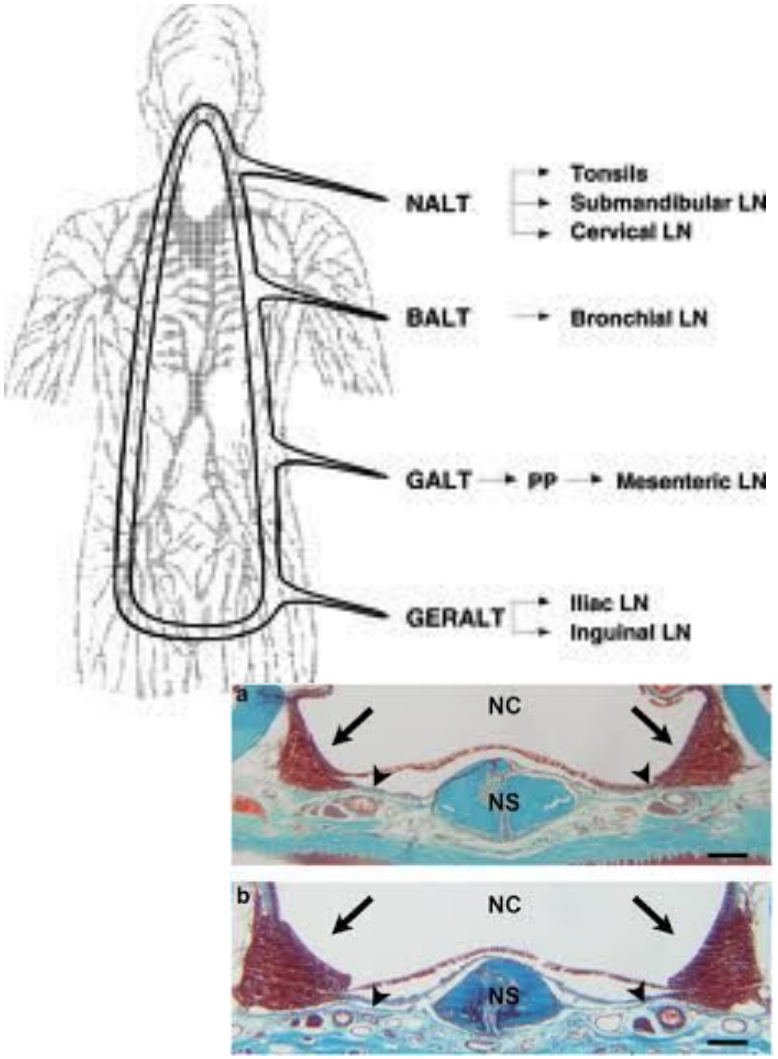
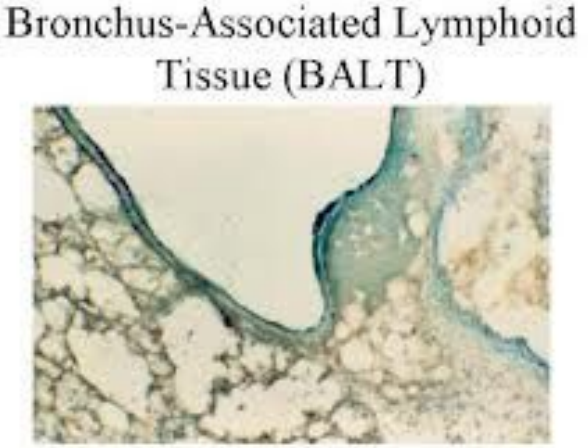


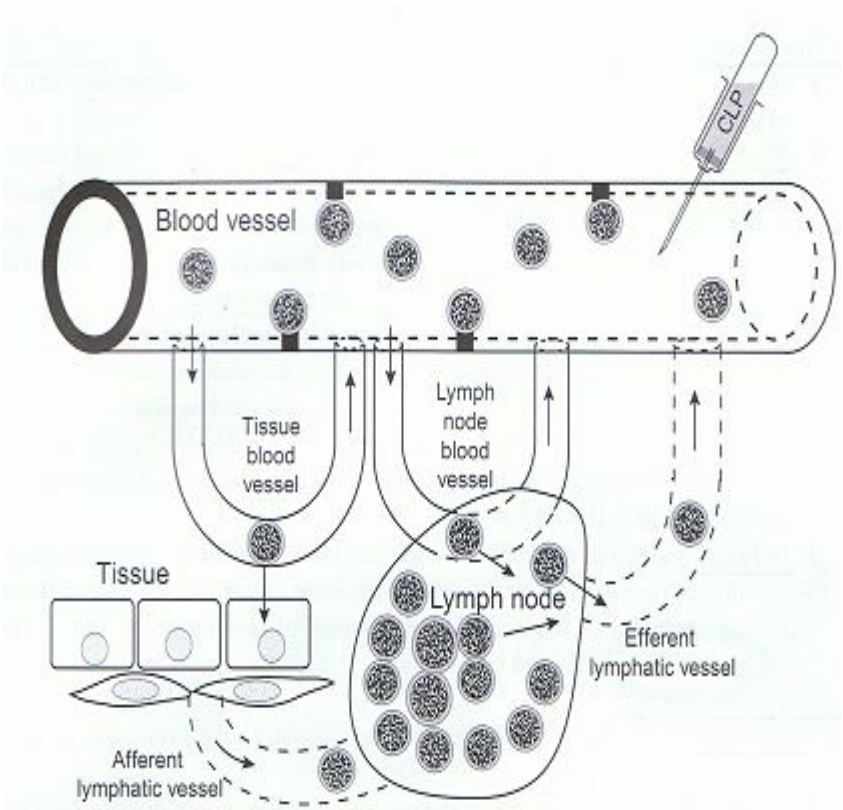
Lymfocyten


NALT
Tonsils
Submandibular LN
Cervical LN
BALT
Bronchial LN
GALT
PP
Mesenteric LN
GERALT
Iliac LN
Inguinal LN
a
NC
NS
b
NC
NS


Bronchus-Associated Lymphoid Tissue (BALT)


Oesophagus H&E
MALT

Lymfocyten



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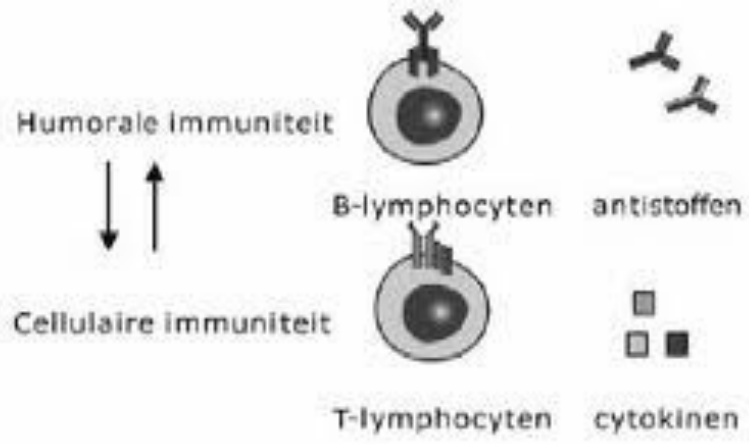
- Levensduur
  - Enkele dagen
  - Jaren (memory)
- Recirculatie
  - Goede verdeling lymfocyten in het lichaam
- Bloedbaan
  - Vnl. T cellen 85%

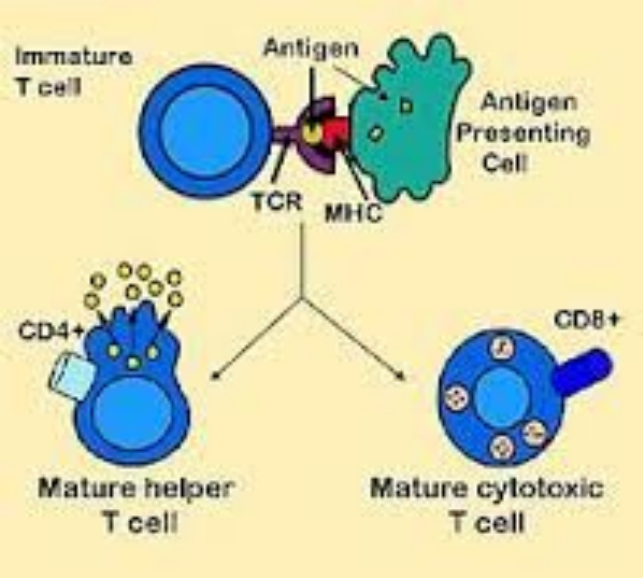
Lymfocyten: functie

- Functie B-lymfocyten
  - Humorale immuniteit
    - Vorming van immunoglobulines
    - Plasmacellen!! Eindstadium van differentiatie van B-lymfocyten

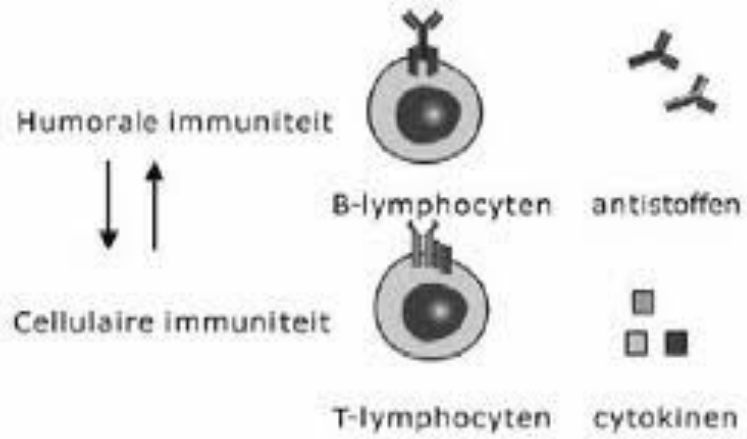


Figuur 1. De specifieke afweer: humorale en cellulaire immuniteit.

Lymfocyten: functie



- Functie T lymfocyten
  - Cellulaire immuniteit
  - 2 Types cellen: helper cellen en cytotoxische cellen



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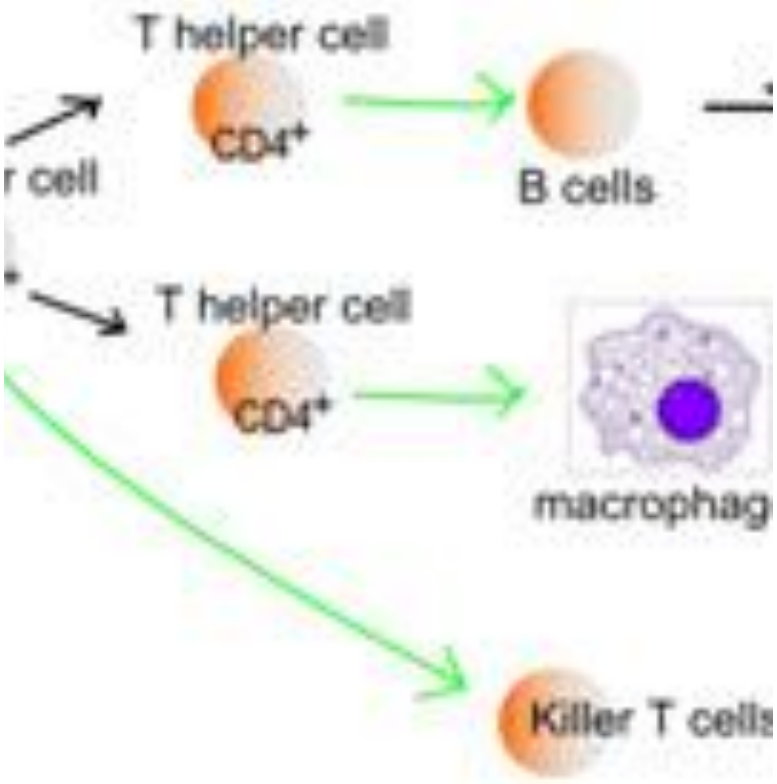
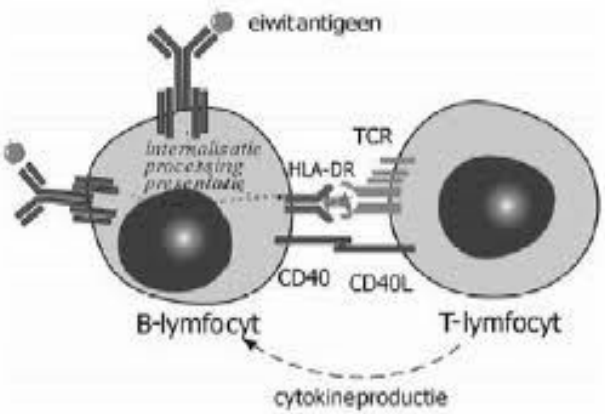
Lymfocyten: functie

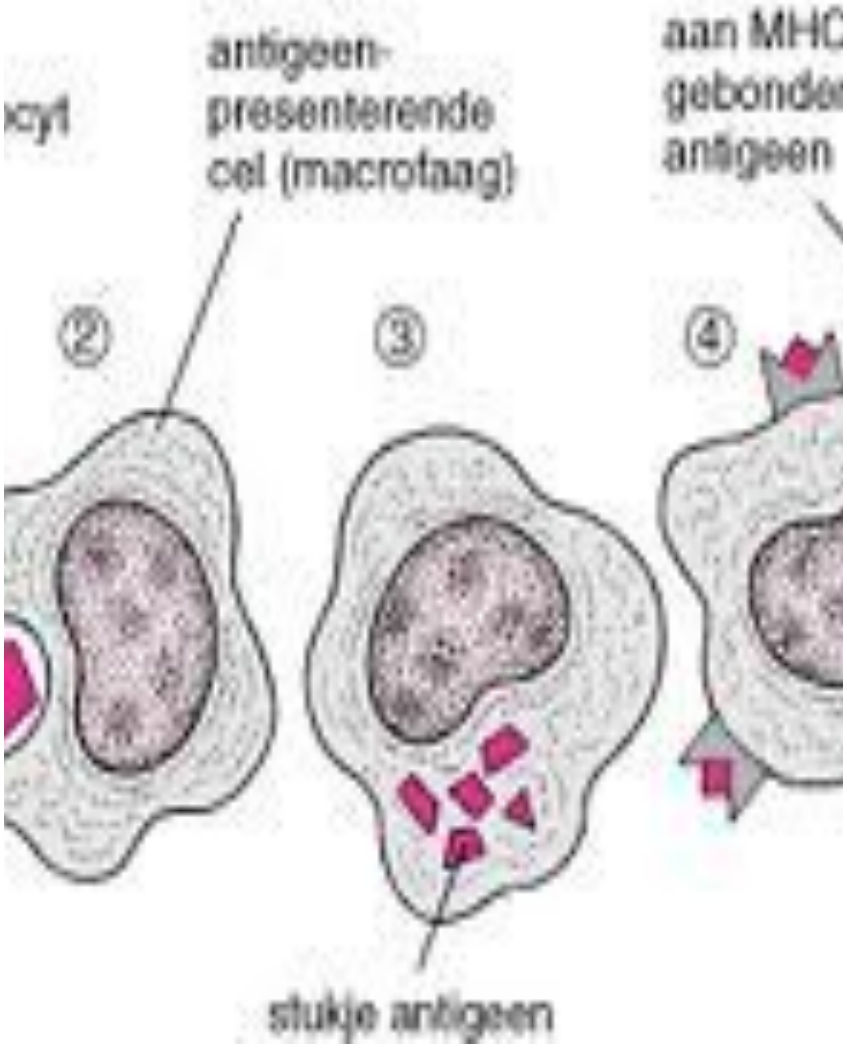


- Functie: Th cellen
  - CD4+
  - Secretie van cytokines
    - samenwerking met B-lymfocyten
    - Stimuleren deling en activatie: Tc cellen, NK cellen, macrofagen, …..

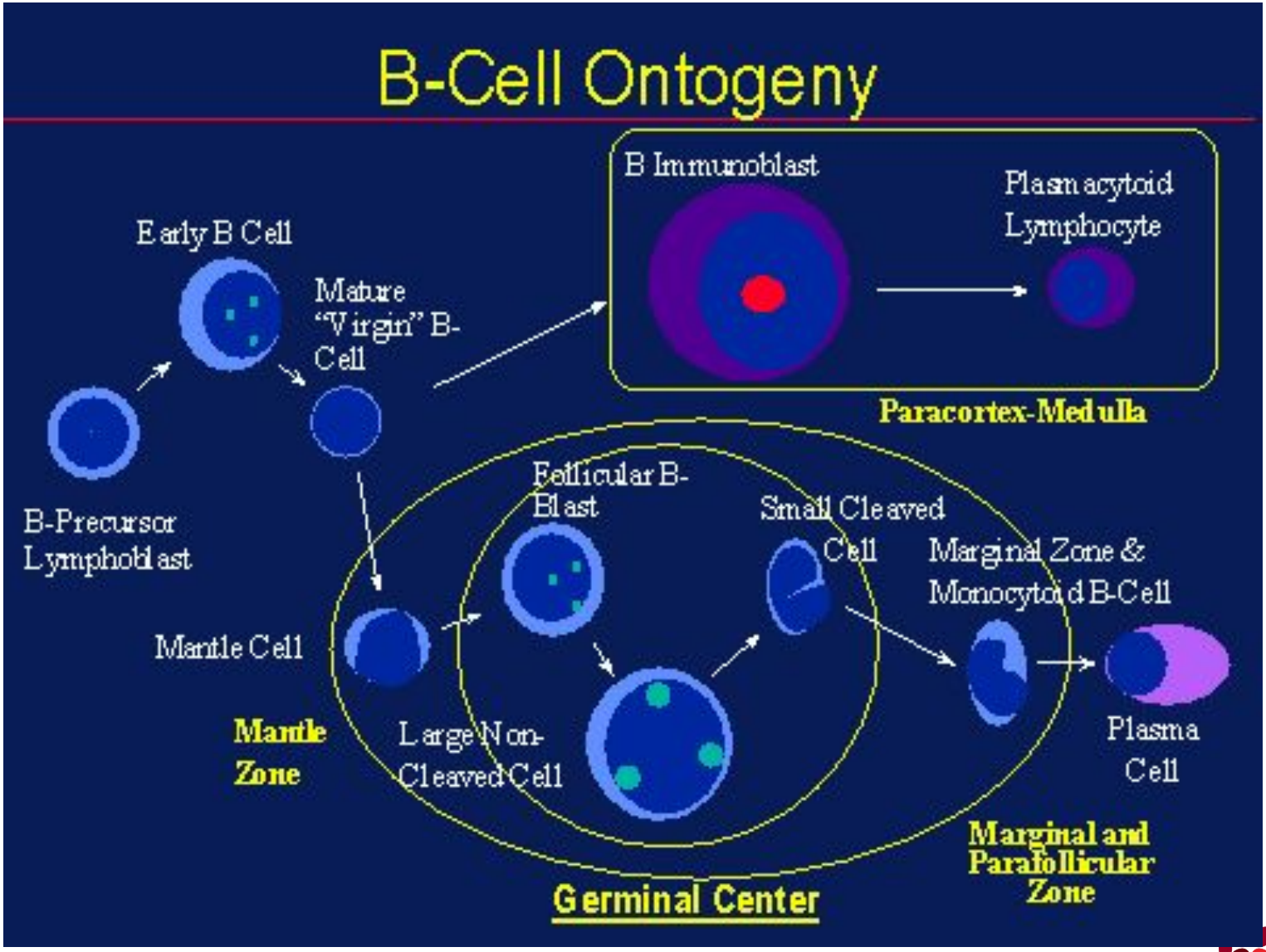


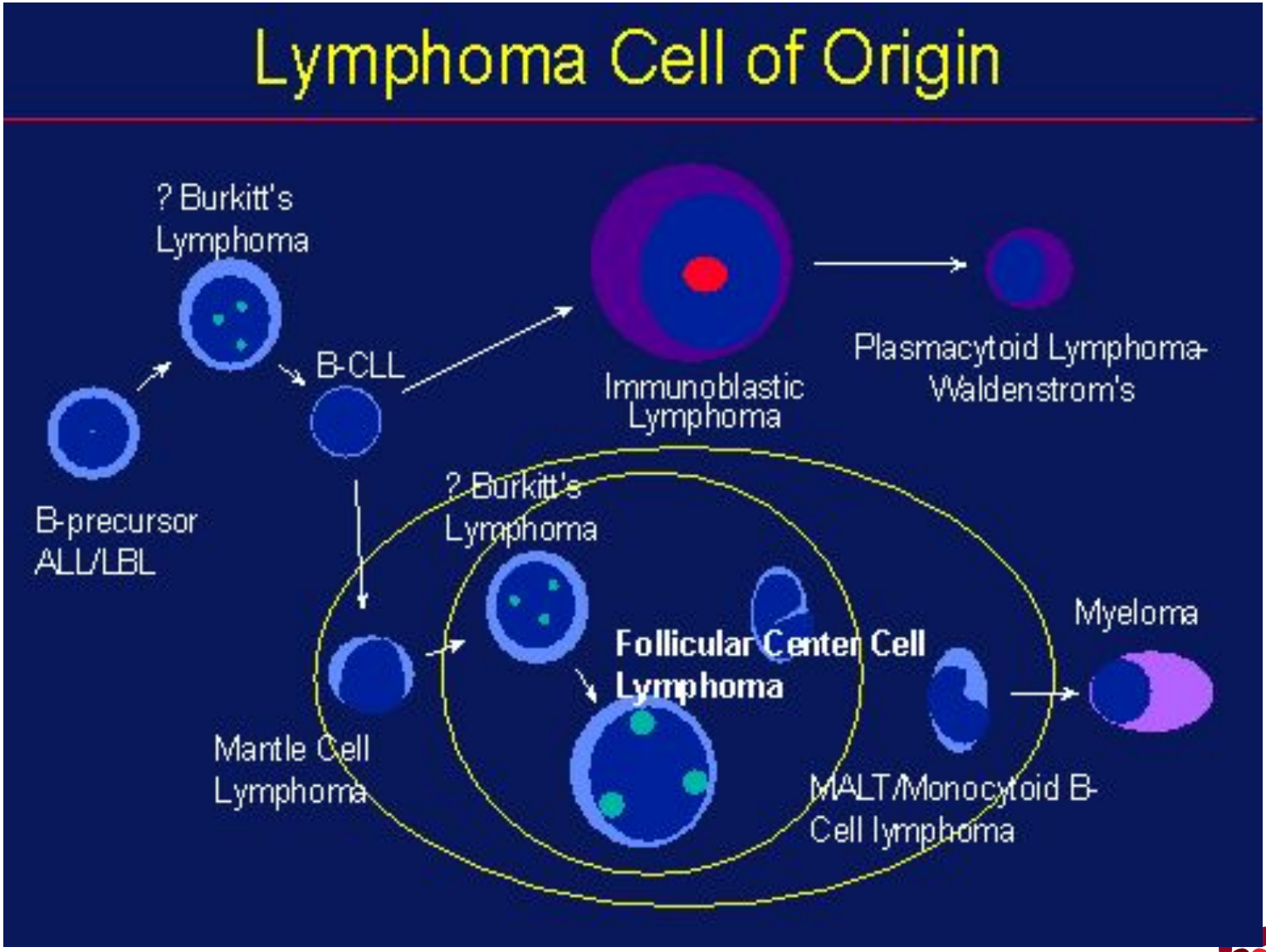
Figuur 4. Samenwerking tussen T- en B-lymfocyten.

Lymfocyten: functie



- Functie Tc cellen
  - CD8+
  - Herkennen en doden van geïnfecteerde cellen


B-Cell Ontogeny
B Immunoblast
Plasmacytoid Lymphocyte
Early B Cell
Mature "Virgin" B-Cell
Paracortex-Medulla
B-Precursor Lymphoblast
Follicular B-Blast
Small Cleaved Cell
Marginal Zone & Monocytoid B-Cell
Mantle Cell
Mantle Zone
Large Non-Cleaved Cell
Plasma Cell
Marginal and Parafollicular Zone
Germinal Center


Lymphoma Cell of Origin
? Burkitt's Lymphoma
B-CLL
B-precursor ALL/LBL
Immunoblastic Lymphoma
Plasmacytoid Lymphoma-Waldenstrom's
? Burkitt's Lymphoma
Follicular Center Cell Lymphoma
Myeloma
Mantle Cell Lymphoma
MALT/Monocytoid B-Cell lymphoma

Deel 2
Classificatie van lymfomen

Indeling

- Verschillende soorten lymfoproliferatieve aandoeningen
  - Leukemie
    - Acuut
    - Chronisch
  - Lymfomen
  - Multipel myeloom
  - Plasmacytomen
- Lymfoom generische term voor veel verschillende aandoeningen
- Alle organen

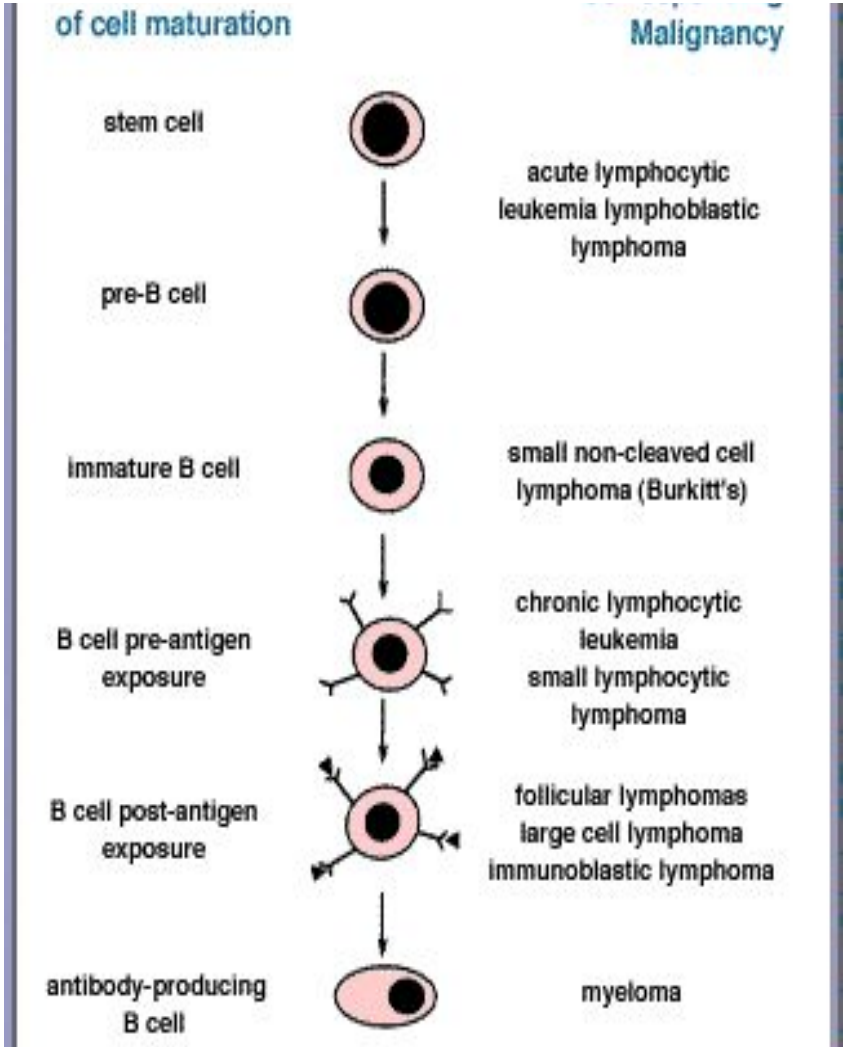


Table 1. Frequency distribution in 602 cases of feline lymphoproliferative disease classified according to the NC1 working formulation.

Tumor type	Acronym	Number	%
Low grade			
Chronic lymphocytic leukemia	CLL	10	1.7
Small lymphocytic lymphoma	SLL	13	2.2
Small lymphocytic intermediate lymphoma	SLLI	30	5.0
Small lymphocytic plasmacytoid/plasmacytoma lymphoma	SLLP	12	2.0
Follicular small cleaved-cell lymphoma	FSC	1	0.1
Follicular mixed-cell lymphoma	FM	3	0.5
Intermediate grade			
Follicular large-cell lymphoma	FL	2	0.3
Small cleaved-cell lymphoma	SCC	35	5.8
Mixed cell lymphoma	MC	45	7.4
Large cell lymphoma	LC	51	8.5
Large cleaved-cell lymphoma	LCC	77	12.8
High grade			
Acute lymphocytic leukemia	ALL	22	3.7
Immunoblastic lymphoma	IB	178	29.6
Immunoblastic small-cell lymphoma	IBS	18	3.0
Immunoblastic polymorphous lymphoma	IBP	13	2.2
Small noncleaved-cell lymphoma	SNC	79	13.1
Lymphoblastic lymphoma	LB	2	0.3
Lymphoblastic convoluted-cell lymphoma	LBC	11	1.8
Total		602	100.0

Table 2. Frequency distribution in 602 cases of feline lymphoproliferative disease classified according to the International Lymphoma Study Group REAL system.

Tumor type	NCI WF acronyms	Number	%
B-cell lymphoma			
Precursor B-cell lymphoma: B-lymphoblastic leukemia/lymphoma	ALL, LB, LBC	22	3.7
B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma	CLL, SLL	23	3.9
Lymphoplasmacytoid lymphoma/immunocytoma	SLLP	8	1.3
Mantle cell lymphomas	SCC, SLLI, MCL	65	10.8
Follicle center lymphoma	FSC, FM, FL	6	0.9
Marginal zone B-cell lymphoma			
Extranodal (MALT type ± monocytoid B cells)			
Nodal (±monocytoid B cells)			
splenic (±villous lymphocytes)	MALT	...	...
Hairy cell leukemia	...	...	...
Plasmacytoma/myeloma	Plasmacytoma, myeloma	4	0.7
B-cell large cell lymphoma, subtype: thymic B-cell lymphoma	DM, DL, DLC, IB	382	63.5
Burkitt's lymphoma	SNC	79	13.1
Provisional category: high-grade B-cell lymphoma, Burkitt's like	...	...	...
T-cell and putative NK-cell lymphomas			
Precursor T-cell lymphoma: T-precursor lymphoblastic lymphoma/leukemia	ALL, LB, LBC	13	2.1
Peripheral T-cell lymphomas			
T-cell chronic lymphocytic leukemia/prolymphocytic leukemia	CLL	...	...
Large granular lymphoproliferative (LGL) disorder	...	...	...
T-cell type			
NK-cell type			
Mycosis fungoides/Sezary's syndrome	...	...	...
Peripheral T-cell lymphomas, unspecified (medium, mixed, large)	...	...	...
Provisional subtype: lymphoepithelioid cell lymphoma	...	...	...
Adult T-cell lymphoma/leukemia (ATL/L)	...	...	...
Angioimmunoblastic lymphoma	...	...	...
Angiocentric lymphoma	...	...	...
Intestinal T-cell lymphoma (±enteropathy associated; ITCL)	...	...	...
Anaplastic large cell lymphoma, CD30+, T-cell, and null-cell types	...	...	...
Total		602	100

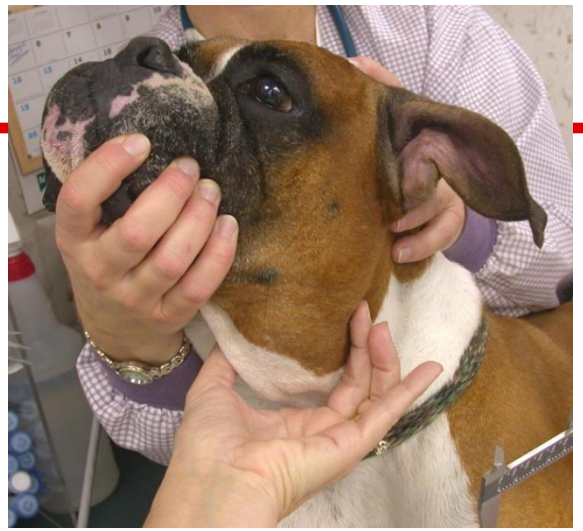
Anatomische Indeling

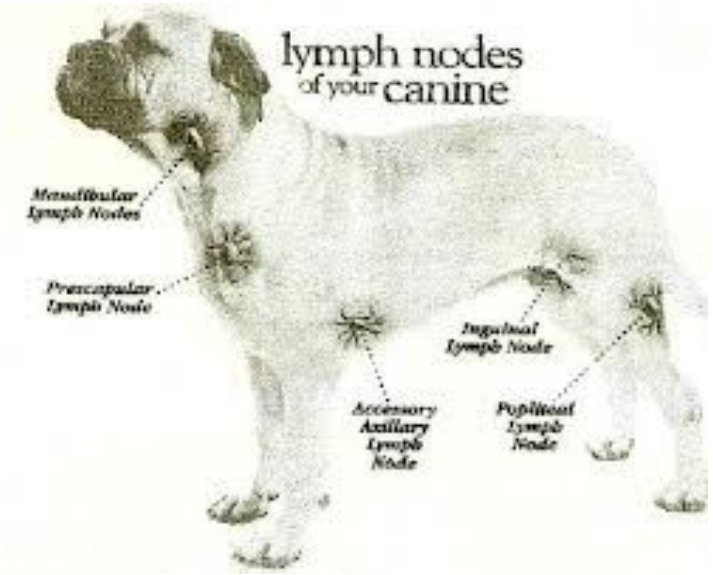
- Alimentair Lymfoom
- Mediastinaal Lymfoom
- Multicentrisch (Nodaal) Lymfoom
- Extra-Nodaal Lymfoom
  - Nasaal
  - Renaal
  - Enz……..

Deel 3
Epidemiologie
Etiologie

Hond

- Multicentrisch **70%**
- Andere
  - GI 7%
  - Lever-milt
  - Milt
  - Nasaal
  - Mediastinaal
  - CZS
  - Huid
  - Oog





Etiologie en Epidemiologie

Epidemiologie

- 100/200.000
- **Neemt toe** ondanks afname FeLV

VOOR DE JAREN 80	NA DE JAREN 80
70% FeLV +	15-25% FeLV+
Mediastinaal!!! Nodaal CZS	Abdominaal!!!!! Renaal Atypisch: nasaal
Fenotype T Hoge graad	B en T Hoge EN lage graad
Mediaan 4-6 jaar	Mediaan 11 jaat

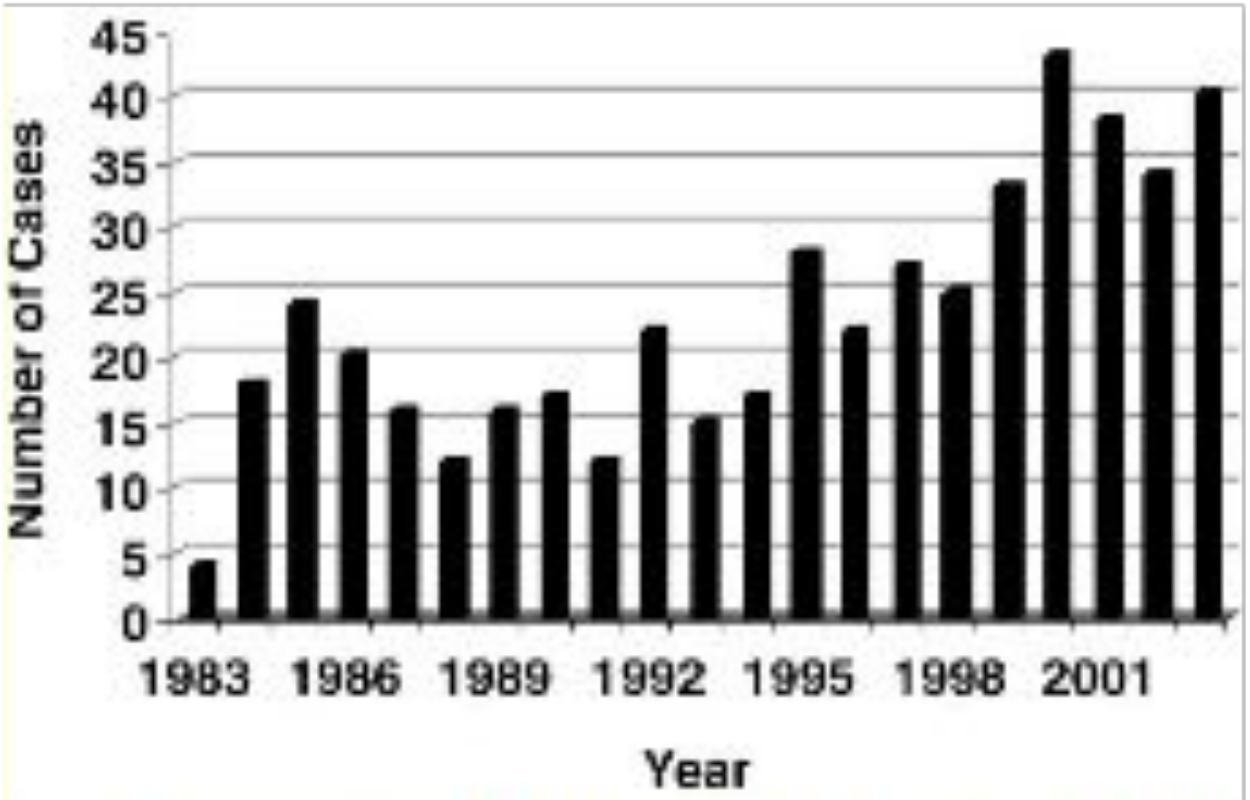
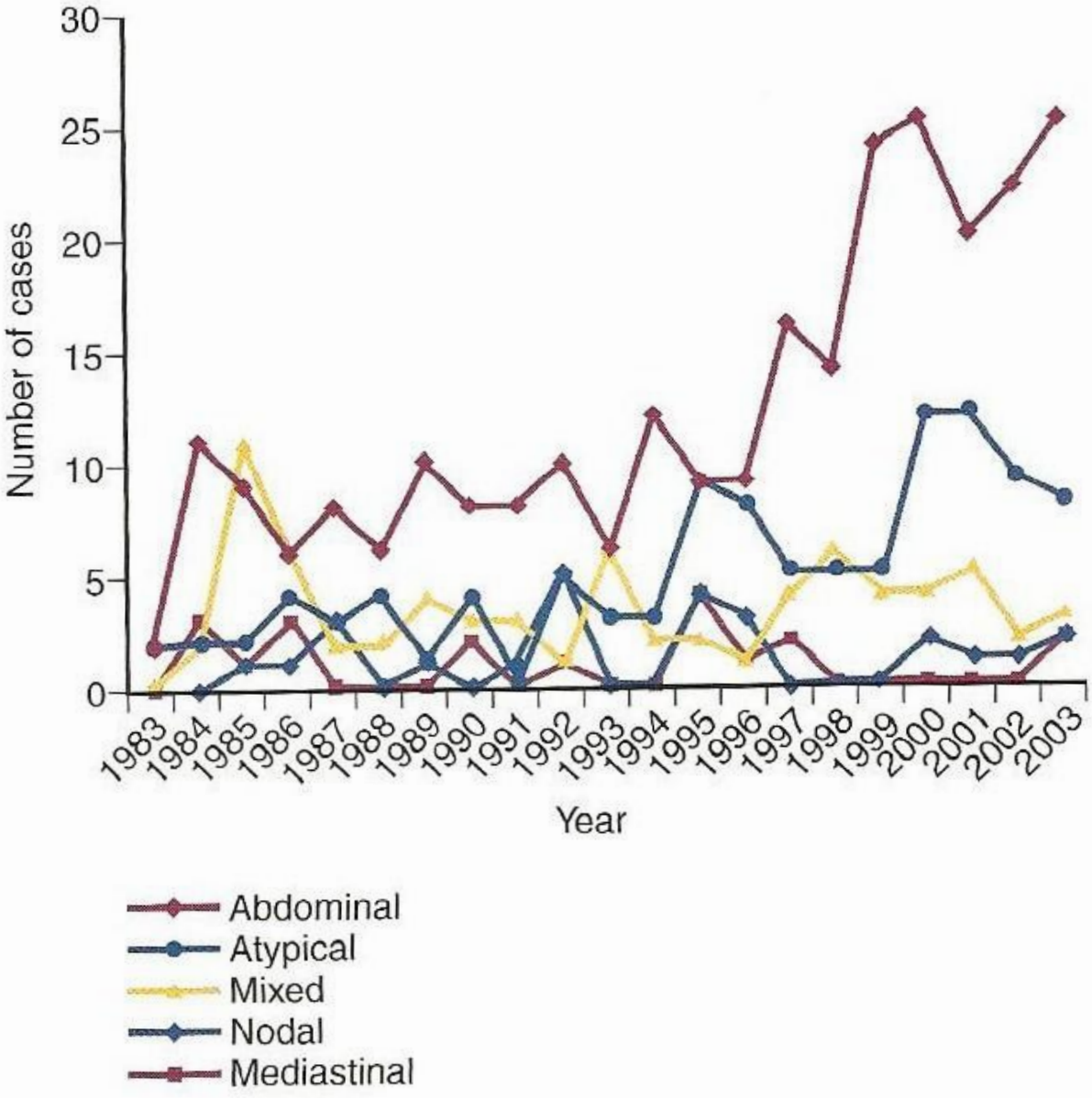


Fig 1. Increase in feline lymphoma incidence from 1983 to 2003. All cases of feline lymphoma presented each year to the University of California, Davis, Veterinary Medicine Teaching Hospital from 1983 to 2003 are shown.


30
25
20
15
10
5
0
Number of cases
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
Year
Abdominal
Atypical
Mixed
Nodal
Mediastinal

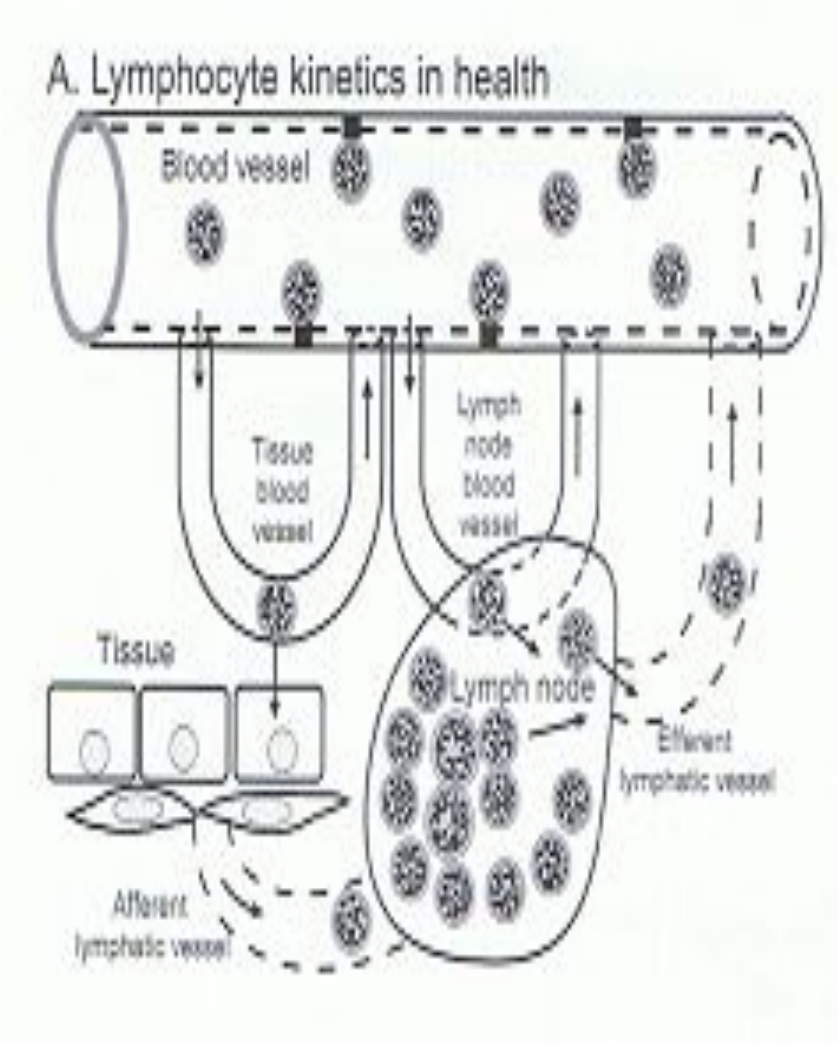
Etiologie

- Genetische factoren
  - FeLV *62 (+FIV *77)
- Immunosupressie
  - FIV
  - CYCLOSPORINE !!!
- Chronische ontsteking
  - IBD
  - Bacteriën
- Passief roken
  - 1 pak/dag *3

Deel 4
STAGING

Staging

- Lymfocyten circuleren permanent in het lichaam
- Belangrijk voor de prognose
  - beenmerg!!
- Opvolging effect behandeling



Staging

	WHO staging
Stadium 1	1 lymfeklier of lymfeweefsel van 1 orgaan aangetast
Stadium 2	Verschillende lymfeklieren in 1 streek
Stadium 3	Veralgemeende aantasting van lymfeklieren
Stadium 4	Infiltratie lever en/of milt +/- 1-3
Stadium 5	Infiltratie beenmerg +/- stadium 1-4

- 1-2 gunstige prognose
- 4 zeer slechte prognose indien gamma-delta
- 5 slechte prognose

Staging of feline lymphoma[7]

Stage I
- A single tumour (extranodal) or single anatomic area (nodal), includes primary intrathoracic tumours

Stage II
- A single tumour (extranodal) with regional lymph node involvement
- Two or more nodal areas on the same side of the diaphragm
- Two single tumours (extranodal), with or without regional lymph node involvement, on the same side of the diaphragm
- A resectable primary GI tract tumour, usually in the ileocaecal area, with or without involvement of associated mesenteric nodes

Stage III
- Two single tumours (extranodal) on opposite sides of the diaphragm
- Two or more nodal areas above and below the diaphragm
- All extensive primary unresectable intra-abdominal disease
- All paraspinal or epidural tumours, regardless of other tumour site(s)

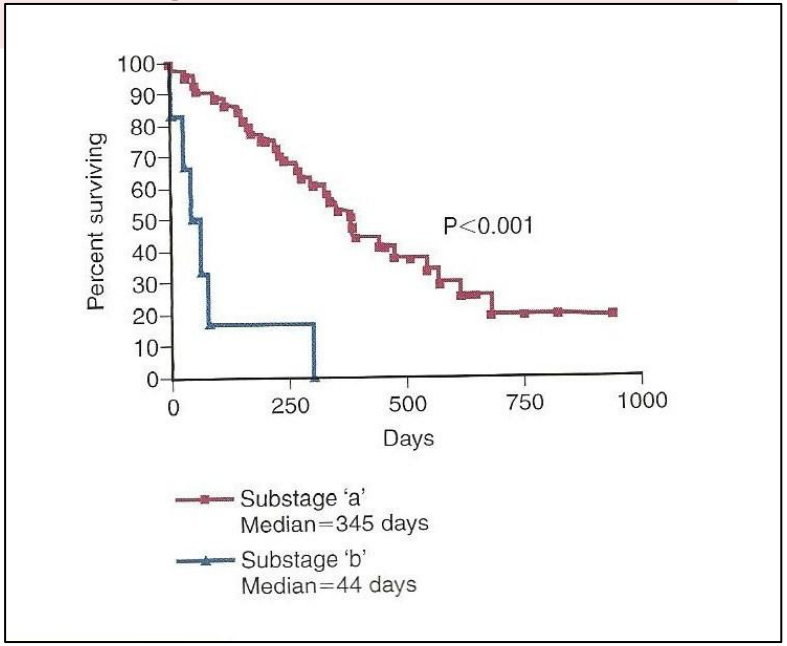
Stage IV
- As for stages I–III with liver and/or spleen involvement

Stage V
- As for stages I–IV with initial involvement of the central nervous system and/or bone marrow

Staging

Stadium	kliniek
a	Geen algemene symptomen
b	Algemene symptomen: lusteloos, anorexie, koorts, PU/PD, vermageren

Klinisch stadium **b:**
ongunstig

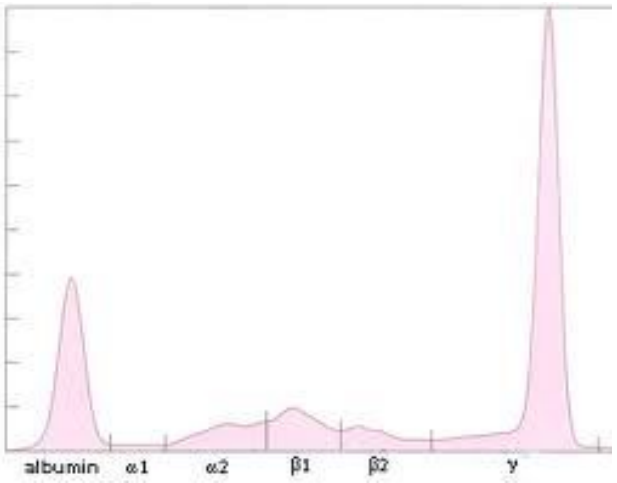


Staging

1. Hematologie
    1. Cytopenie
    2. Abnormale cellen in circulatie
    3. Leucocytose en lymfocytose
    4. Monocytose
    5. IMHA en/of IMT

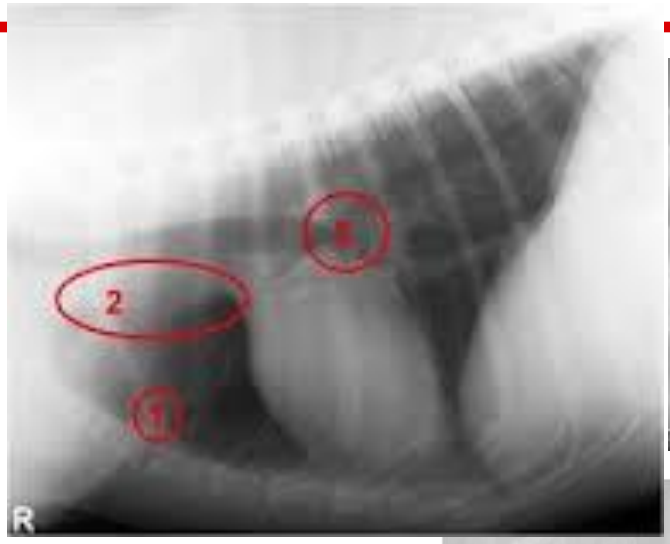
Staging

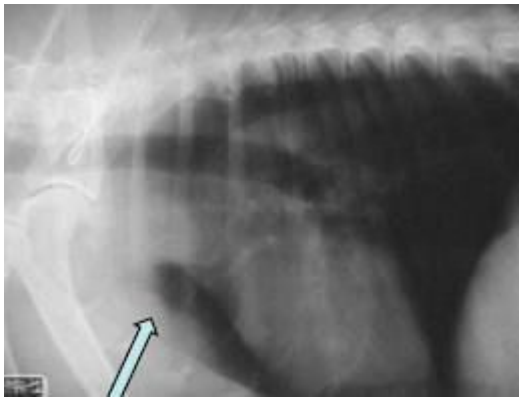
1. Hematologie
2. Biochemie
    1. Nierwaarden
    2. Leverwaarden
    3. Ca
    4. Electroforese
        1. Monoclonale gammopathie

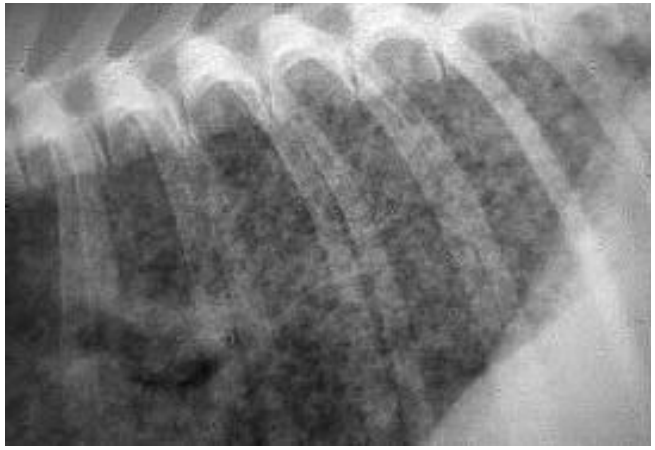


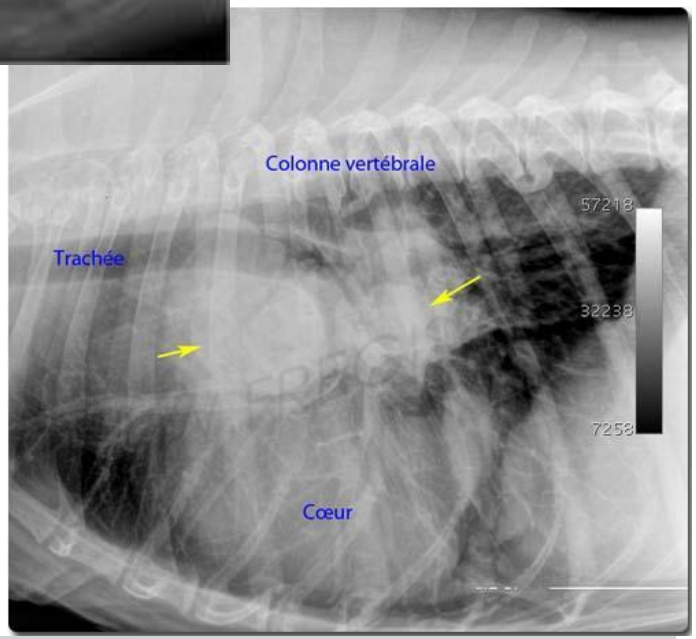
Staging

1. Hematologie
2. Biochemie
3. RX thorax
    1. Mediast
    2. Ln
    3. Parenchym: interstitieel!!



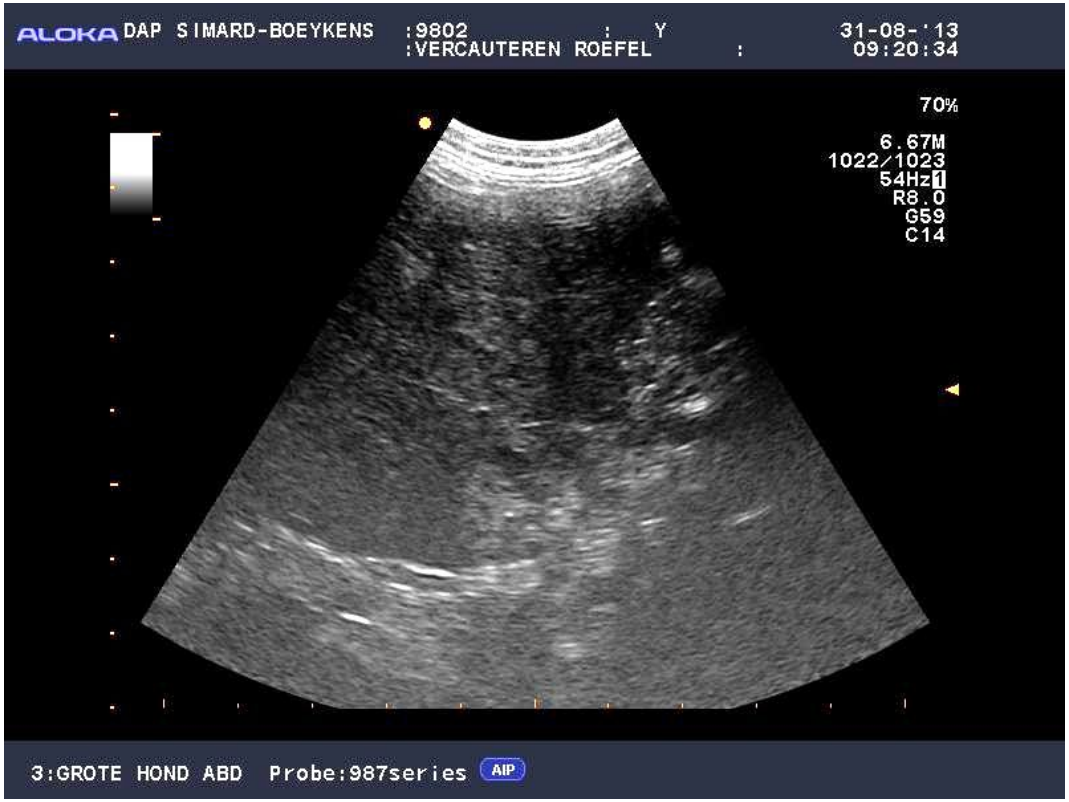






Staging

1. Hematologie
2. Biochemie
3. RX thorax
4. Echo abdomen
    1. Lever
    2. Milt
    3. Lymfeklieren
    4. Darmen



Staging

1. Hematologie
2. Biochemie
3. RX thorax
4. Echo abdomen
5. Beenmerg? Indien geen afwijkingen in bloedbeeld?

Staging

Veterinary and Comparative Oncology

Original Article

DOI: 10.1111/vco.12024

Peripheral blood abnormalities and bone marrow infiltration in canine large B-cell lymphoma: is there a link?

V. Martini[1], E. Melzi[1], S. Comazzi[1] and M. E. Gelain[2]

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[2]Department of Comparative Biomedicine and Food Science, Faculty of Veterinary Medicine, University of Padua, Padua, Italy

2013

Staging

Peripheral blood abnormality	Number of cases	BM infiltration (%)	
		Median	Min–max
Low haemoglobin concentration	17 (28.3%)	3.03	0.3–74.5
Normal haemoglobin concentration	43 (71.7%)	3.07	0.03–48.62
Low platelet count[ab]	15 (25%)	18	0.35–74.5
Normal platelet count	45 (75%)	2.49	0.03–27
High leucocyte number[a]	12 (20%)	21.55	0.34–74.5
Normal leucocyte number	48 (80%)	2.58	0.03–51.42
High lymphocyte number[a]	11 (18.3%)	24.43	1.2–74.5
Normal lymphocyte number	49 (81.7%)	2.2	0.03–51.42
Presence of atypical cells	5 (8.3%)	1.35	0.3–74.5
Absence of atypical cells	55 (91.7%)	3.25	0.03–71.26
Any abnormality	30 (50%)	3.97	0.13–74.5
No abnormalities	30 (50%)	2.58	0.03–22.4

[a]Significant difference in BM infiltration based on Mann–Whitney test ($P \leq 0.05$).

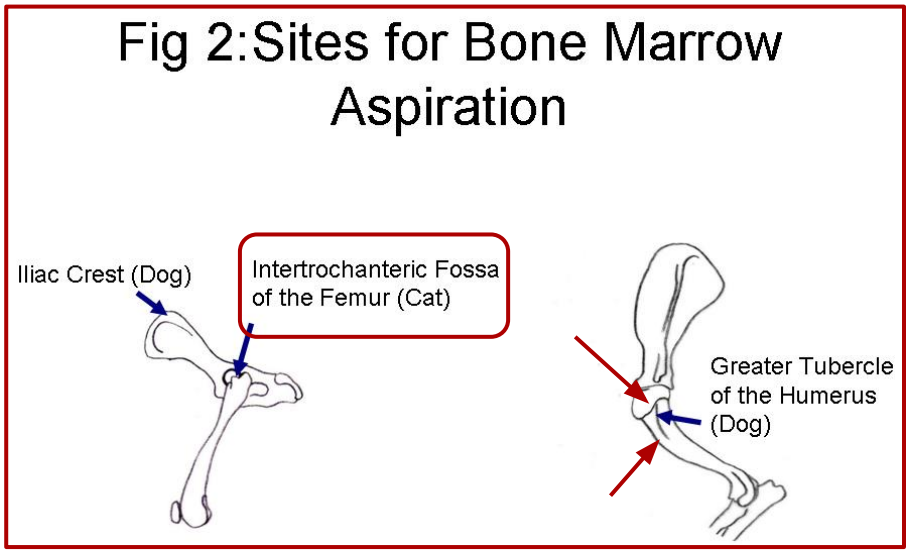
[b]Significant correlation with BM infiltration based on generalized linear models ($P \leq 0.05$).

Staging

- **Besluit**
  - Bloedresultaten kunnen infiltratie beenmerg NIET voorspellen
    - 50 % normaal bloedbeeld bij infiltratie
  - Mate van infiltratie BM was erger bij
    - Thrombocytopenie
    - Leucocytose of lymfocytose
  - Deze afwijkingen op zich voorspellen geen infiltratie
  - Punctie uitvoeren voor betere staging en prognose
  - Klinische relevantie moet nog bepaald worden

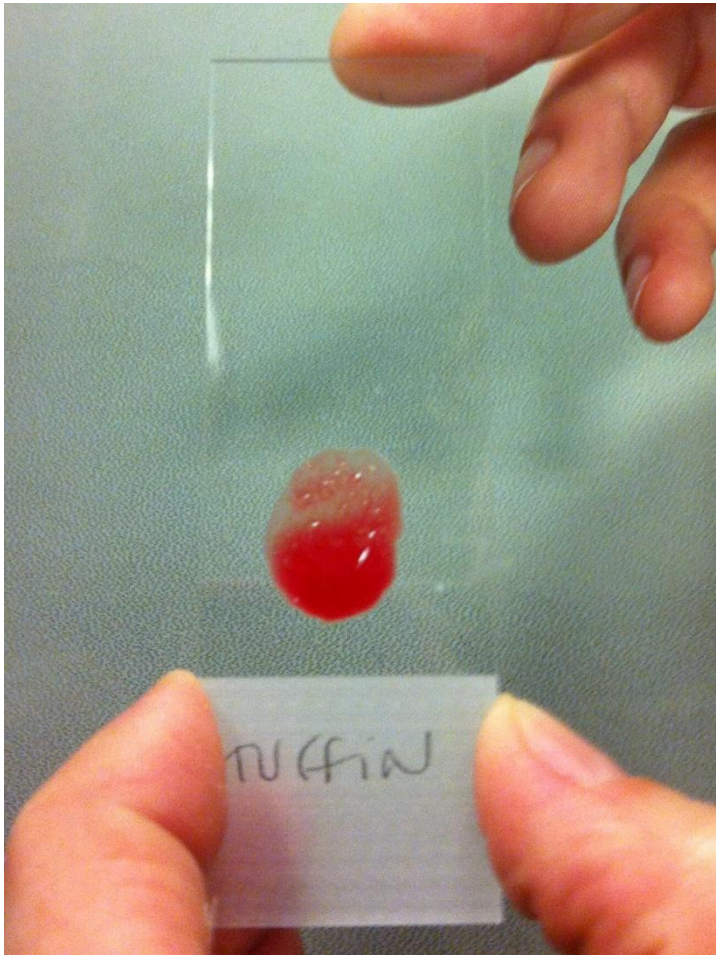
Beenmergpunctie

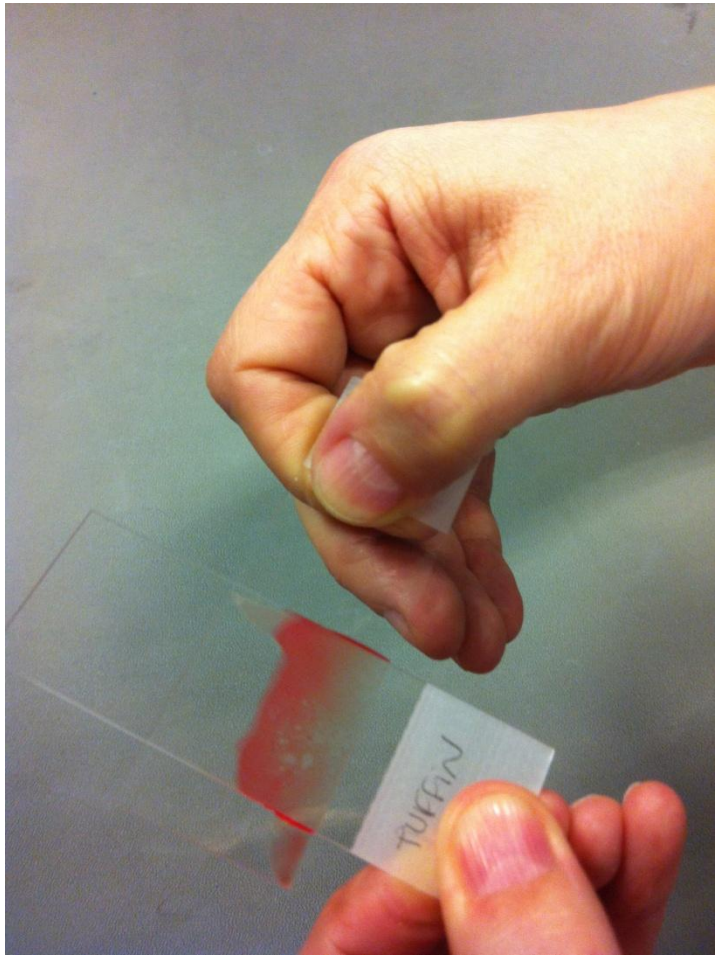
- **Proximale humerus**
- **Fossa femur**
  - Goed staal
  - Fijne cortex
  - Roze naald (geel <2.5 kg)
  - Citraat in naald en spuit
  - Sedatie of anesthesie
  - Scheren en ontsmetten
  - Penetratie cortex
  - verschillende malen na elkaar snel aspireren
  - Onmiddellijk en voorzichtig uitstrijken



Beenmergpunctie

Beenmergpunctie





Deel 5
Paraneoplastische syndromen

Paraneoplastische syndromen

- Frequent (hond>kat)
- Dikwijls als EERSTE symptoom
- Duidelijk een reden om lymfoproliferatieve aandoeningen gericht op te zoeken

Paraneoplastische syndromen

- **CACHEXIE**
  - Alleen bij hoge graad lymfomen
  - Storing in stofwisseling tgv cytokinen
  - prognostische factor

- **Koorts**
  - Cytokienen
  - NK cells, T-cells

Paraneoplastische syndromen

- **Hypercalcemie**
  - Eerder zelden bij katten
    - Frequent bij honden met mediastinaal lymfoom
    - ±100% T-cel lymfomen
      - Mediastinaal
    - Andere tumoren dan lymfomen
  - PTHrp gebonden: hypercalcemie meestal uitgesproken!!!
  - Secundaire nierinsufficiëntie!!

Hypercalcemie

- Sterkste stijging Ca
  - Paraneoplastisch (humoraal): PTHrp
  - Vit. D intoxicatie
  - PHPT (afhankelijk van de duur)

TABLE 2 VETERINARY MEDICINE

Causes of Hypercalcemia: GOSH DARN IT

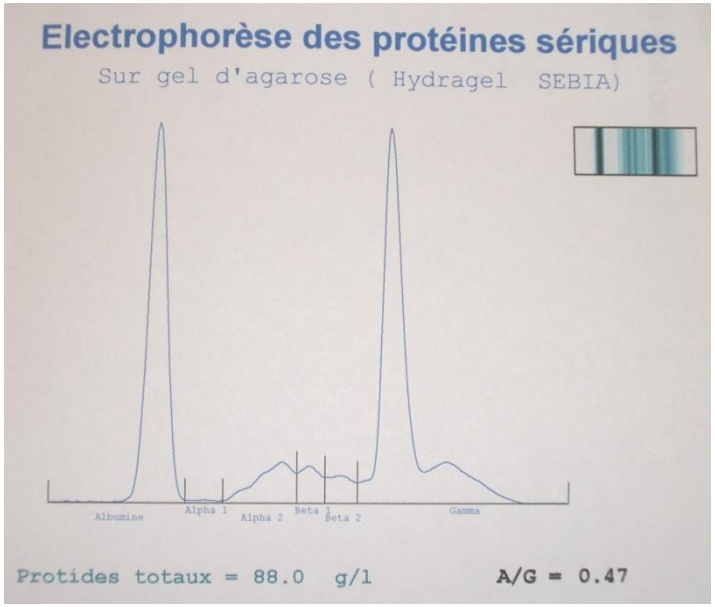
G	**Granulomatous disease** (fungal, parasitic, bacterial)
O	**Osteolytic disease** (tumor, infection)
S	**Spurious** (laboratory error, lipemia, hemolysis)
H	**Hyperparathyroidism**
D	**Drug related** (thiazide diuretics, calcium-containing phosphate binders)
A	**Addison's disease** (hypoadrenocorticism)
R	**Renal failure** (acute, chronic)
N	**Nutritional** (excess vitamin D, vitamin A, or calcium)
I	**Idiopathic**
T	**Tumors**

Mild	11.6 mg/dL
Matig	13.2
Erg	14.8

Hypoglycemie

- Glucose < 70 mg/dL
- Lymphoma mogelijke oorzaak
- Diffuse infiltratie van de lever
- Insuline-like growth factor

Monoclonale gammopathie



- Meestal B-cel
- Monoclonaal
  - Neo 1ste oorzaak
- Symptomen tgv hyperviscositeit
  - Bloedingen
    - CZS
    - Oculair,..
    - Nieren
    - infecties

Monoclonale gammopathie

- **Differentiaal Diagnose**
  - Chronische infecties
    - FIP, FIV, FeLV
    - Schimmelinfecties
    - “Tick-Borne”
  - IBD
  - IMHA
  - NEO: 1!!!
    - Lymphoma
    - Plasmacytoma
    - Multiple Myeloma

Serum protein electrophoresis in 155 cats

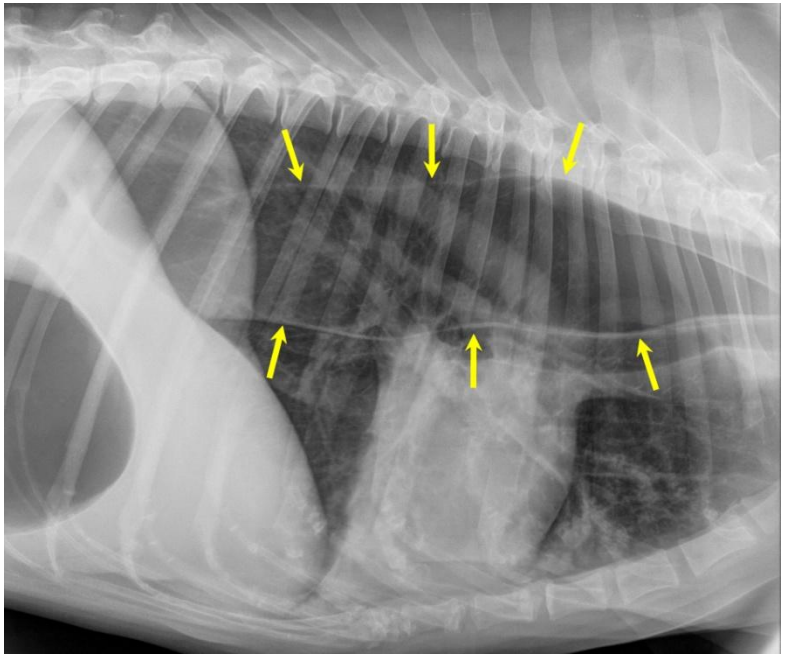
Samantha S Taylor BVetMed, CertSAM, DipECVIM-CA, MRCVS[1]*, Simon W Tappin MA, VetMB, CertSAM, DipECVIM-CA, MRCVS[1,a], Steve J Dodkin BSc, MSc[2], Kostas Papasouliotis DVM, PhD, DipRCPath, DipECVCP, MRCVS[2], Domingo Casamian-Sorrosal DVM, CertSAM, CertVC, MRCVS[1], Séverine Tasker BSc, BVSc, PhD, DSAM, DipECVIM-CA, PGCertHE, MRCVS[1]

4/155 monoclonale gammopathie

- 1 FIP
- 2 plasmacel tumoren
- 1 lymfoom

Myasthenia gravis Megaoesophagus

- Thymomen meest voorkomende oorzaak



Paraneoplastische syndromen

- **Hematologie**
  - Anemie
  - Neutrofilie
  - Eosinofilie
  - Thrombocytopenie
  - Leukemie: lymfoom stadium 5

Paraneoplastische syndromen

- **Anemie**
  - Verschillende mogelijke oorzaken!!!
  - Soms verschillende oorzaken samen
  - Differentiëren door bloedonderzoek
    - Regeneratief
    - Niet-regeneratief

Paraneoplastische syndromen

Regeneratieve anemie

- **IMHA**
  - Sferocytose, hemolyse, reticulocyten
- **Bloeding**
  - Darm
  - Nasaal
- **Erythrophagocytosis**
  - Extra-nodaal T-cel lymphoma (mastcel, MM, Hyst. Sarcoma)

Paraneoplastische syndromen

Niet-regeneratieve Anemie

- **Anemia of chronic disease**
  - Normochroom, normocytair
- **Myelophtisis**
  - Invasie van beenmerg door tumorale cellen
    - Vnl. leukemieën
    - Stadium5 lymfoom
- **Beenmerghypoplasie**
  - Renale lymfomen: EPO↓
- **Iatrogeen**
- **FeLV**

Paraneoplastische syndromen

Thrombocytopenie

- Immuungemedieerd
  - Samen met IMHA = Evan's syndrome
- Infiltratie beenmerg
- Sequestratie in de milt

Neutrofilie

- Regelmatig voorkomend
- 20-25.000
- 90-95% neutrofielen, soms metamyelocyten
- G-CSF of GM-CSF

Paraneoplastische syndromen

Eosinofilie

- Vnl. bij lymfomen en mastcel tumoren
- IL-5!!! Andere cytokienen

Leukemie

- Atypische lymfocyten in perifeer bloed
- Eindstadium lymfoom STADIUM 5
  - Beenmerg infiltratie
- Afwezigheid van leukemie sluit infiltratie beenmerg NIET uit
  - Slechts in 50% van infiltratie leukemie
    - = ***aleukemische leukemie***

Thymidine kinase

Een nieuwe biomarker??

Original Article

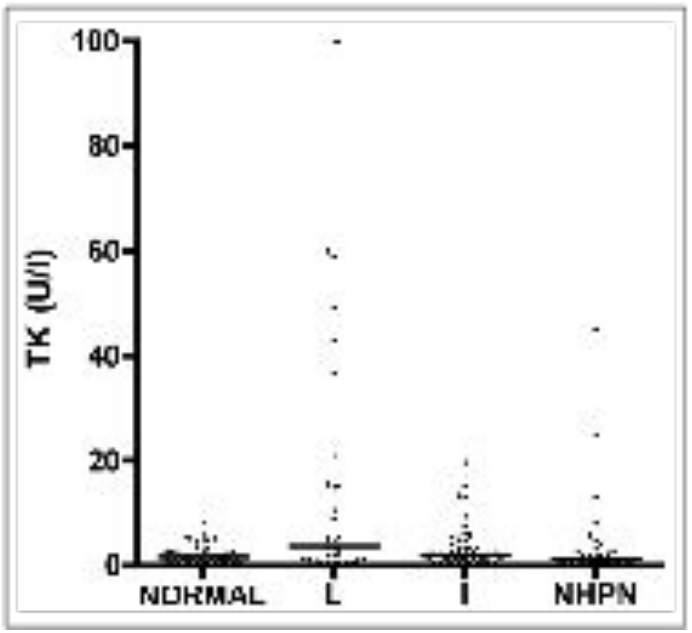
jfms

Journal of Feline Medicine and Surgery
15(2) 142–147

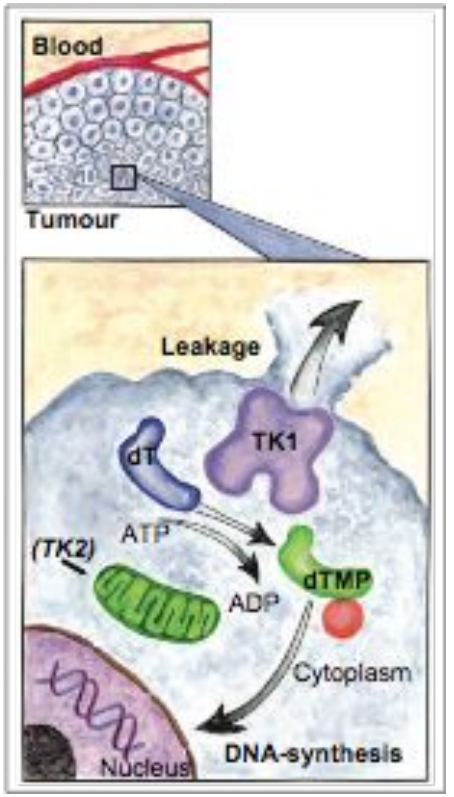
DOI: 10.1177/1098612X12463928
jfms.com
SAGE

Serum thymidine kinase activity in clinically healthy and diseased cats: a potential biomarker for lymphoma

Samantha S Taylor[1,*], Steve Dodkin[1], Kostas Papasouliotis[1], Helen Evans[2], Peter A Graham[2], Zoe Belshaw[3,†], Sara Westberg[4] and Henrik P von Euler[5]



Cut-off 8.9 U/L
Specificitiet 94,8%



Deel 6
Alimentair lymfoom

70% van alle gevallen

GI lymfoom

- Synoniem
  - Intestinaal lymfoom
  - Abdominaal lymfoom (met aantasting van andere organen)
  - Alimentair lymfoom
- Symptomen **ATYPISCH!!!**
  - Anorexie
  - Vermageren
  - Braken/diarree
- Klinisch onderzoek
  - afhankelijk van type!!!
- Bloedonderzoek NIET SPECIFIEK

GI lymfoom

- Differentiaal diagnose
  - IBD
  - Chronische pancreatitis
  - Andere tumoren
    - Adenocarcinoom
    - Mastocytoom
  - Hypereosinofiel syndroom
  - Metabole aandoeningen

GI lymfoom

- Verschillende klinische vormen !!!!!
  - Focaal versus Diffuus infiltratief
  - d.d. versus D.D.
  - Lymfeklieren
    - Sterk/matig/bijna niet opgezet
  - Massa maagwand
  - Oude katten: invaginatie
    - Hypomotiliteit aangetast segment

GI lymfoom REAL/WHO

- Low grade diffuse **small lymfocytic**
  - B-cell small lyphocytic
  - Eptheliotropic T-cell
- High-grade **immunoblastic**
  - Diffuse large B-cell immunoblastic nuclear type
  - T-cell lymphoblastic
- **LGL** Large Granular Lymph.

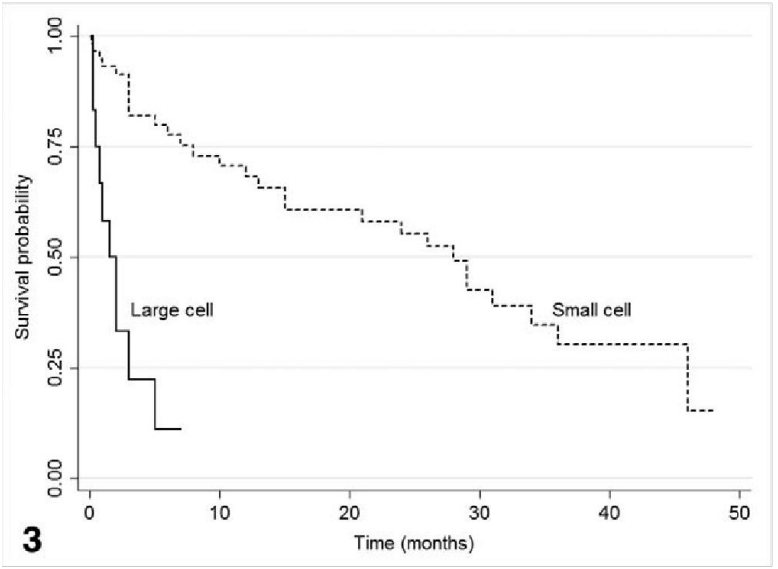


Figure 3. Kaplan-Meier plot of survival comparing cats with T-cell lymphoma, small-cell type (median survival 28 months) with cats with T-cell lymphoma, large-cell type (median survival 1.5 months).

Table 1. Histologic classification of 50 cases of feline GIT lymphoma.

REAL/WHO*	NCI WF†	NCI WF Grade	No. Tumors (n = 49)‡
Diffuse Large B-Cell of Immunoblastic Nuclear Type	Immunoblastic	High	16
Diffuse Large B-Cell Lymphoma of Centroblastic Nuclear Type	Diffuse large	Intermediate	2‡
Large Granular Lymphocyte	Immunoblastic	High	3
B-Cell Small Lymphocytic	Diffuse small lymphocytic	Low	3
Epitheliotropic Small T-Cell Lymphoma	Diffuse small lymphocytic	Low	15
B-Cell Lymphocytic Intermediate Type	Diffuse small cleaved	Intermediate	4
T-Cell–Rich Large B-Cell	Diffuse mixed	Intermediate	2
T-Cell Lymphoblastic	Lymphoblastic	High	4

* REAL/WHO classification system.

† NCI WF classification system.

‡ One tumor classified as "diffuse large cell lymphoma" by the NCI WF had cells positive for both BLA.36 and CD3. For this reason it was not assigned a REAL/WHO classification.

GI lymfoom

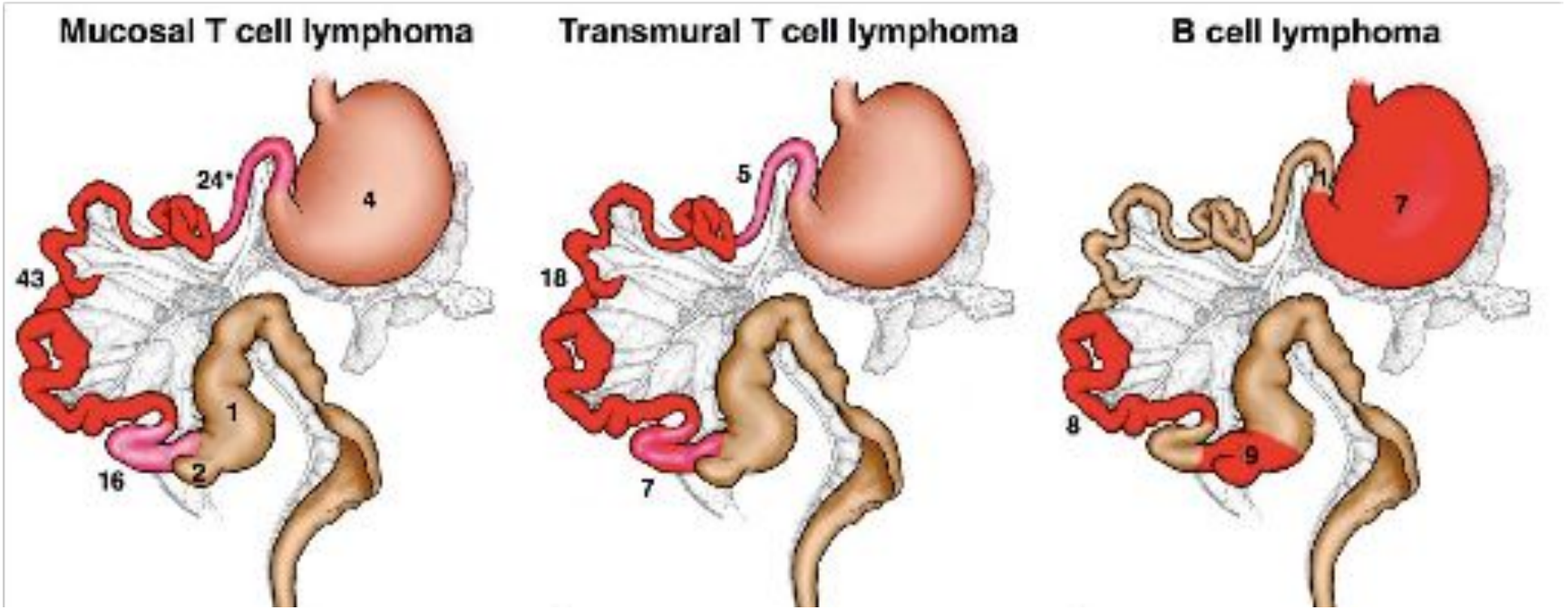
	Intermediaire/ Hoge graad	**Lage Graad**	**Large Granular Lympfocyte Lymphomae**
Leeftijd (mediaan)	12 jaar	13 jaar	10 jaar
FeLV	>70% -	>99% -	>96% -
Immuno-phenotype	B- en T-cel	> 90% T-cel	>90% T-cel
Abdominale palpatie	Intestinale massa !!! Extra-intestinaal lymfekieren (mes.) lever, milt nier	NORMAAL Diffuse verdikking darmen Vergrote lymfeklieren Massa (zelden)	Focale massa Lymfeklieren Lever, milt nieren

GI lymfoom

	Intermediaire/ Hoge graad	**Lage Graad**	**Large Granular Lympfocyte Lymphomae**
Behandeling	CHOP	Prednisolone Chlorambucil	CHOP
Toediening	IV	ORAAL	IV
CR	36-87%	56-97%	<5%!!!
Mediane overleving	7-10 maanden	19-29 maanden	17 dagen

GI lymfoom REAL/WHO

- NAARGELANG CELTYPE VERSCHILLENDE LOKALISATIE



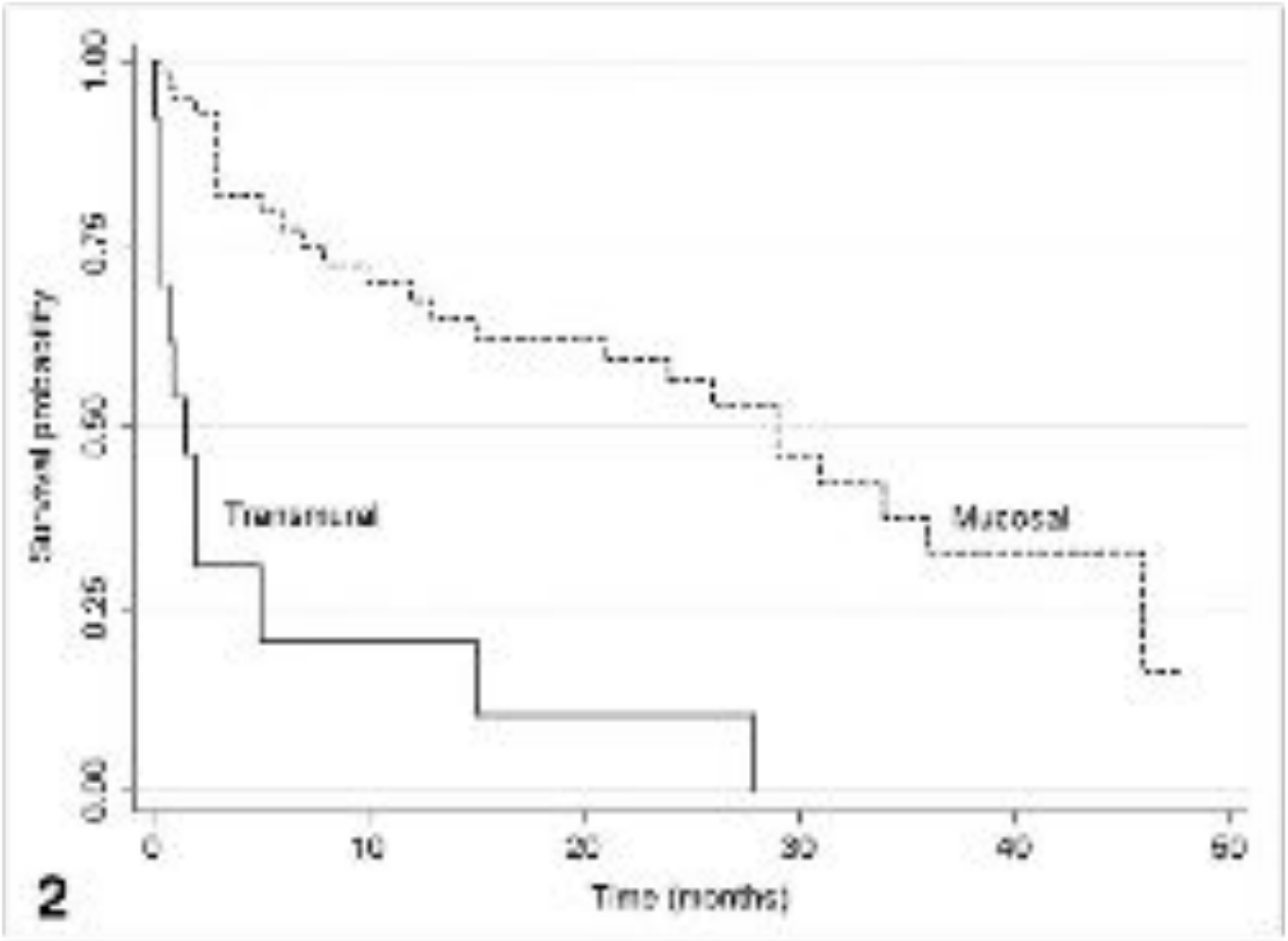
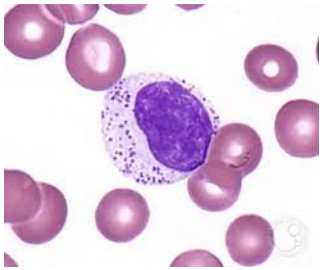
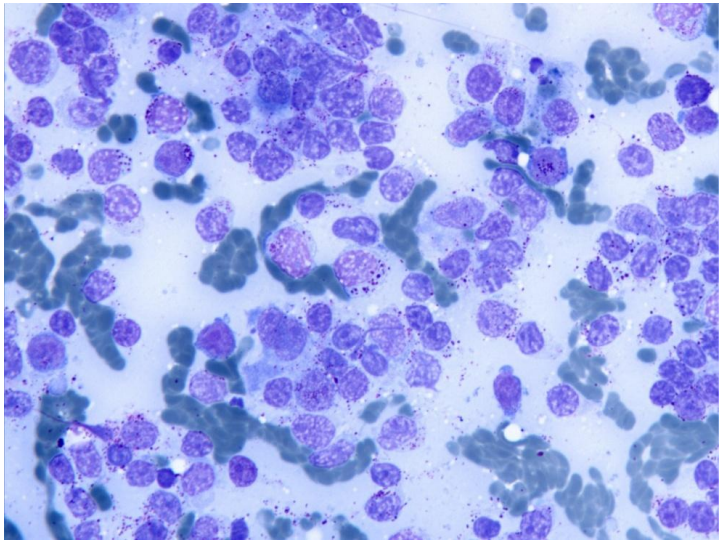


Figure 2. Kaplan-Meier plot of survival comparing cats with mucosal T-cell lymphoma (median survival 29 months) with cats with transmural T-cell lymphoma (median survival 1.5 months).

GI lymfoom: LGL

- LARGE GRANULAR LYMFOCYTE LYMPHOMA
  - Darmen
  - Andere organen
  - Zeer slechte prognose
  - Reageert niet op chemo
  - Overleving <2 maand





- Vet Comp Oncol.2008 Jun;6(2):102-10.

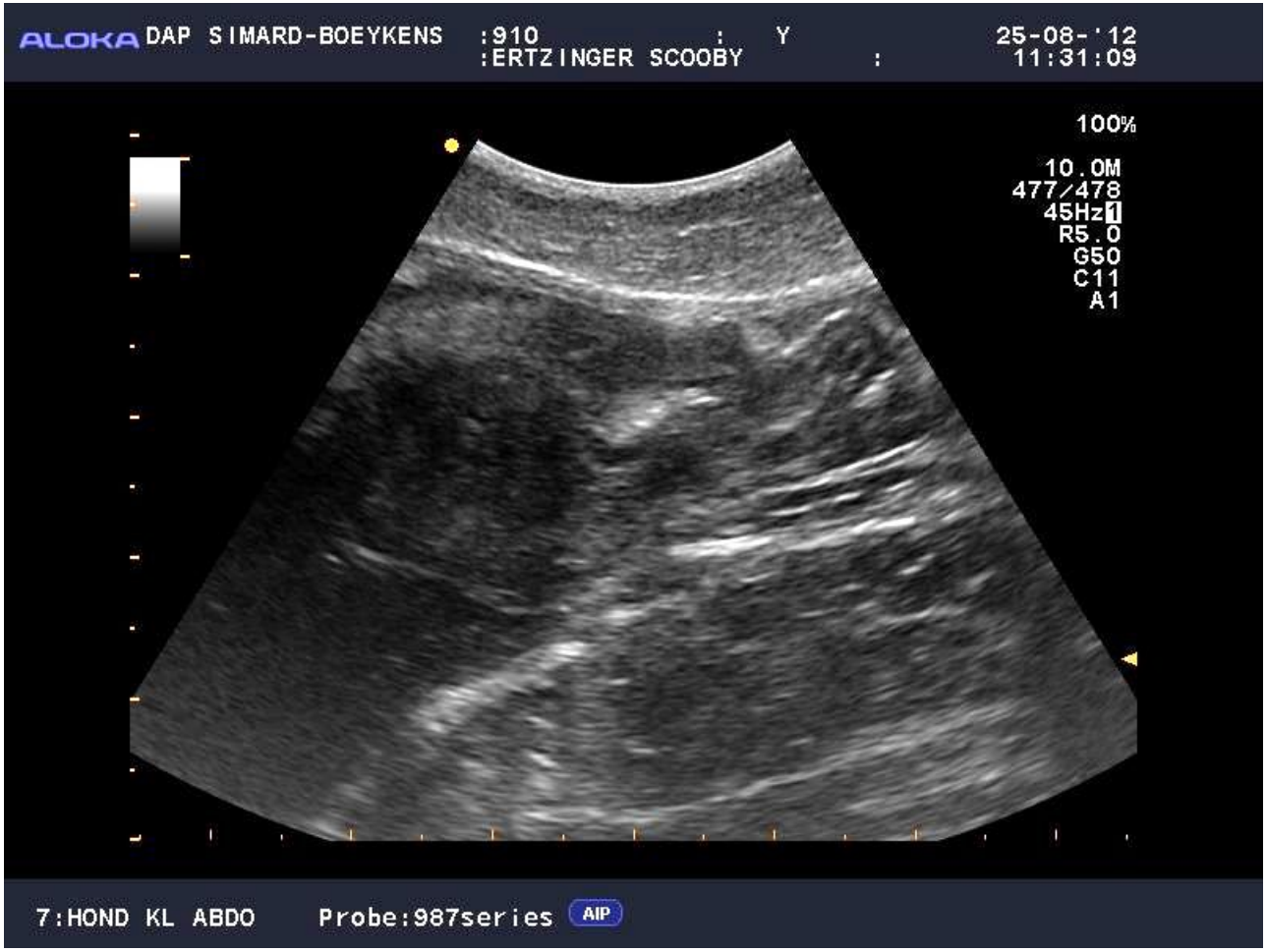
- **Description of clinical and pathological findings, treatment and outcome of feline large granular lymphocyte lymphoma**

(1996-2004) Krick EL, Little L, Patel R, Shofer FS, Sorenmo K, Clifford CA, Báez JL.

GI lymfoom Diagnose

- Echografie
  - Tumor

GI lymfoom: diagnose



VERLIES VAN LAGEN : HOOGGRADIG

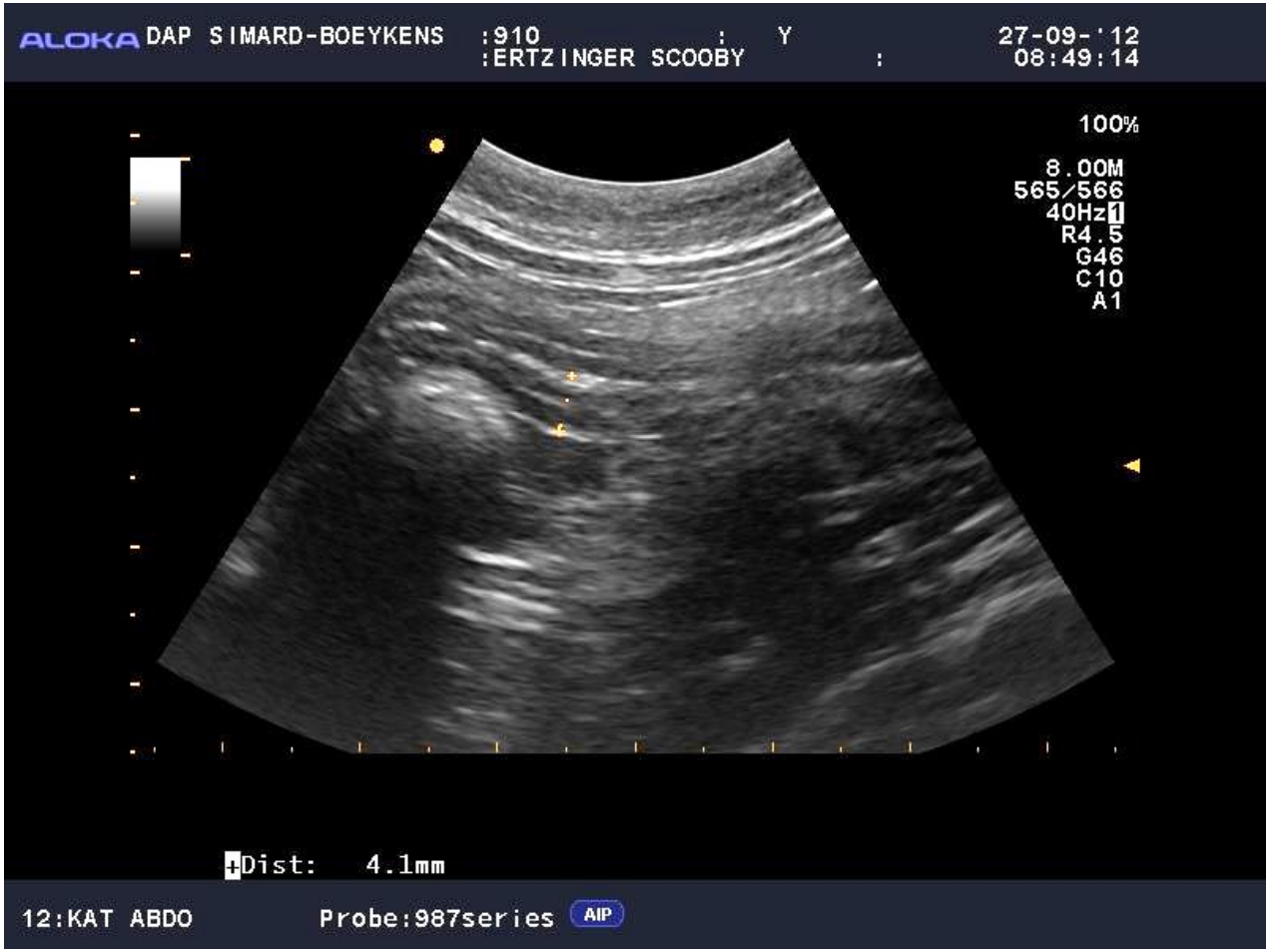
GI lymfoom: diagnose

- Echografie
  - Tumor
  - Opgezette Inn

GI lymfoom: diagnose

- Echografie
  - Tumor
  - Opgezette lnn

GI lymfoom: diagnose



- Verdikte wanden

GI lymfoom: diagnose

- ECHOGRAFIE
  - Tumor
  - Opgezette lnn
  - Verdikte wanden
  - **Hepatomegalie**
  - **Splenomegalie**
  - **Δ echodensiteit lever en/of milt**

Hooggradig	**Laaggradig**
Transmurale verdikking (symmetrisch!!)	Normaal !!! 1 laag verdikt
Verminderde echogeniciteit	Verdikking van de muscularis
Verlies van gelaagdheid	Behoud van gelaagdheid
Gelocaliseerde hypomotiliteit	Hypomotiliteit zelden
Vergrote lymfklieren	Vergrote lymfeklieren
Extra-intestinaal	Lever en milt normaal

LGAL vs. IBD : Echografie

- Verdikking muscularis (alleen of)

  SAMEN

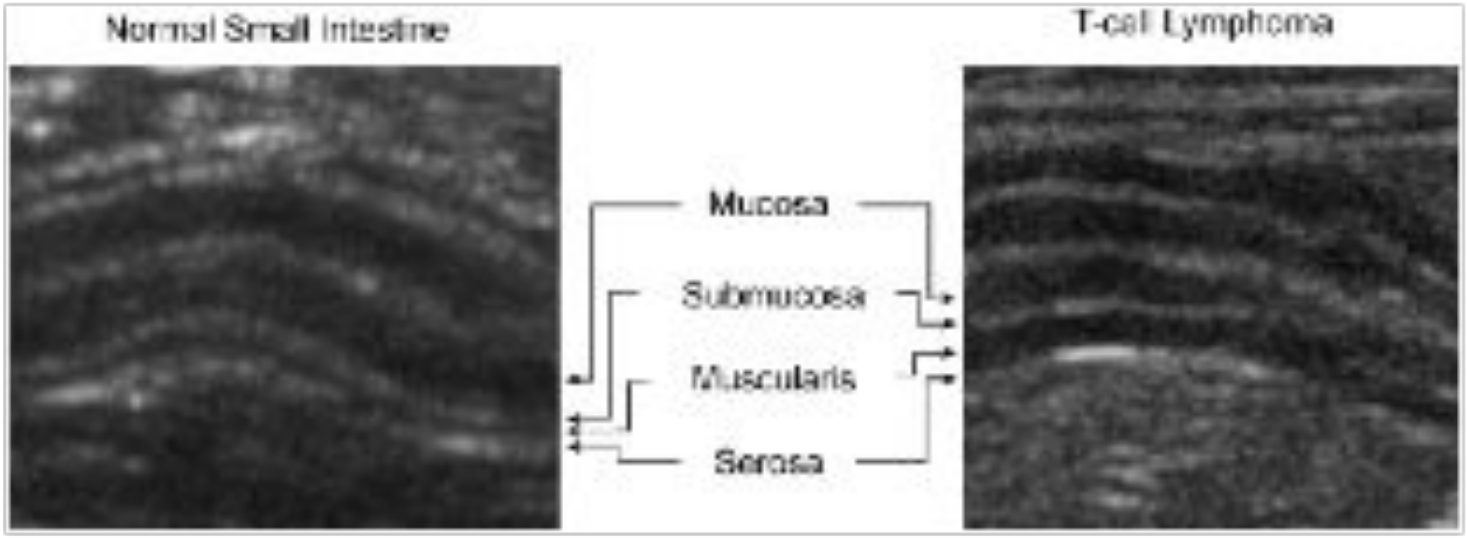
- Lymphadenopathy

J Vet Intern Med 2010;24:289–292

Ultrasonographic Evaluation of the Muscularis Propria in Cats with Diffuse Small Intestinal Lymphoma or Inflammatory Bowel Disease

A. L. Zwingenberger, S. L. Marks, T. W. Baker, and P. F. Moore

STERKE INDICATIE VOOR LYMFOOM



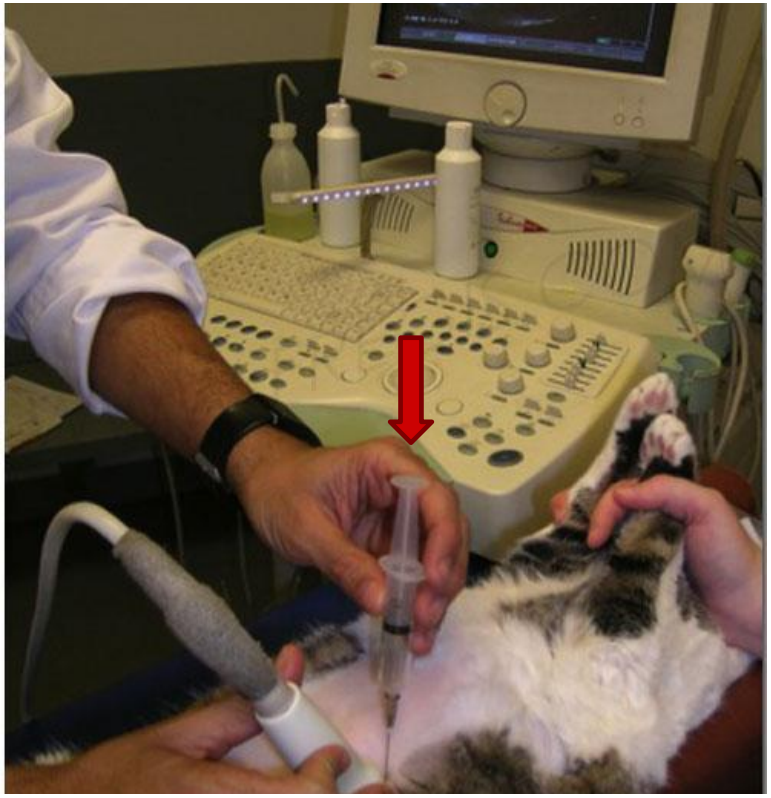
GI lymfoom: cytologie

1. Niet bij diffuse vormen
   a. technisch zeer moeilijk
   b. kleine lymfocyten met normaal uitzicht

2. Lymfeklieren
   a. Laaggradig : kleine lymfocyten???
   b. Hooggradig
      i. meestal diagnose
      ii. reactieve lymfeklieren mogelijk!!!

GI lymfoom: diagnose

- Echografie
- Cytologie
- Endoscopie
  - Biopsie
  - Macroscopische afwijkingen niet specifiek
  - Technisch moeilijk indien dunne darm: JEJUNUM!!
  - Kwaliteit biopsie???



GI lymfoom: diagnose

- LAPARATOMIE
  - Diagnose ++++
  - Kwaliteit biopsie ++++
    - Alle lagen van GI stelsel: MUSCULARIS
    - Andere Organen
  - Focale vormen EXCISIE: diagnose EN behandeling
    - obstructie

- ***Comparison of endoscopic and full thickness biopsy specimens for diagnosis of IBD and alimentary tract lymphoma in cats***. *Sarah E.Evans et al. JAVMA 2006*: lymfoom maag endoscopie gemakkelijk en diagnostisch; dunne darm verkies laparatomie.

- ***Perioperative complications sfter full-thickness gastrintestinal surgery in cats with alimentary lymphoma.*** *Smith AL et al. Vet Surg 2011: niet meer kans op dehiscentie*

Cytologie vs Histopathologie

- **Nodulaire vorm** en sterk opgezette lnn.: cytologie meestal voldoende.
- **LGL**: cytologie>>histologie
- **Diffuse vorm:** histologie verdient voorkeur
  - Ddx lymfoom vs IBD
  - Score IBD (WSAVA GI Standardization Group)
    - Mbt de behandeling

WSAVA
Global Veterinary Development

GI STANDARDIZATION GROUP

Following a 2004 publication in the *Journal of* the American Veterinary Medical Association that identified marked discrepancies in the histopathological evaluation of gastrointestinal biopsies, a group of veterinarians specialising in GI diseases approached the WSAVA with the concept of standardising the collection and assessment of GI biopsies. (See Willard MD, et al. Interobserver variation among histopathological evaluation of intestinal tissues from dogs and cats. *J Am Vet Med Assoc* 2004; 220: 1177).

Based on similar goals and the ultimate success of the Liver Disease Standardization Group (www.wsava.org/LiverStandard.htm), a formal GI Standardization Group was organized, consisting of Dr. Yoshebu (chair), Bilzer, Day, Guilford, Hall, Jergens, Mansell, Minami, Willcock, and Willard, and its remit set. With support from Hill's Pet Nutrition, the group has enjoyed tremendous productivity, including:

- Histopathological Standards for the Diagnosis of Gastrointestinal Inflammation in Endoscopic Biopsy Samples from the Dog and Cat: A Report from the World Small Animal Veterinary Association Gastrointestinal Standardization Group. (J Comp Path 2008;138:S1–S44) This monograph presents a standardised pictorial and textual template of the major histopathological changes that occur in inflammatory disease of the canine and feline gastric body, gastric antrum, duodenum and colon.
- Standardized GI Endoscopy Reporting Forms available online – www.wsava.org/StandardizationGroup.htm

The group recognised early the need to also standardise endoscopic examination and sampling of the GI tract to ensure the highest procedural diagnostic yield. These endoscopy report forms help address this, namely that endoscopic examination is complete and thorough.

Development of an ACVIM Consensus Statement on IBD

The ACVIM Board of Regents invited the WSAVA Gastrointestinal Standardization Group to develop, present and publish an ACVIM Consensus Statement on 'Histopathologic Standards for Canine and Feline IBD'. This was presented in a special session at the 2008 ACVIM Forum in San Antonio and is awaiting ratification and eventual publication in the *Journal of Veterinary Internal Medicine*.

Dr Robert Washabau proposed the Consensus Statement on IBD, based on the work of the WSAVA Standardization Group, at the 2008 ACVIM Forum in San Antonio, Texas. Congratulations to the GI Standardization Group for their outstanding contribution to the betterment of of medicine and hance the lives of dogs and cats throughout the worrld.

For more informat ion visit their committee page on the WSAVA website. ■

LATEST WSAVA NEWS

Periodically, WSAVA produces a News Bulletin that highlights the initiatives and accomplishments of the association, its committees, member associations, and individual members. The most recent News Bulletin is now available for viewing online – www.wsava.org ■

Cytologie vs histopathologie

- **Diffuse vorm**: histologie verdient voorkeur
  - Ddx lymfoom vs IBD
  - Score IBD (WSAVA GI Standardization Group)
  - Graad lymfoom
  - Bij twijfel bijkomende onderzoeken nodig!!
    - Beginnend diffuus lymfoom
    - Lage graad lymfoom
    - Erge infiltratie van ontstekingscellen (IBD)

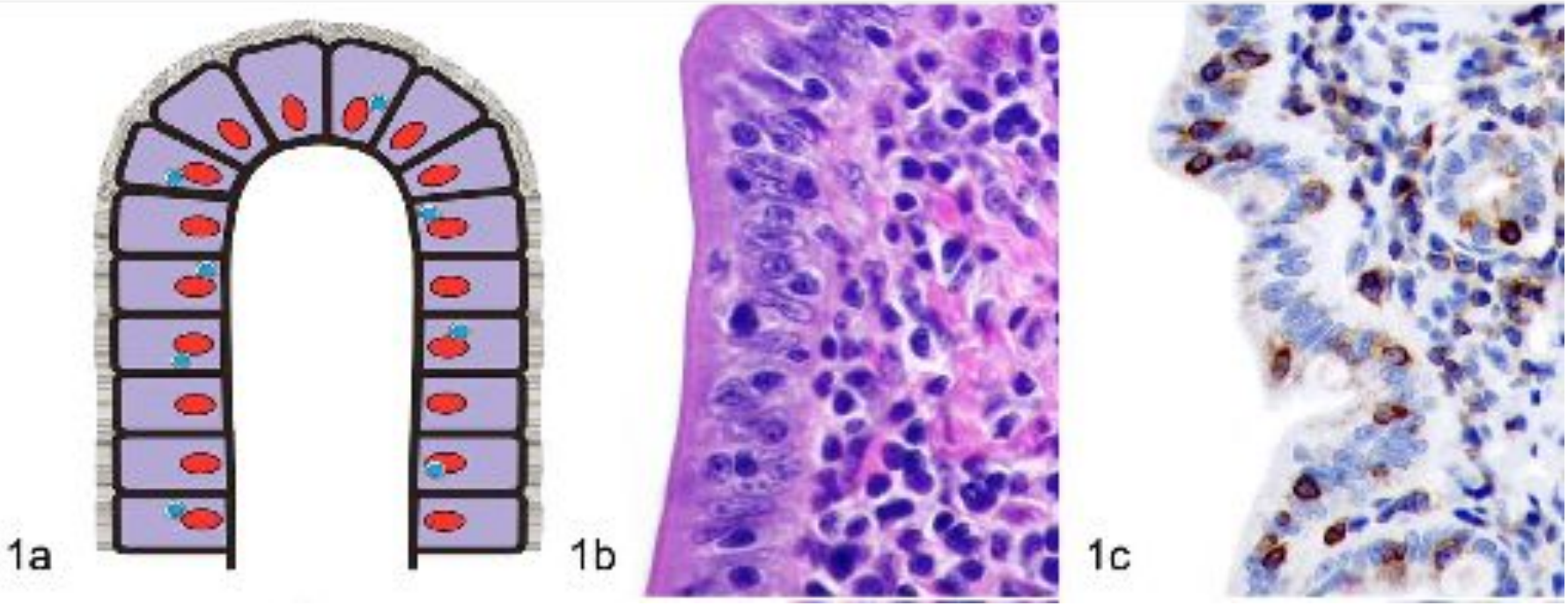
Histopathologie

- **Hystologische parameters indicatief voor lymfoom**
  - Infiltratie onder de submucosa (muscularis)
    - onmogelijk met endoscopie
  - Intra-epitheliale infiltratie (100% specifiek)
  - Monomorfe populatie kleine lymfocyten (versus lyfocytaire-plasmacytaire infiltratie)
  - Intravasculaire infiltratie
  - Hoge mitotische index

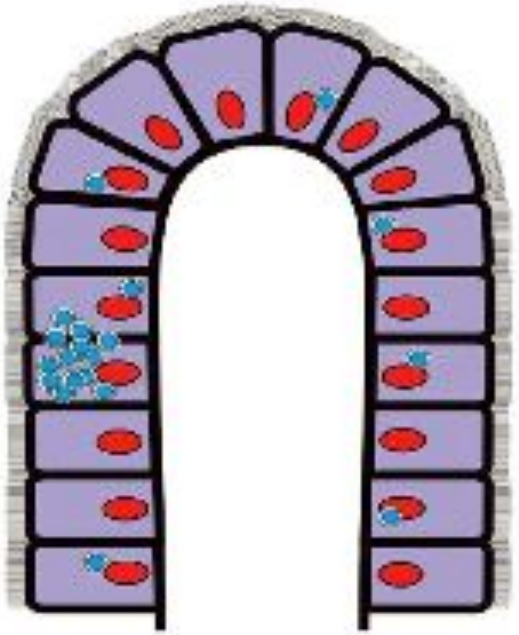
Immunohistochemie

- Fenotype bepalen: B versus T
  - MALT vnl. T lymfocyten
  - IBD en int. T cel lymfoom : proliferatie T-cellen uit MALT
  - Meer T-cel dan B-cel lymfoom in jejunum
  - 100% B-cellen : lymfoom
  - Invasie epitheel : lymfoom
    - Epitheliotroop T-cel lymfoom

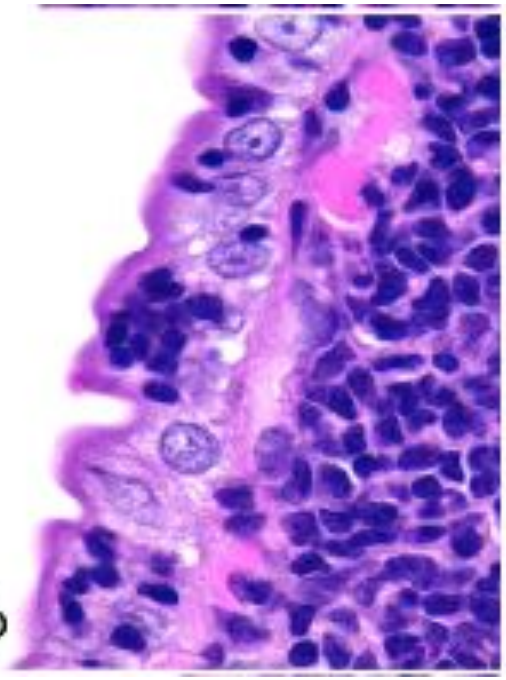
- Na immunochemie verandering van diagnose!!!!
  - IBD naar LGAL


1a
1b
1c

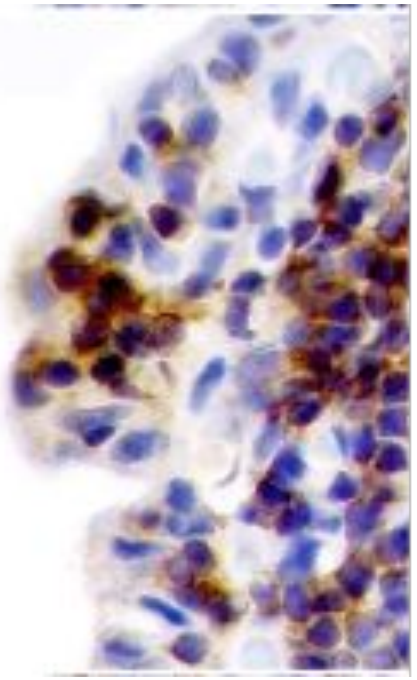
2a

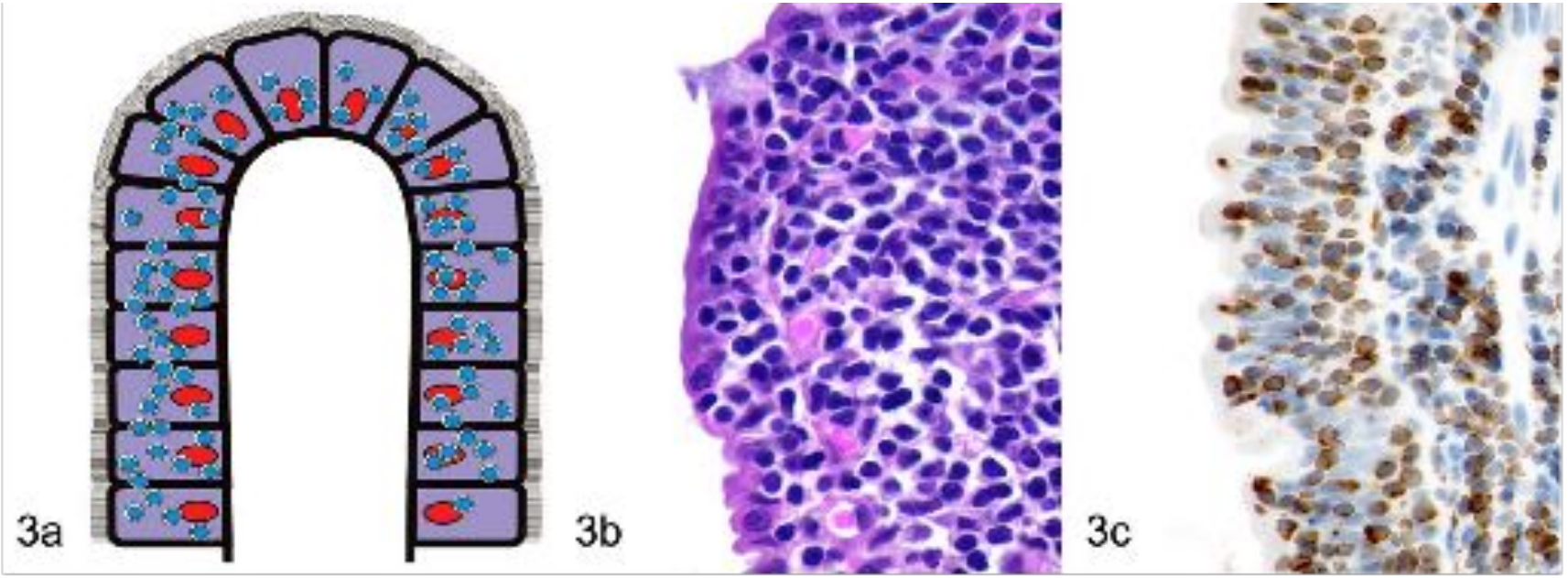


2b

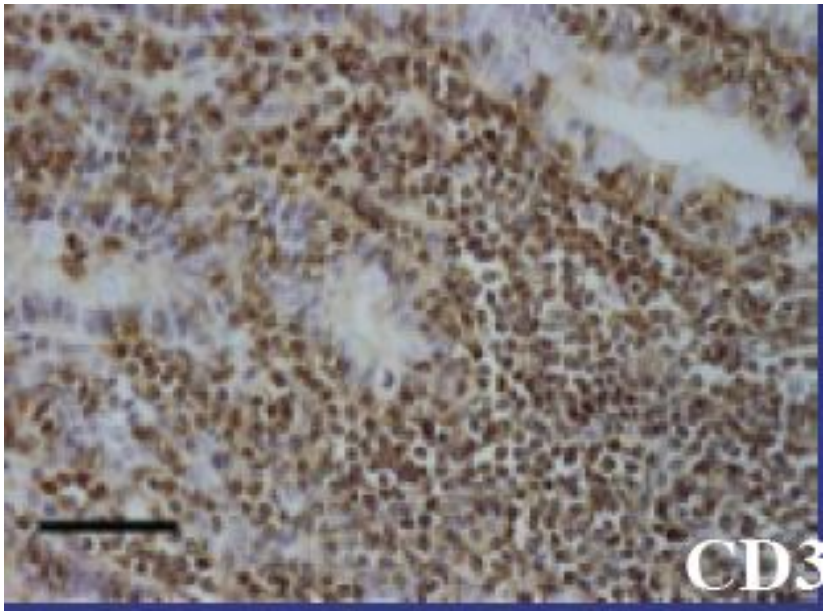


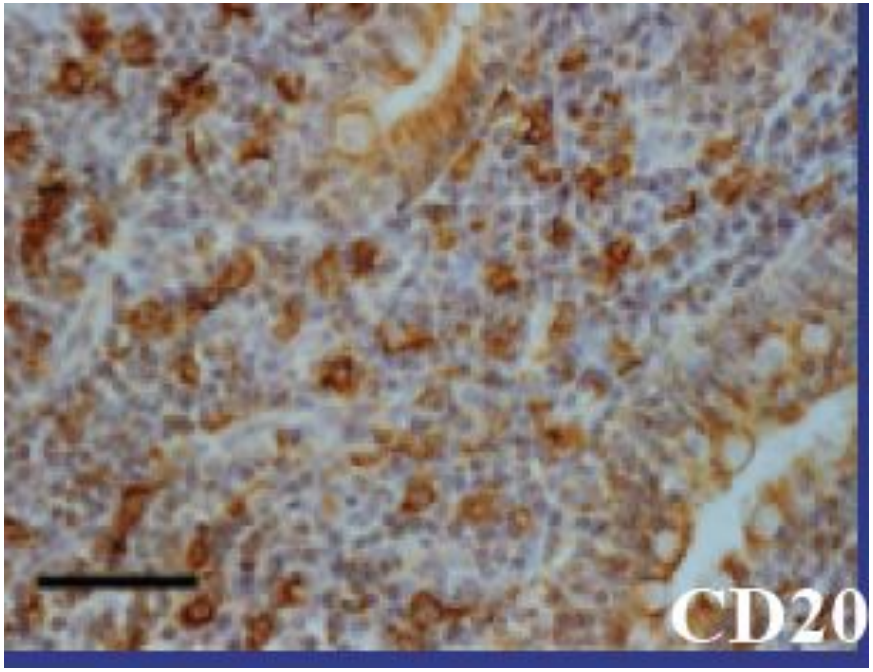
2c



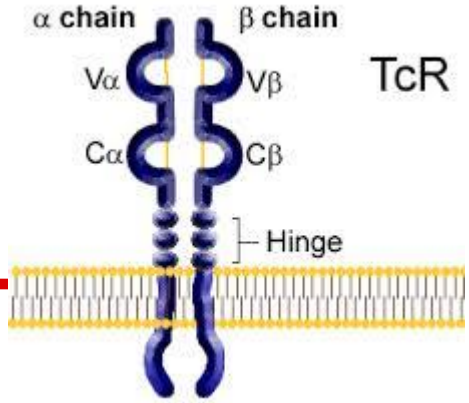

3a
3b
3c

Immunohistochemie

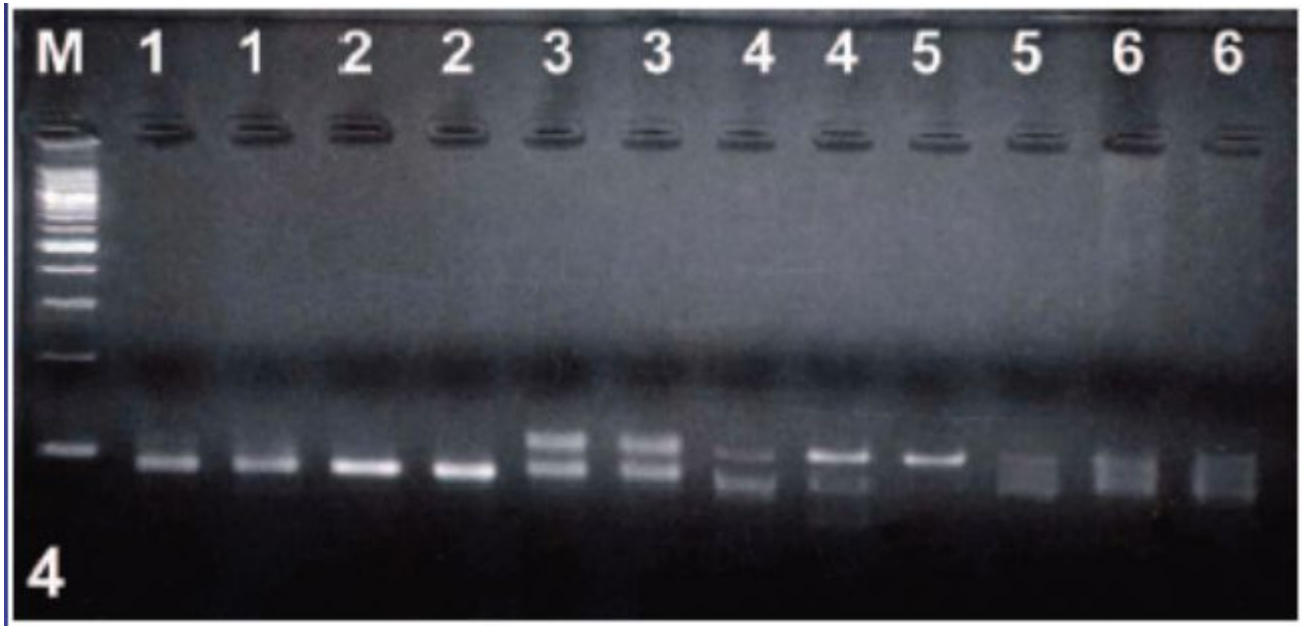




Clonaliteit: PARR



- PCR for Antigen Receptor Rearrangement
  - IBD : polyclonaal
  - LGAL : mono- of oligoclonaal
- PARR combineren met histo en IHC!!!!



Kiupel 2011

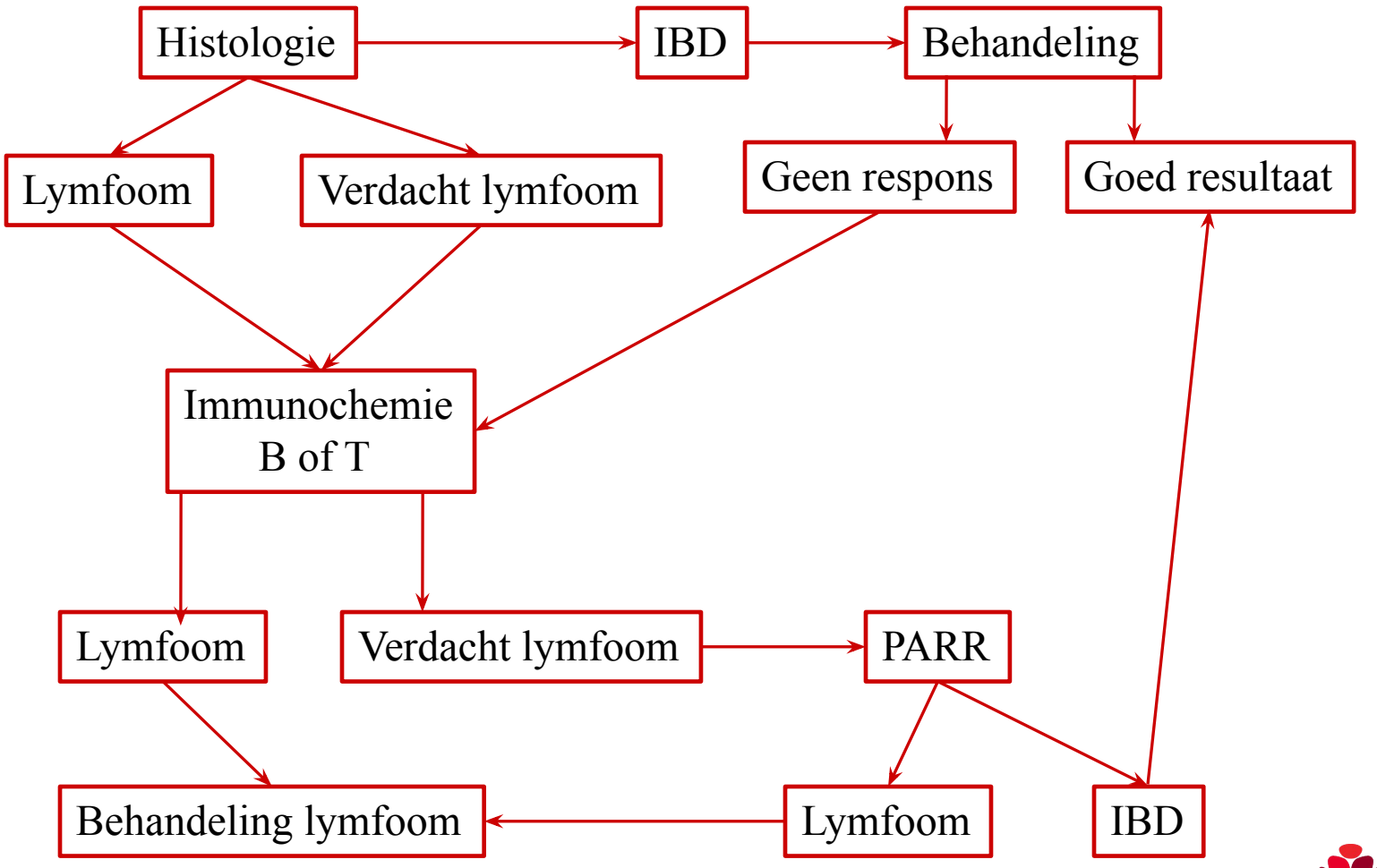
Change of Diagnosis	HE + IHC	HE + IHC + PCR
IBD → T cell lymphoma	5	10
IBD → B cell lymphoma	0	0
T cell lymphoma → IBD	1	3
T cell lymphoma → B cell lymphoma	2	2
B cell lymphoma → T cell lymphoma	1	1
B cell lymphoma → IBD	0	0

The bottom box highlights the numbers of cases for which the diagnosis was changed after combining the morphologic evaluation with immunophenotyping and with immunophenotyping plus clonality analysis. HE, hematoxylin and eosin; IBD, inflammatory bowel disease; IHC, immunohistochemistry; PCR, polymerase chain reaction.

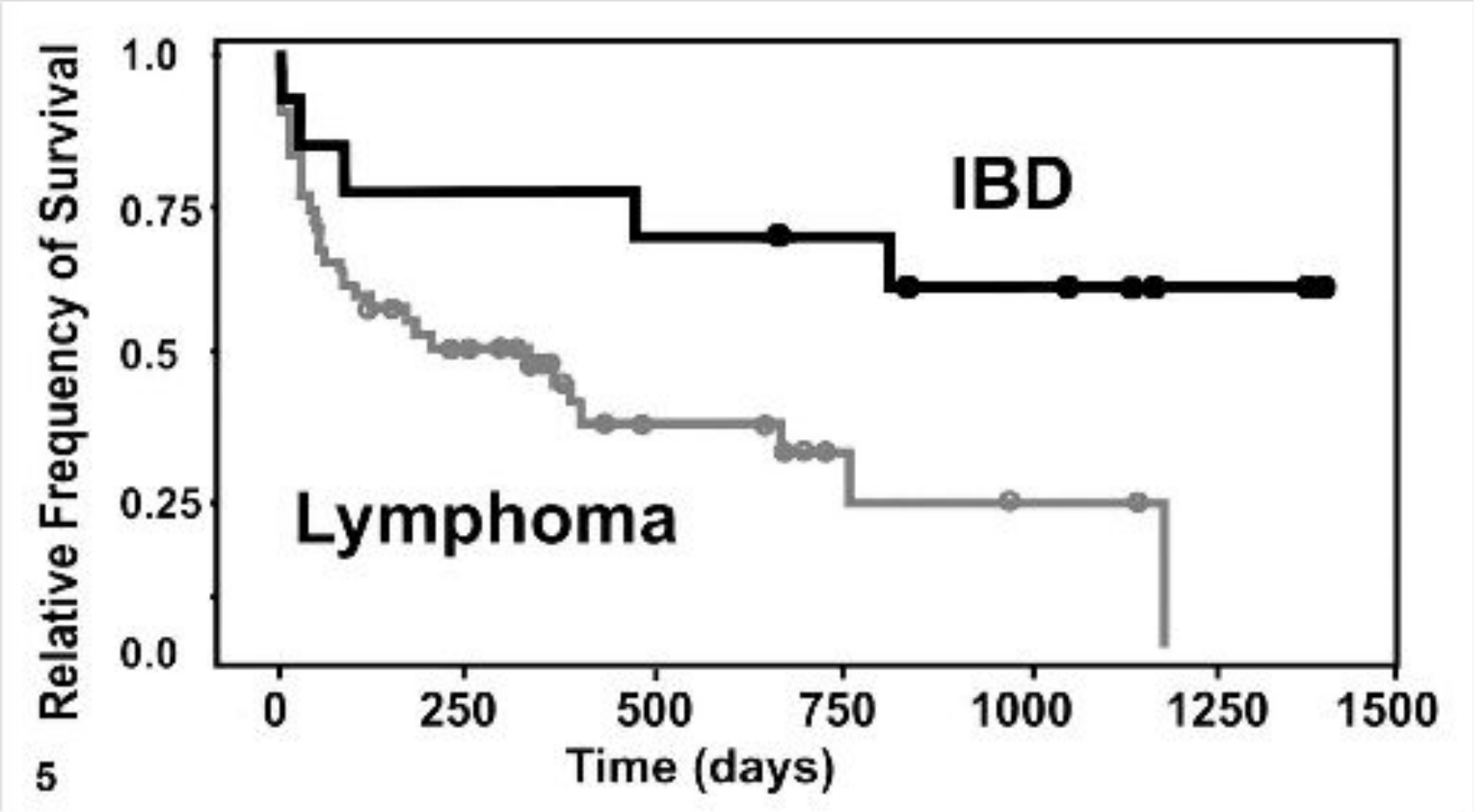
Diagnostic Algorithm to Differentiate Lymphoma From Inflammation in Feline Small Intestinal Biopsy Samples

M. Kiupel[1], R. C. Smedley[1], C. Pfent[1], Y. Xie[2], Y. Xue[2], A. G. Wise[1], J. M. DeVaul[1], and R. K. Maes[1]

DDx Lymfoom IBD



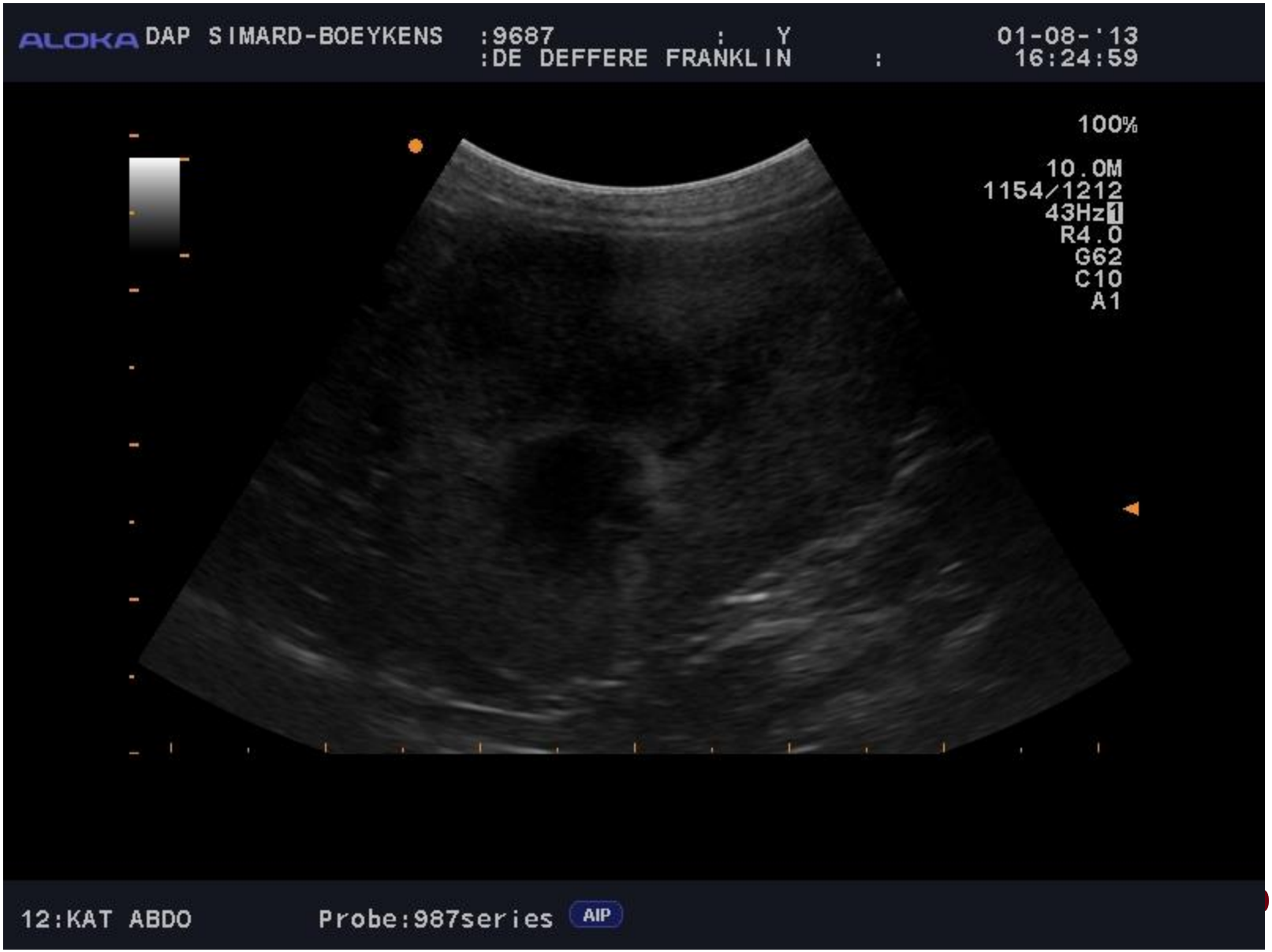
Kiupel 2011

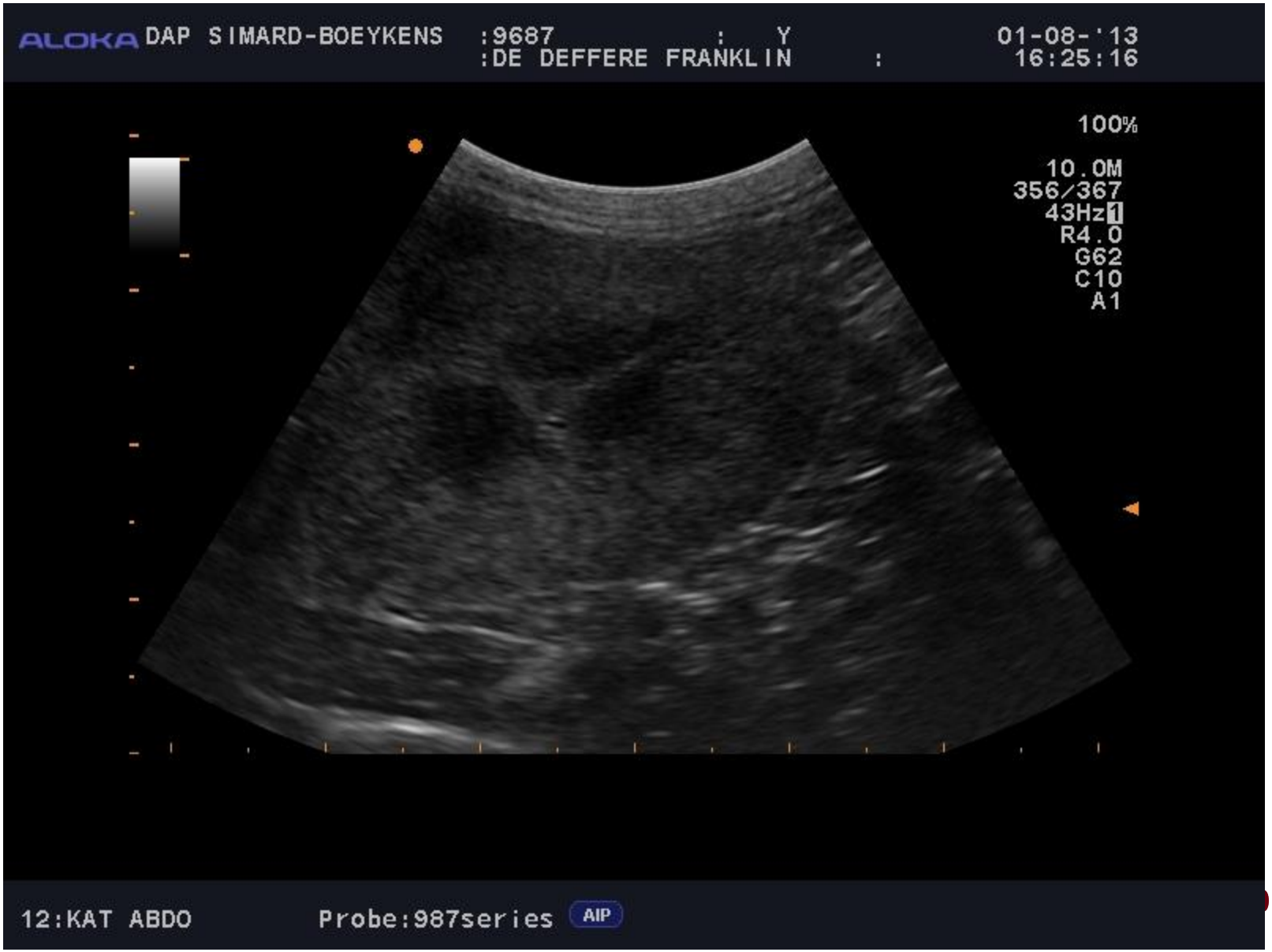

Relative Frequency of Survival
1.0
0.75
0.5
0.25
0.0
IBD
Lymphoma
0
250
500
750
1000
1250
1500
Time (days)

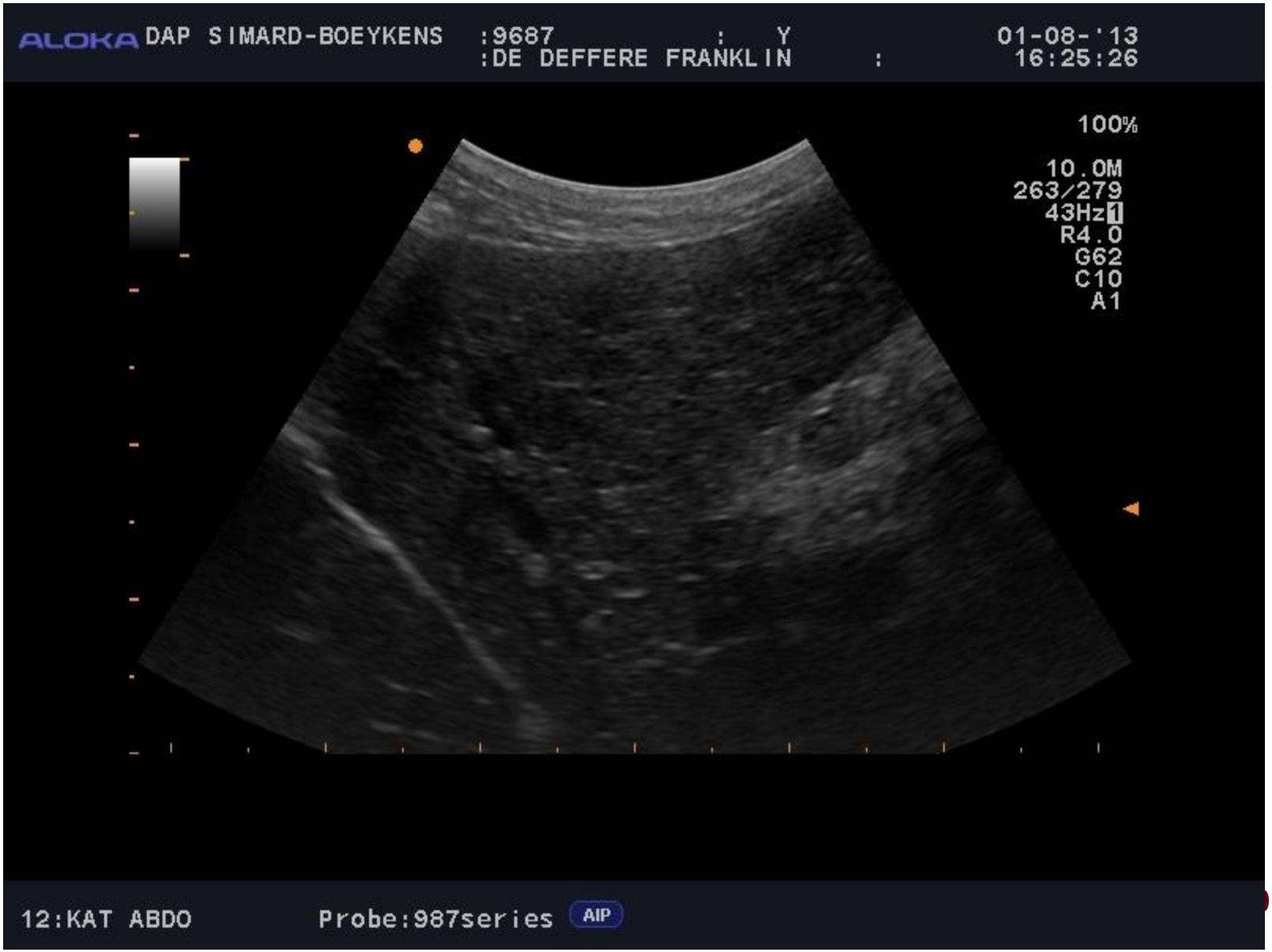
Franklin

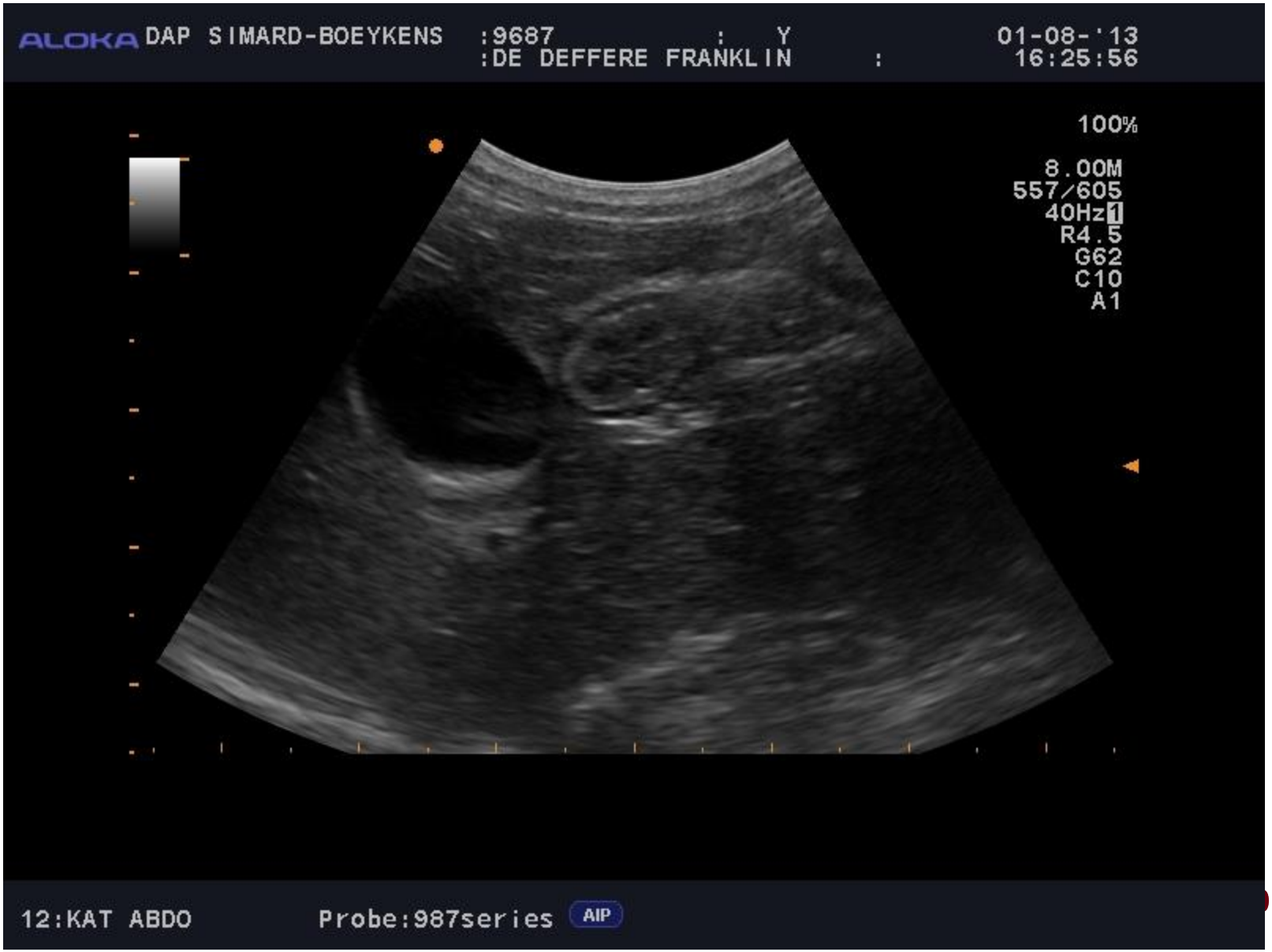
- Brits Korthaar, man, 15/7/2002, chocolade wit
- HCM, PKD negatief; FIV, FeLV negatief (4/5/2004)
- Opvang 3/5/2013 3.6kg
- Voorgeschiedenis: chronische diarree (duur? Tx?)
- Diverse behandelingen
- Bloedonderzoek
- Lichte niet-regeneratieve anemie
- Hypergammaglobulinemie
- Opnieuw ontwormen, daarna cortisone
- Mestonderzoek negatief
  - parasieten
  - pathogene kiemen

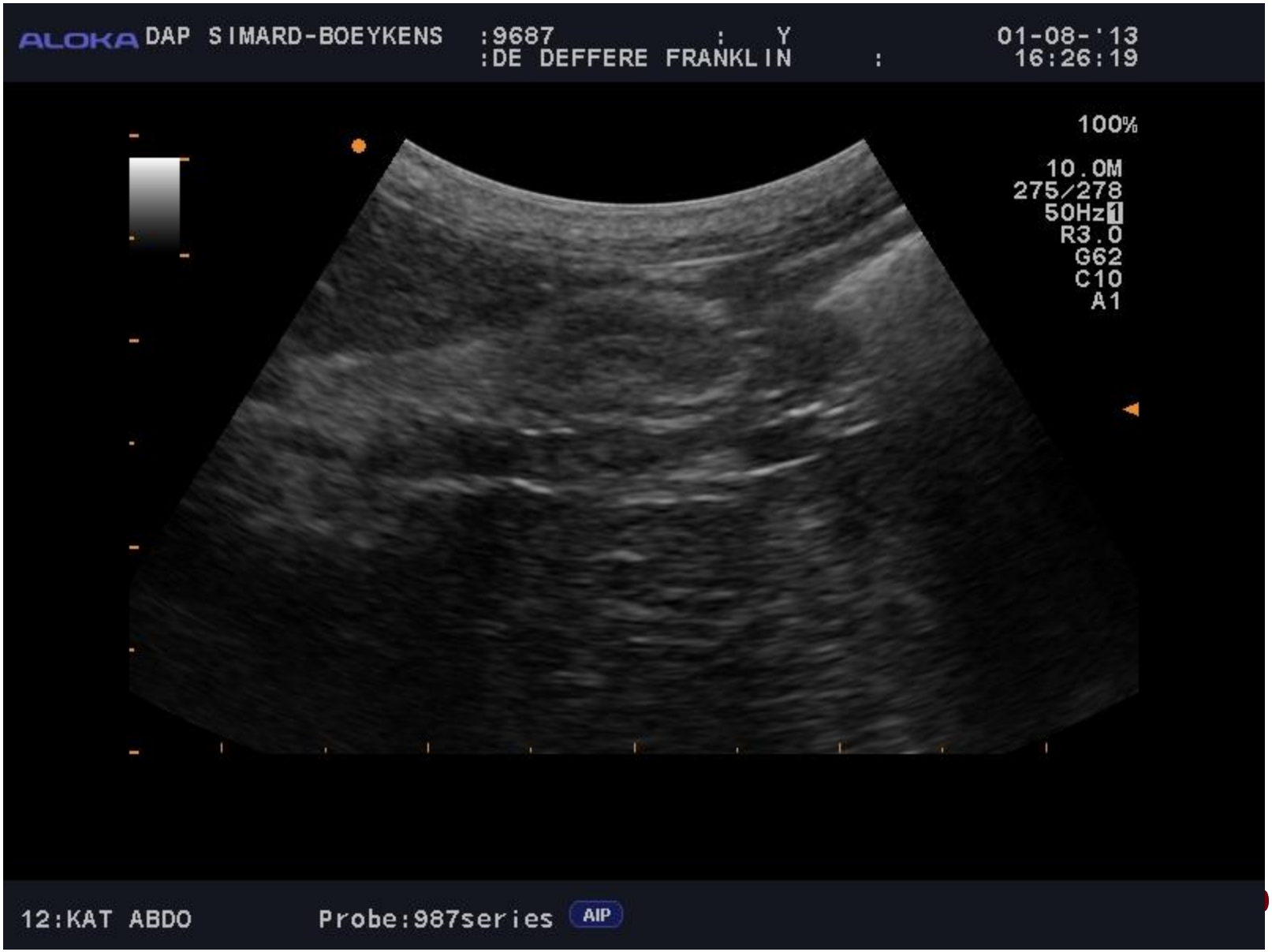
- 28/5 Nieuwe kuur Ab
- 1/6 Stop Ab
- 7/6 stoelgang beter
- 12/6 paardenvlees, hypoallergene voeding
- 13/6 diarree
- 14/6 dieet aangepast
- 16/6 geen natvoer meer
- 17/6 stoelgang ok, chip en vaccinatie
- Geplaatst, na enkele dagen diarree
- **Eind juli aangeboden**
  - LO normaal, mager, bijgeruis 2/6
  - Advies Echo (gepland 1/8)

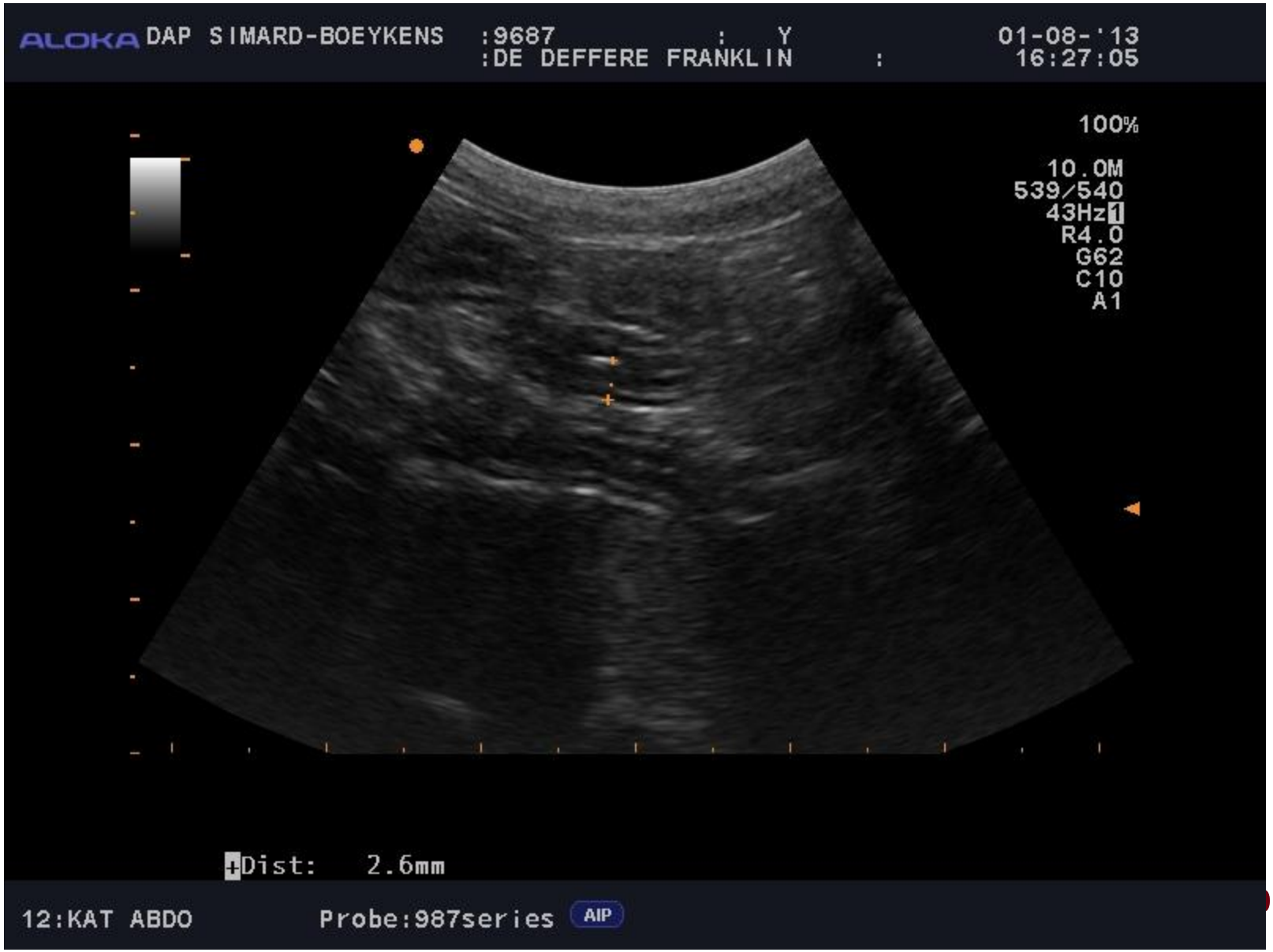

ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:24:59
100%
10.0M
1154/1212
43Hz1
R4.0
G62
C10
A1
12:KAT ABDO
Probe:987series
AIP

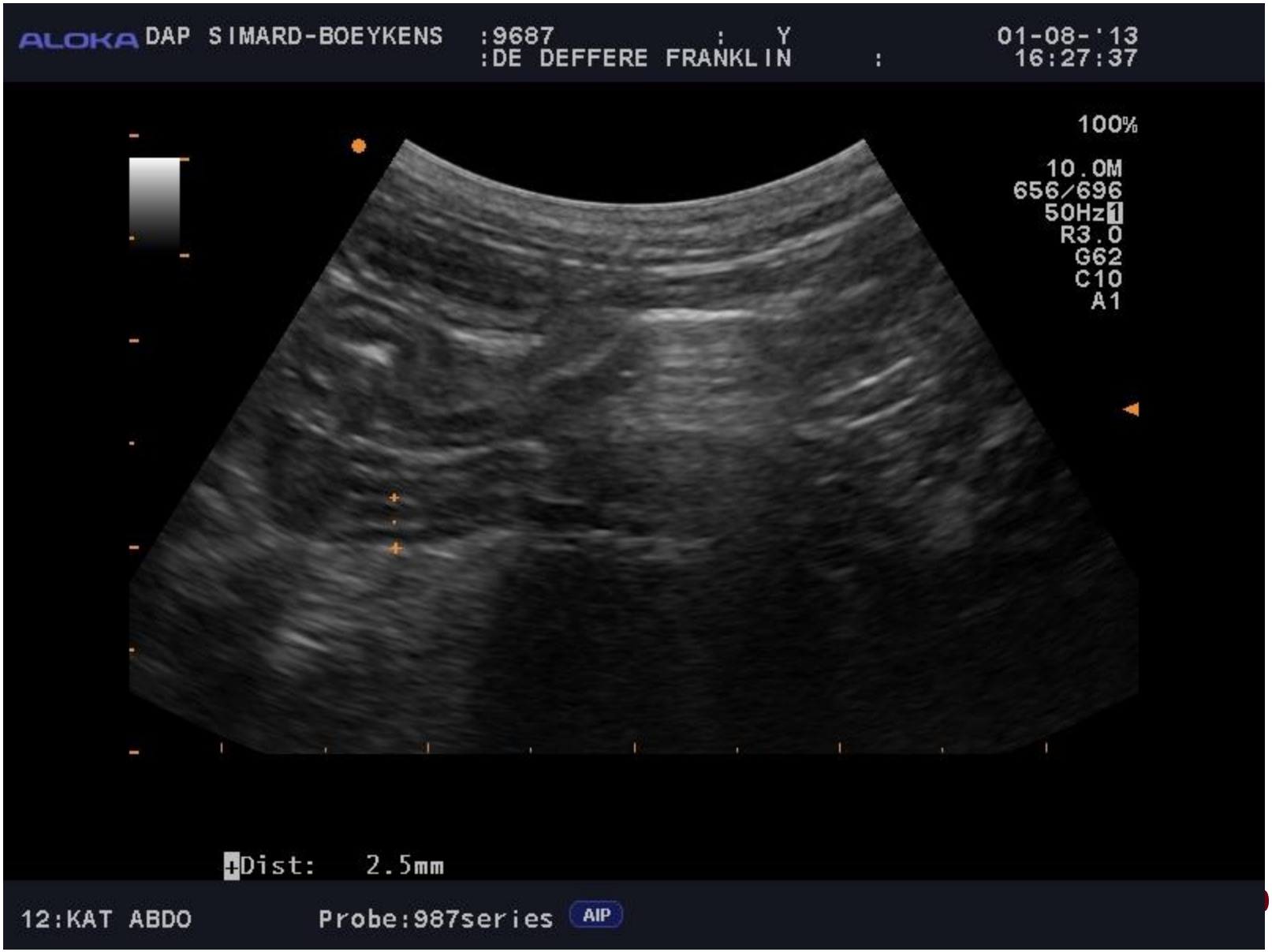

ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:25:16
100%
10.0M
356/367
43Hz1
R4.0
G62
C10
A1
12:KAT ABDO
Probe:987series
AIP

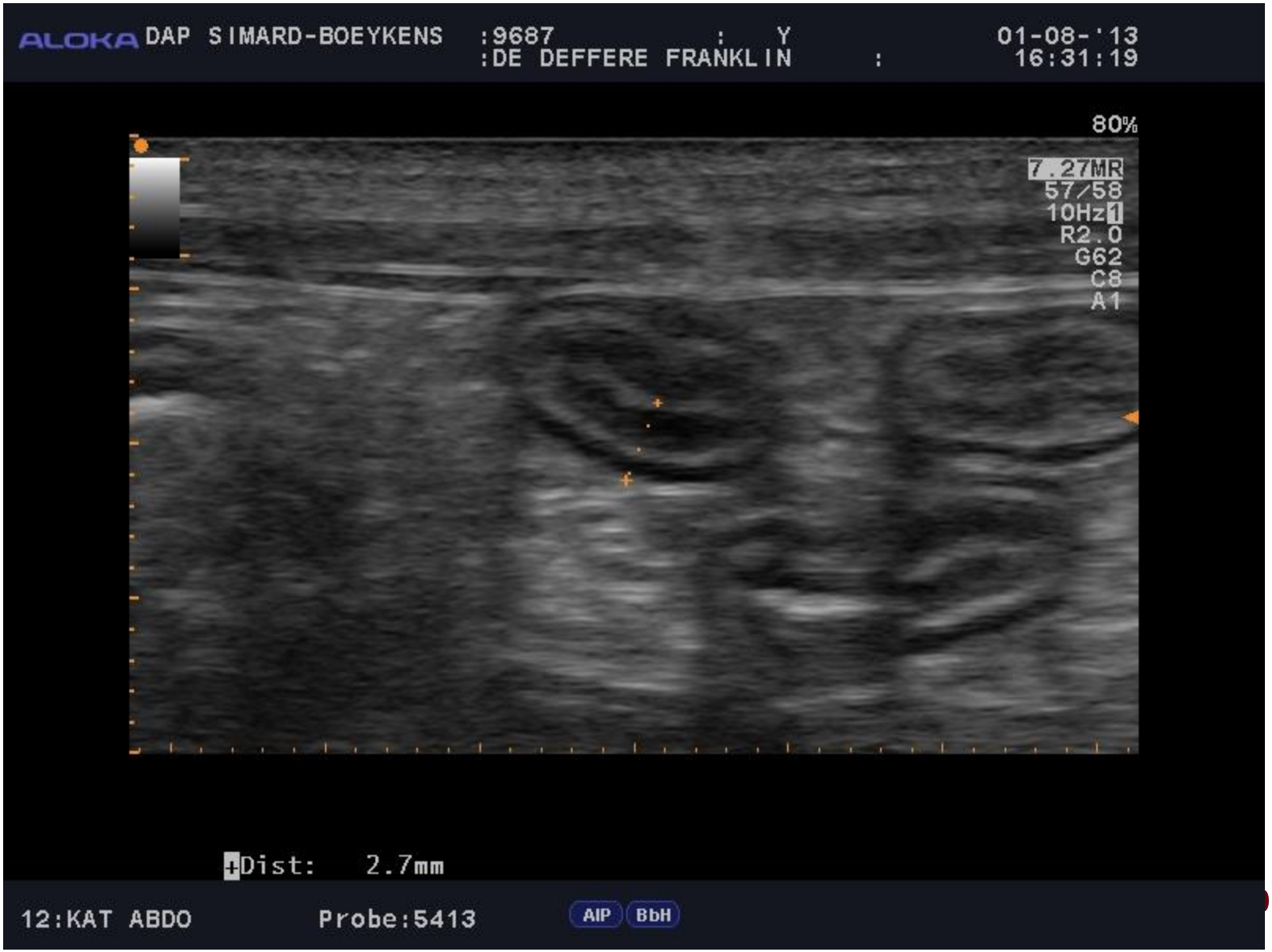

ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:25:26
100%
10.0M
263/279
43Hz1
R4.0
G62
C10
A1
12:KAT ABDO
Probe:987series
AIP

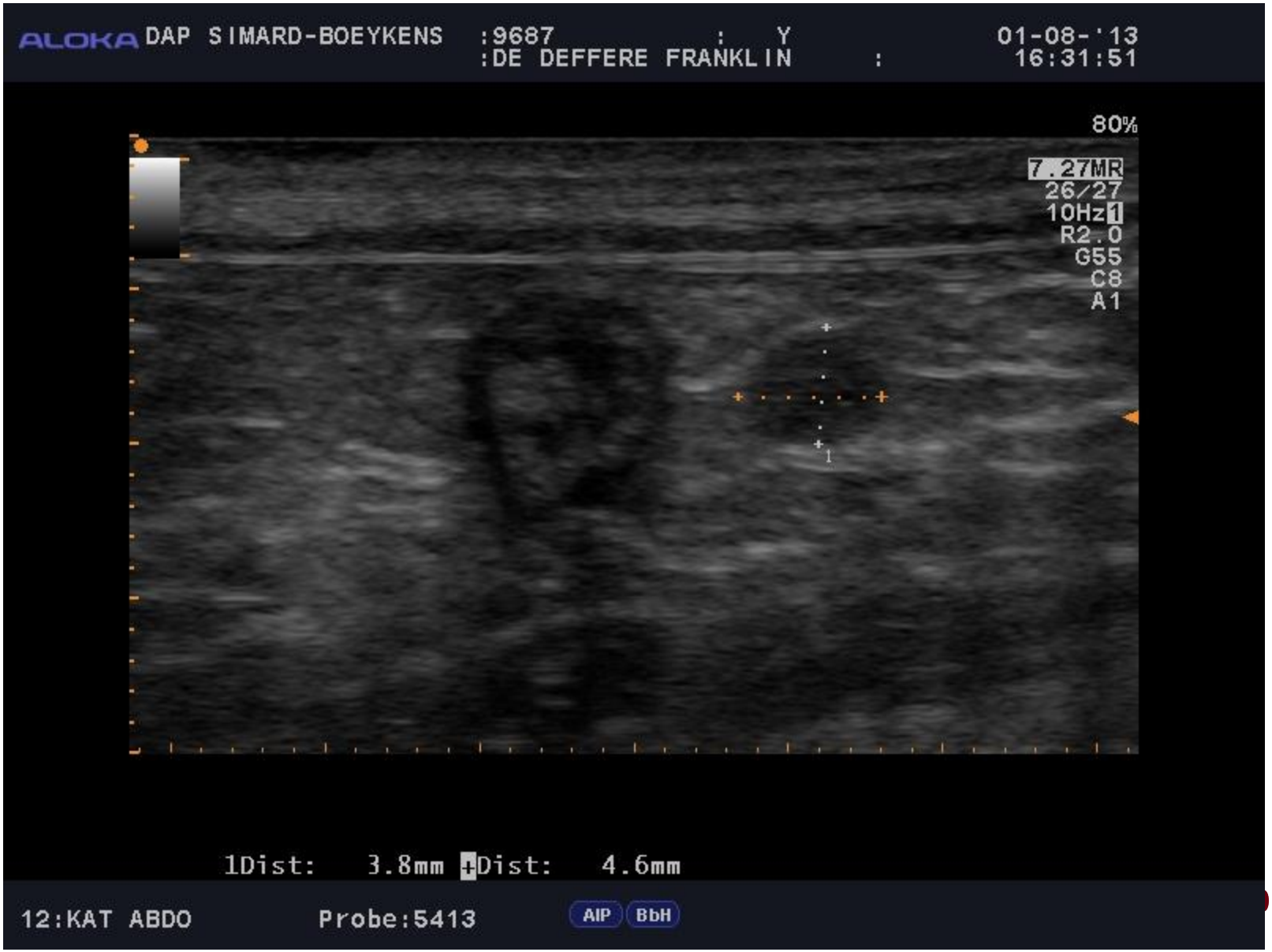

ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:25:56
100%
8.00M
557/605
40Hz1
R4.5
G62
C10
A1
12:KAT ABDO
Probe:987series
AIP

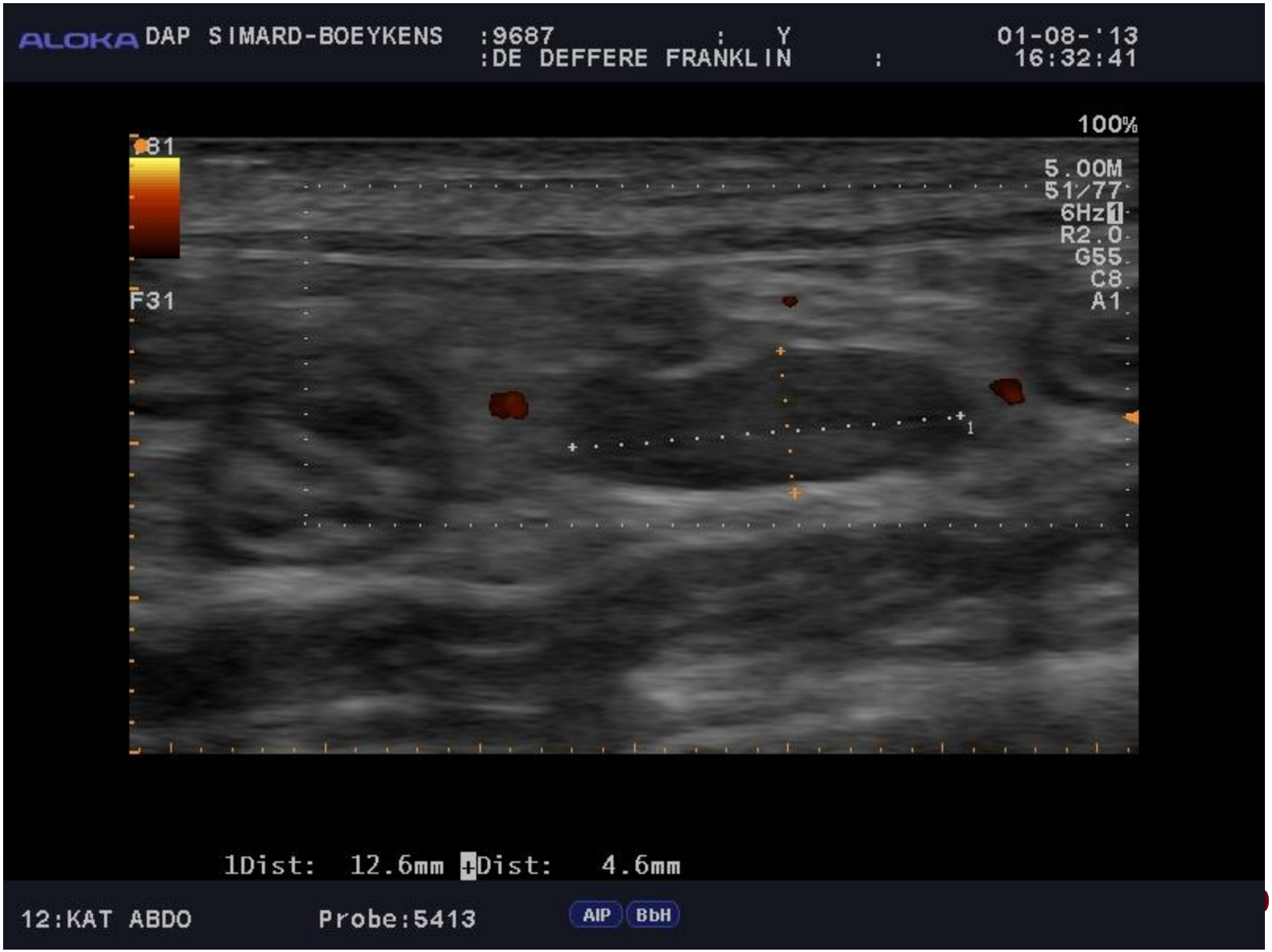

ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:26:19
100%
10.0M
275/278
50Hz1
R3.0
G62
C10
A1
12:KAT ABDO
Probe:987series
AIP


ALOKA DAP SIMARD-BOEYKENS :9687 : Y
:DE DEFFERE FRANKLIN :
01-08-'13
16:27:05
100%
10.0M
539/540
43Hz1
R4.0
G62
C10
A1
+Dist: 2.6mm
12:KAT ABDO
Probe:987series
AIP


ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:27:37
100%
10.0M
656/696
50Hz1
R3.0
G62
C10
A1
Dist: 2.5mm
12:KAT ABDO
Probe:987series
AIP


ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:31:19
80%
7.27MR
57/58
10Hz1
R2.0
G62
C8
A1
+Dist: 2.7mm
12:KAT ABDO Probe:5413
AIP BbH

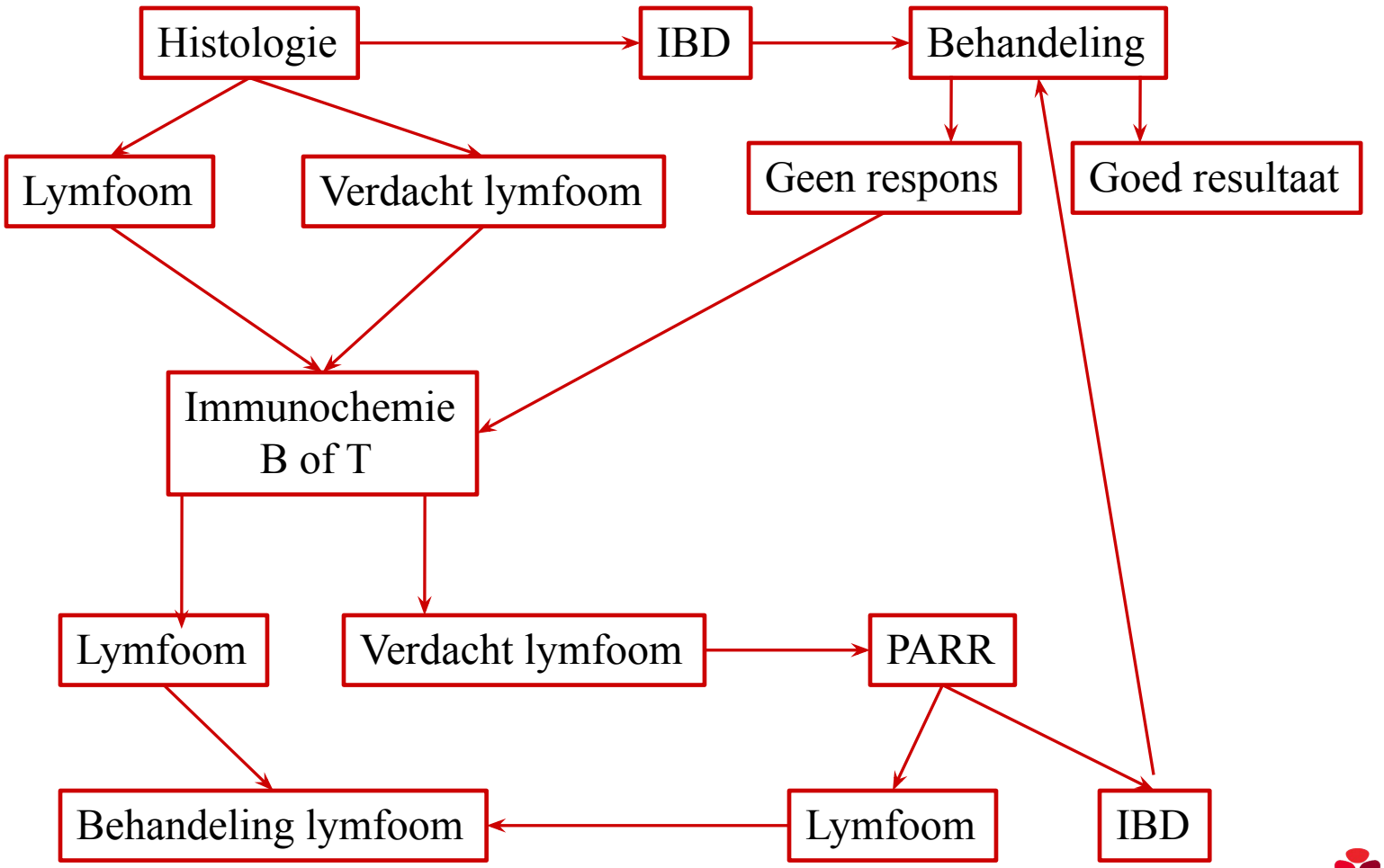

ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:31:51
80%
7.27MR
26/27
10Hz1
R2.0
G55
C8
A1
1Dist: 3.8mm +Dist: 4.6mm
12:KAT ABDO Probe:5413
AIP
BbH


ALOKA DAP SIMARD-BOEYKENS :9687 : Y 01-08-'13
:DE DEFFERE FRANKLIN : 16:32:41
100%
81
F31
5.00M
51/77
6Hz1
R2.0
G55
C8
A1
1Dist: 12.6mm +Dist: 4.6mm
12:KAT ABDO Probe:5413
AIP
BbH

Franklin

- 1/8 Advies biopsie darm en ln, **geweigerd**: Hills WD
- 4/8 Veel beter
- 8/8 Verslecht
- 9/8 Laparatomie
- 13/8
  - Matige lymfoplasmocytaire enteritis, reactieve lymfeklier
  - Dx: IBD? (diarree ondertussen onder controle)
  - Tx: Hills WD

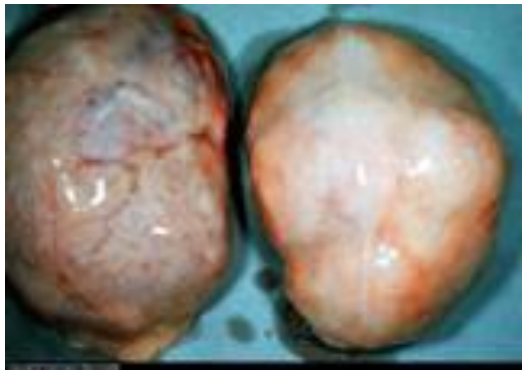
DDx Lymfoom IBD



Deel 7
Renaal Lymfoom

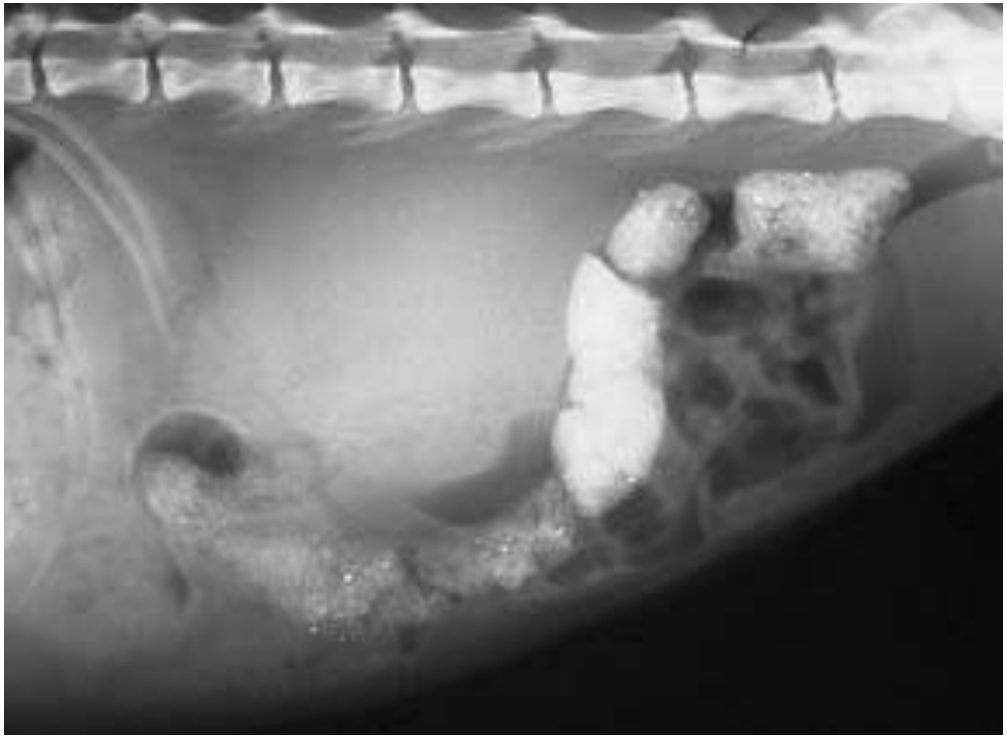
Renaal lymfoom

- Kliniek
  - Niet specifiek
    - Vermageren, braken,…
    - **Pu/pd**
  - **Renomegalie**
  - ALTIJD BILATERAAL
- Labo
  - Nierfalen (omkeerbaar)
  - FeLV -
  - Australië 50% FIV +



Renaal lymfoom: radiografoe

- Renomegalie
- > 3*lengte L2



Renaal lymfoom: echografie

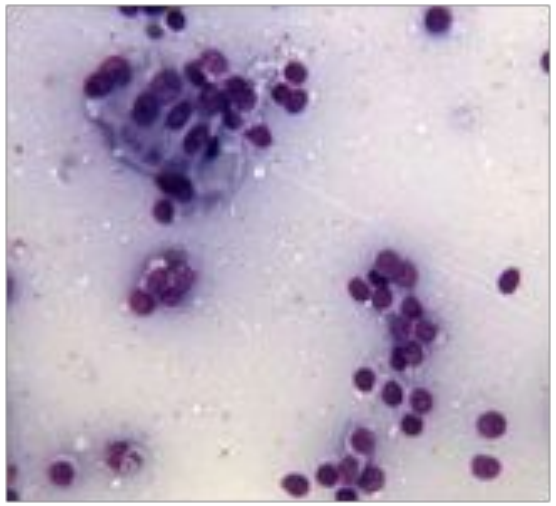
- Sterke aanwijzing
- Hypoëchoïsche haarden
- Diffuse toename echogeniceteit cortex: Ddx!!!!
- Dunne hypoëchoïsche lijn
  - perifeer

Renaal lymfoom

- Staging
  - **Zelden alleenstaand** (16/68)
  - 20/68 alleen abdominaal verspreiding
    - mesenteriale lnn
    - lever, milt
    - GI
  - 30/68 verspreid
    - lymfeklieren: perifeer, sternaal
    - long, hart
    - beenmerg
    - ogen
    - huid
    - CZS

Renaal lymfoom

- Cytologie
  - Onder echo begeleiding
  - Meestal B-cel
    - Primair
    - Andere organen
- Prognose en Behandeling
  - Combinatie chemotherapie
    - 60% CR
    - mediaan 5-7 maanden



Deel 8 : Extranodale Lymfomen

Nasaal Lymfoom

- Epidemiologie
  - NEOPLASIE meest voorkomende aandoening
  - 70% lymfomen
- Kliniek Niet specifiek
  - Neusvloei (bloed, etter)
  - Niezen
  - Stridor
  - Oogvloei
  - Misvorming aangezicht

Nasaal Lymfoom

- Radiografie
  - niet specifiek

Investigation of nasal disease in the cat—a retrospective study of 77 cases

S.M. Henderson*, K. Bradley, M.J. Day, S. Tasker, S.M.A. Caney, A. Hotston Moore, T.J. Gruffydd-Jones

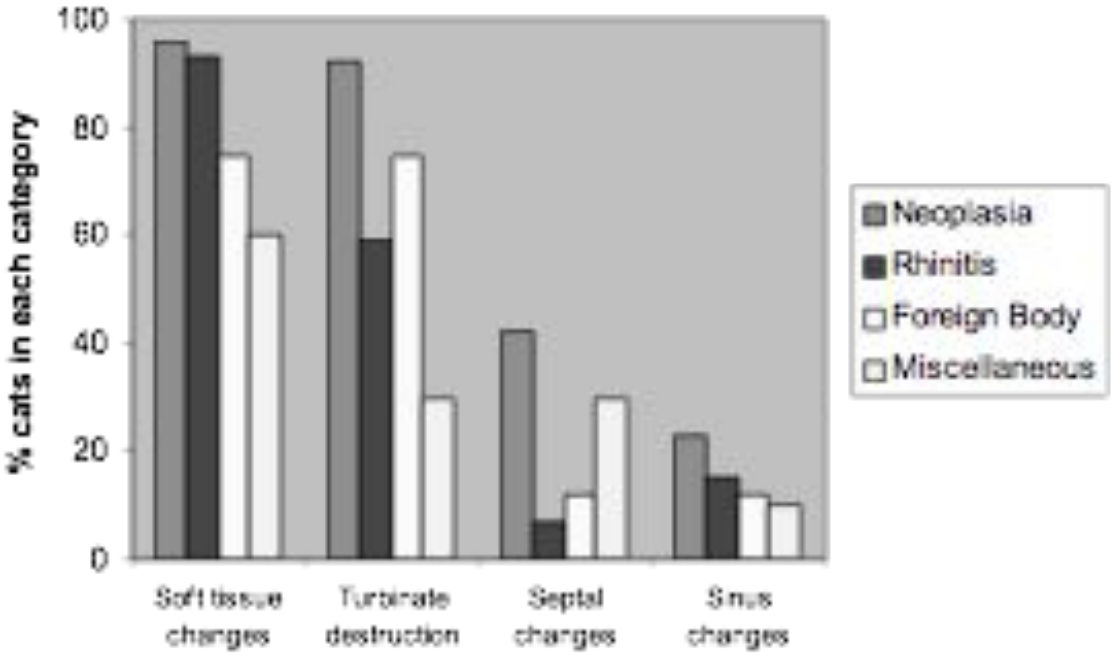
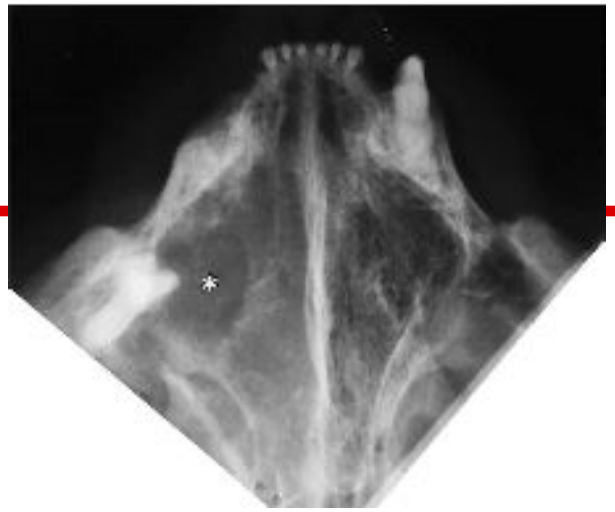
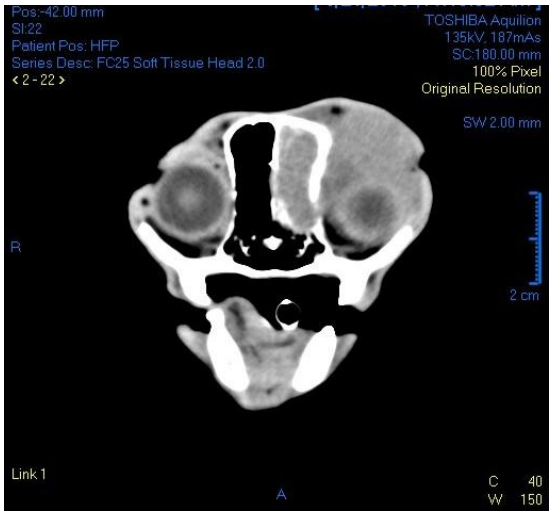


Figure 6 Radiographic changes in cats with nasal disease.

Nasaal Lymfoom



- Radiografie
  - niet specifiek
  - toegenomen densiteit neusgangen
  - opacificatie sinussen
  - < dan bij rhinitis
- CT
  - Indien Radiotx

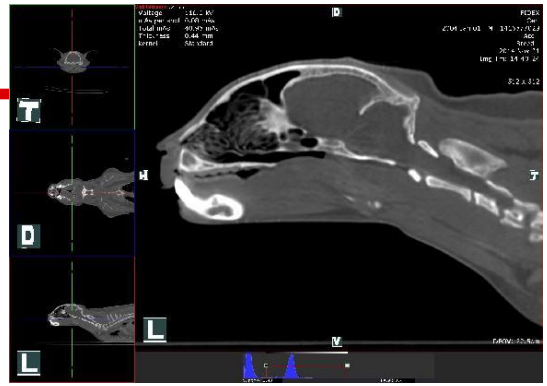


Nasaal Lymfoom

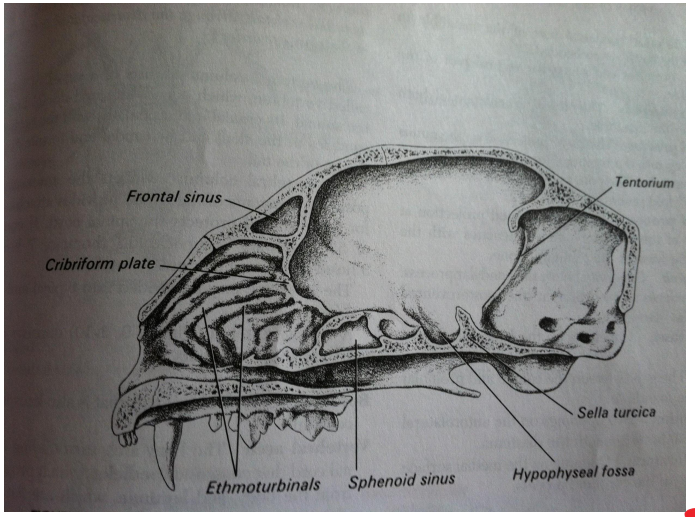
- “NASAL FLUSHING”
- Rhinoscopie
  - Cytologie/histo
- STAGING
  - Meestal B-cel
  - Stage 1a (goede eetlust)
  - FeLV - (>90%)
  - 31% meerdere organen
  - 60% extensie uit neusholte CT

●!! Indien alleen Radiotx

Nasaal Lymfoom



- Prognostische Factoren
  - Slechte eetlust
  - Anemie
  - Botaantasting op CT (cribriform plate)
  - CR na behandeling



- Behandeling
  - Radiotherapie (en)
  - Chemotherapie
  - Langste remissies en overleving (mediaan 24 md!!)
    - Sfiligoi Chemo + RadioTx 31,4 maanden

CZS lymfoom

- Epidemiologie
  - Meest voorkomende spinale tumor
  - Tweede meest voorkomende hersentumor
  - Vroeger eerder jonge FeLV+ katten, spinaal extraduraal
  - Recent: intraduraal, oudere katten, 57% FeLV +
- Kliniek
  - Lumbaal
    - meest voorkomende lokalisatie
    - Parese, paralyse AH
  - Hersenen 50%
    - Anorexie, lethargie
    - Vermageren
    - Ataxie, Δ bewustzijn, agressie

CZS lymfoom

- Radiografie 0
- CT, MRI, myelografie
  - Aantonen massa
- CSF
  - 9-67% + op abnormale cellen
- Tx
  - Chemo? <50% CR
  - Radio: locaal (+chemo)
- Staging!!!
  - >50% beenmerginfiltratie
  - Leukemie
  - 50% renaal lymfoom

CZS lymfoom

CASE REPORT
Central diabetes insipidus in a cat with central nervous system B cell lymphoma

Christopher J Simpson BVSc, MACVSc (Small Animal Medicine)*, Caroline S Mansfield BVMS, MVM, DECVIM-CA, Marjorie E Milne BVSc (Hons), FACVS (Radiology), Priscilla J Hodge BVSc (Hons), MACVSc (Pathology)

Deel 9
Mediastinaal Lymfoom

Mediastinaal lymfoom

- Epidemiologie

Jonge katten <2 jaar Alle leeftijden	Jonge Siamesen
FeLV +	FeLV -
T-Cel hoge graad	B-cel
Agressief	Minder agressief
Reageert slecht op chemp	Reageert beter op chemo

Mediastinaal lymfoom

- Epidemiologie

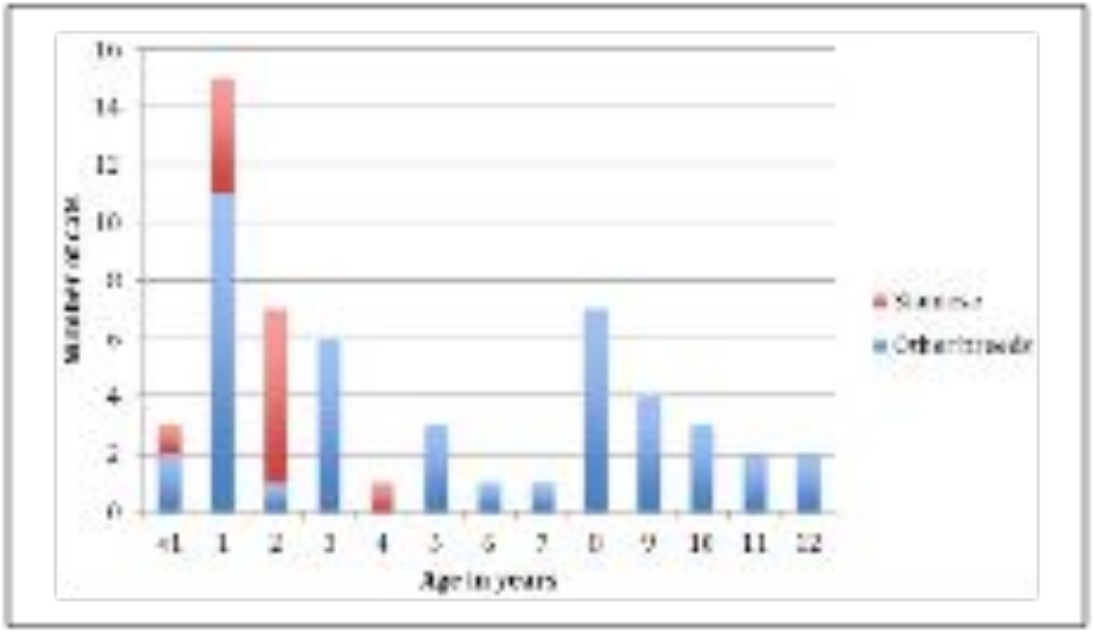
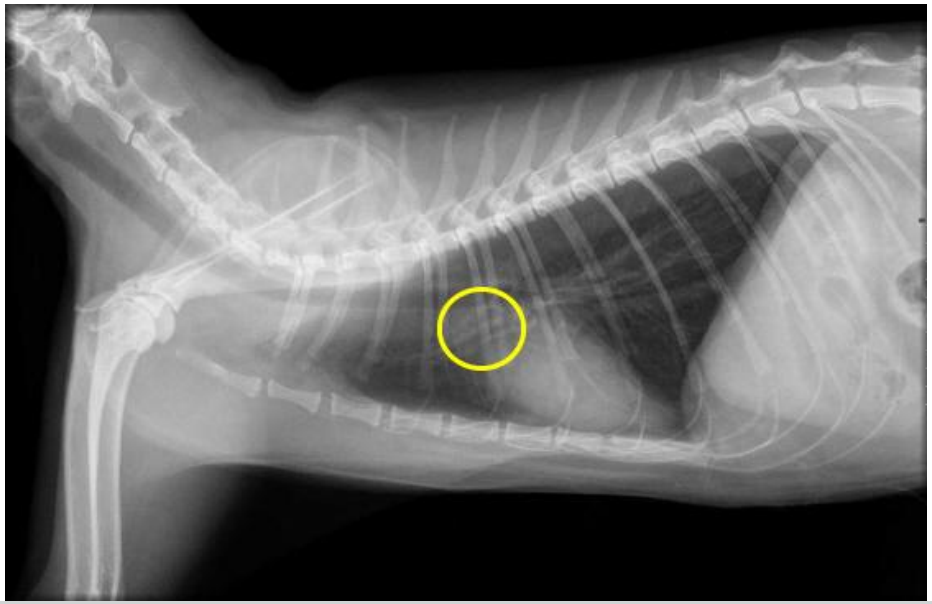


Figure 1 Age distribution of 55 cats with mediastinal lymphoma. Red bars represent Siamese, blue bars represent all other breeds together

Mediastinaal lymfoom

Epidemiologie

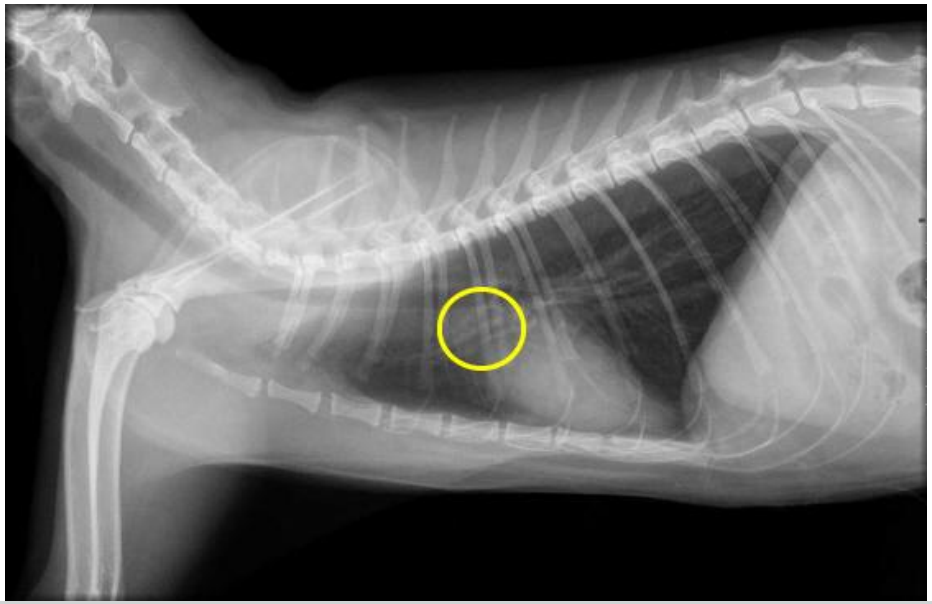
- Thymus
- Sternale lymfeklieren
- Mediastinale lymfeklieren



Mediastinaal lymfoom

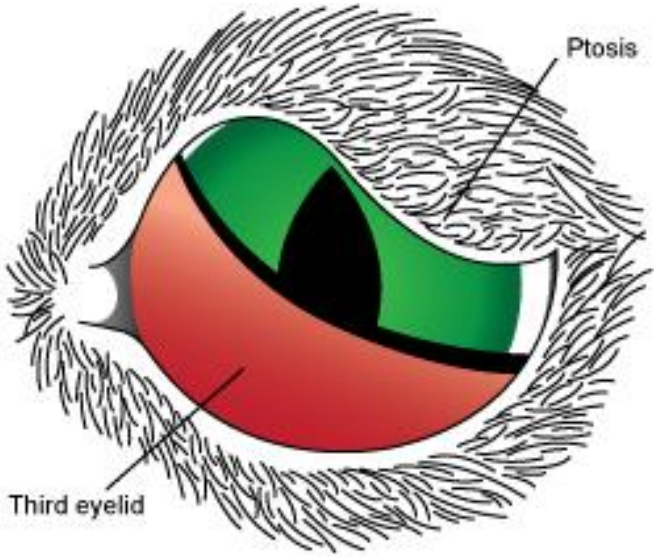
Lymfoom

- Thymus 63%
- Pleurale effusie : 17-20%



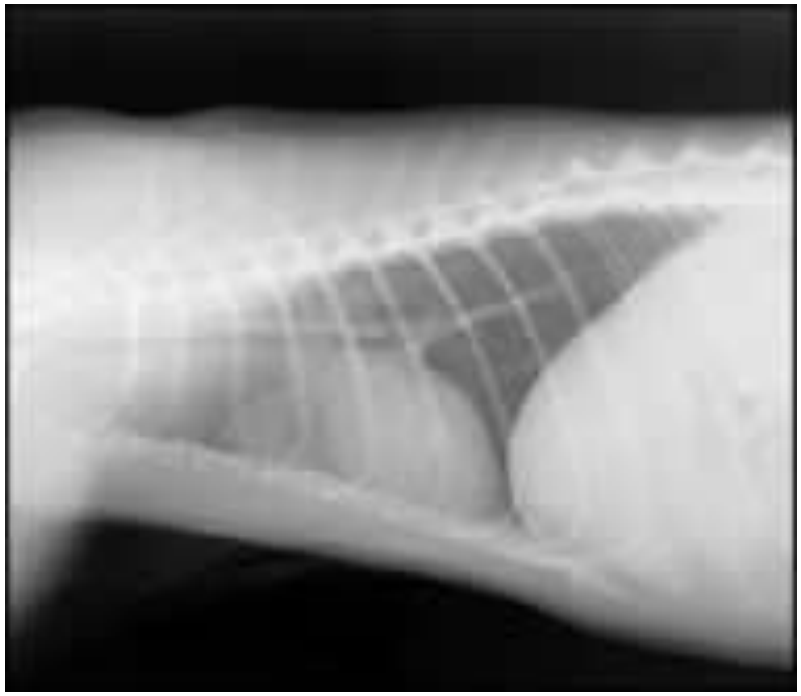
Mediastinaal lymfoom

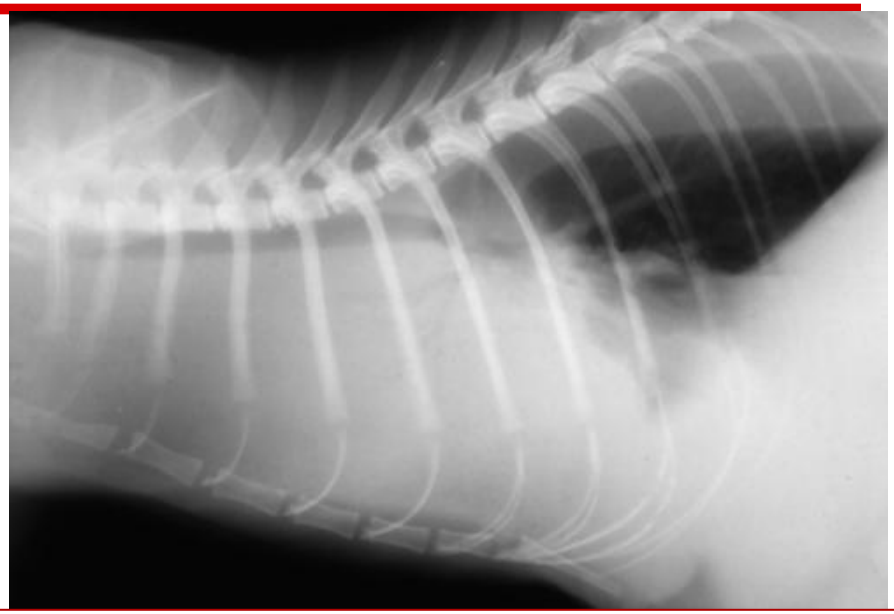
- Kliniek
  - AH!!
    - Tachypnoe
    - Pendelend indien pleurale effusie
  - Thoracale compressie
  - Horner
- Zelden hyper-Ca



Mediastinaal lymfoom

- Radiografie ++
  - massa
  - pleurale effusie

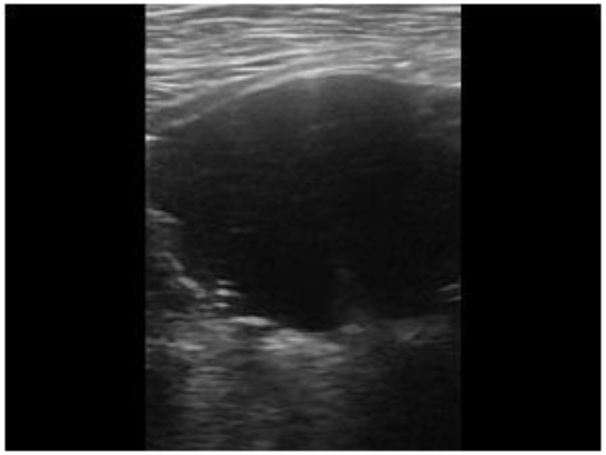


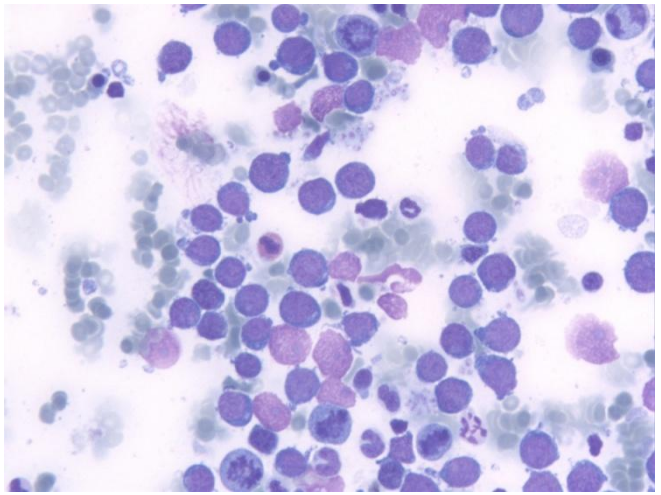


➔ DDx Massa craniaal/ventraal mediasitinum
- ◆ Normale thymus
- ◆ Neoplasie
  - Thymoom
  - Lymfoom
  - Ectopische schildklier
  - Andere
- ◆ Sternale lympadenopathie
- ◆ Abces/granuloom/hematoom
- ◆ Cyste (branchiale cyste)

Mediastinaal lymfoom

- Echografie
  - Aantonen massa
  - Punctie
  -
- Cytologie
  - Pleuraal vocht 80%+)
  - Tumor
  - Meestal diagnostisch





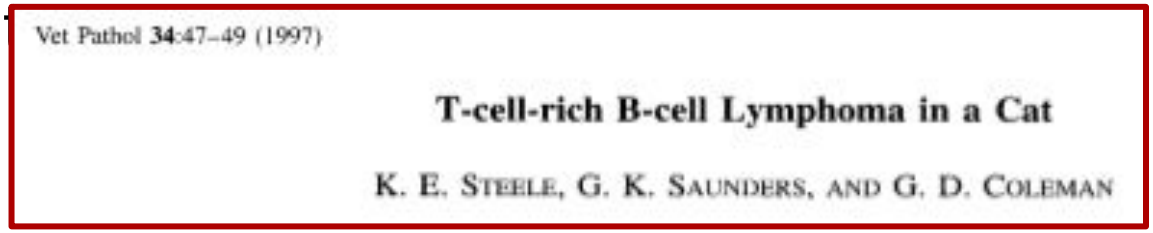
Deel 10
Nodaal Lymfoom

Nodaal lymfoom

- Epidemiologie
  - Zelden: 5%
  - Multicentrisch: zeer zelden
- Kliniek
  - Perifere lymfeklieren opgezet
    - 1 of 2
    - Meestal cervicaal, prescap., submand
  - Snel groeiend
- Cytologie
  - MOEILIJK!!!
  - Excisie en histologie noodzakelijk
  - Mogelijks Hodgkin ipv non-Hodgkin!!

Nodaal lymfoom

- Prognose
  - Eerder gunstig: chirurgische excisie
    - T-cel rich B-cel lymphoma
  - Soms indolen



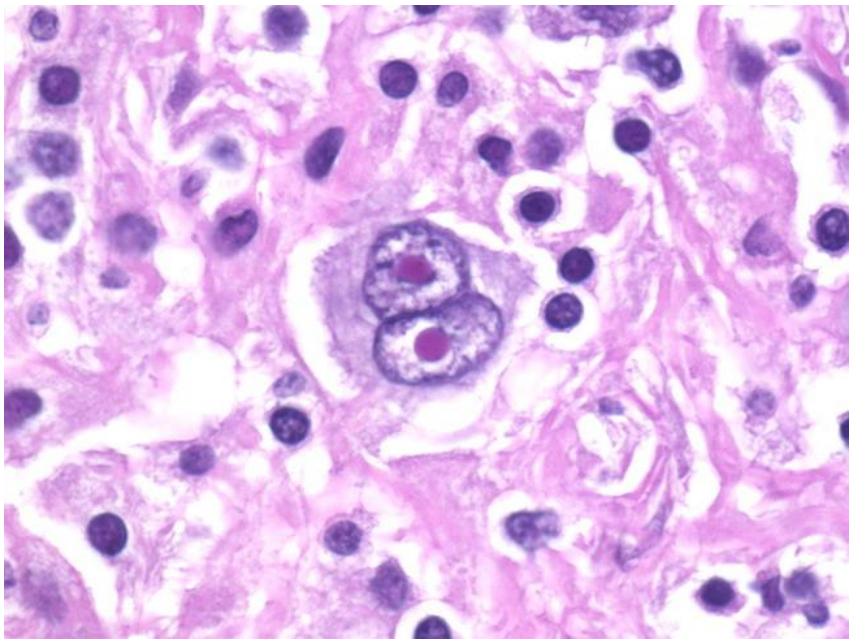
- Diff. Diagnose :!!
  - Lymfeklier hyperplasie bij jonge katten
  - Feline Hodgkin's like Lymphoma
  - Lymphadenopathy resembling Lymphoma
  - Infectieuze en inflammatoire aandoeningen

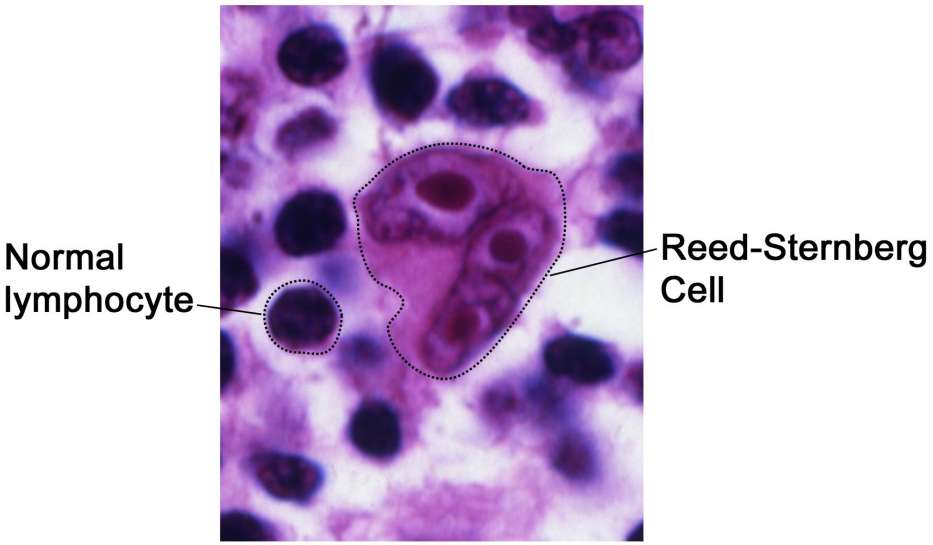
Feline Hodgkin's (like) Lymphoma

- Humaan
  - beperkte groep lymfeklieren
  - verspreiding naar volgende ln.
  - geen extra-nodale uitbreiding
  - Beperkt aantal neoplastische cellen (1-5%)
    - HISTOLOGIE
    - cytologie weinig waarde
  - Gunstige prognose
    - chirurgie
    - bestraling
    - genezing mogelijk!!!!!

Feline Hodgkin's (like) Lymphoma

- Reed-Sternberg cellen
  - dubbelkernige cellen
  - prominente centrale nucleolus

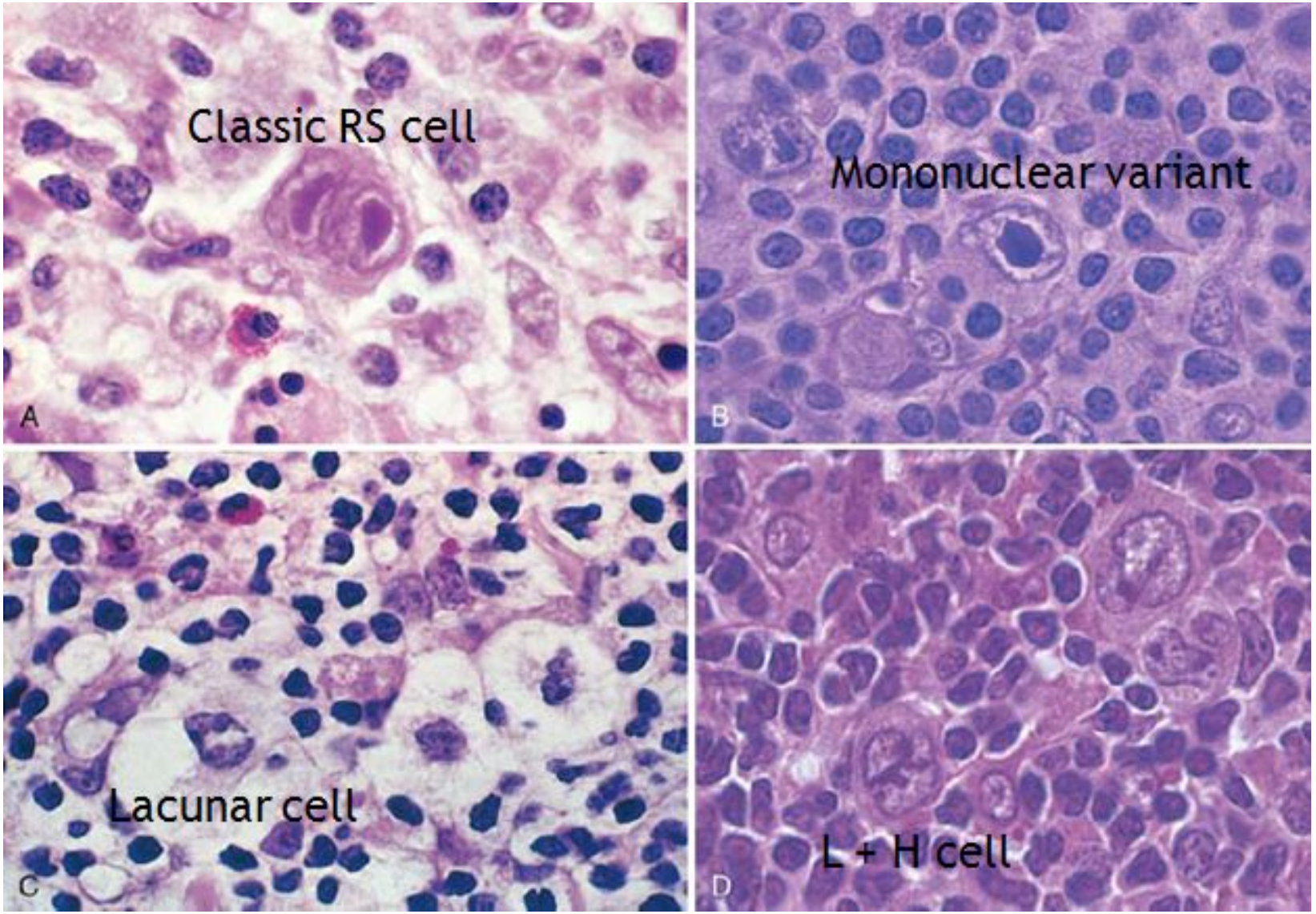




Feline Hodgkin's (like) Lymphoma

- Kliniek: 1 lymfeklier (of 2)
  - mandibulair
  - cervicaal
  - zelden inguinaal of gegeneraliseerd
- Signalement
  - 1-14 jaar
  - geen sex- of raspredispositie
- Verschillende histologische subcategorieën
  - klassieke RS cellen
  - lympho-hystiocytaire cellen
  - lacunaire cellen

Feline Hodgkin's like Lymphoma: 20 cases (1992-1999). *Walton RM, Hendrick MJ. Vet Patol 2001*


Classic RS cell
A
Mononuclear variant
B
Lacunar cell
C
L + H cell
D

Feline Hodgkin's (like) Lymphoma

- Relatief indolent verloop!!!!
  - 11/20 katten geen TX
    - overleving tot 4 jaar (minstens 7 maanden)
  - Excisie, geen chemo

Distinctive Lymph Node Hyperplasia of Young Cats

- Jonde katten: 5m - 2j
- Lymfadenomegalie (2-3*)
  - gegeneraliseerd (14/15)
  - 8/15 gezond
  - lethargie, anorexie
  - mogelijks FeLV+
- Verloop (10/14)
  - 2 euthanasie (FeLV+)
  - 8 in leven na 5 jaar
    - 1 mediastinaal lymfoom

Generalized Lymphadenopathy resembling Lymphosarcoma

- JAVMA Mooney 1987
- 6 katten 1-4 jaar
- Kliniek
  - gegeneraliseerde lymfadenomegalie
  - FeLV-
  - 1 euthanasie vermoeden lymfoom
  - 4 persisterende leukocytose
    - 2 atypische lymfocyten
    - 2 lymfocytosis

Generalized Lymphadenopathy resembling Lymphosarcoma

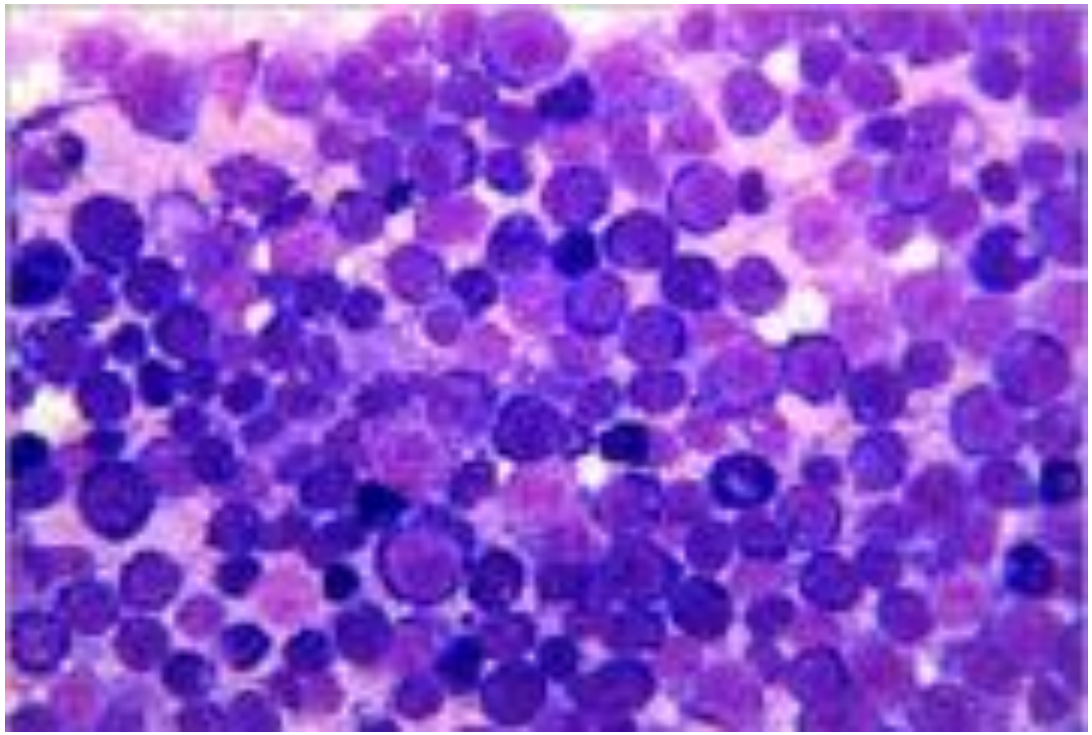
- Moeilijke Histopathologie
  - kenmerken van lymfoom
  - weinig kenmerken van maligniteit

- Spontane regressie na 1-17 weken
  - allemaal in leven na 1-7 jaar
  - gezond

Reactieve hyperplasie

Beeld van reactieve hyperplasie

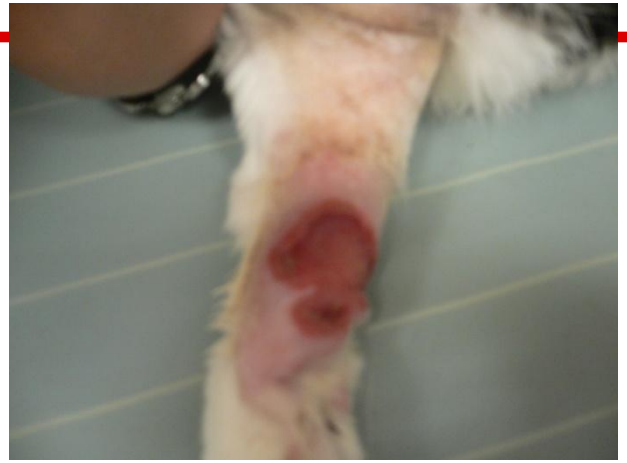
mogelijke verwarring met lymfoom!!!



Deel 11 Andere Extra-nodale Lymfomen

Cutane lymfomen

- Cutaan
  - Epithelitroop T-cel: verschillende vormen
    - Diffuus erytheem
    - Locaal ulceratief en squameus
    - Jeuk +/-
  - Histologie noodzakelijk
- Subcutaan
  - Agressief (hoge graad)
  - Mogelijks ulceratief
  - Cytologie (eenvoudig)



Andere lymfomen : Oculair lymfoom

- Conjunctivaal
  - associatie met chlamydia??
- Intra-oculair
  - uveïtis
  - hypopion
  - massa iris
- Retrobulbair

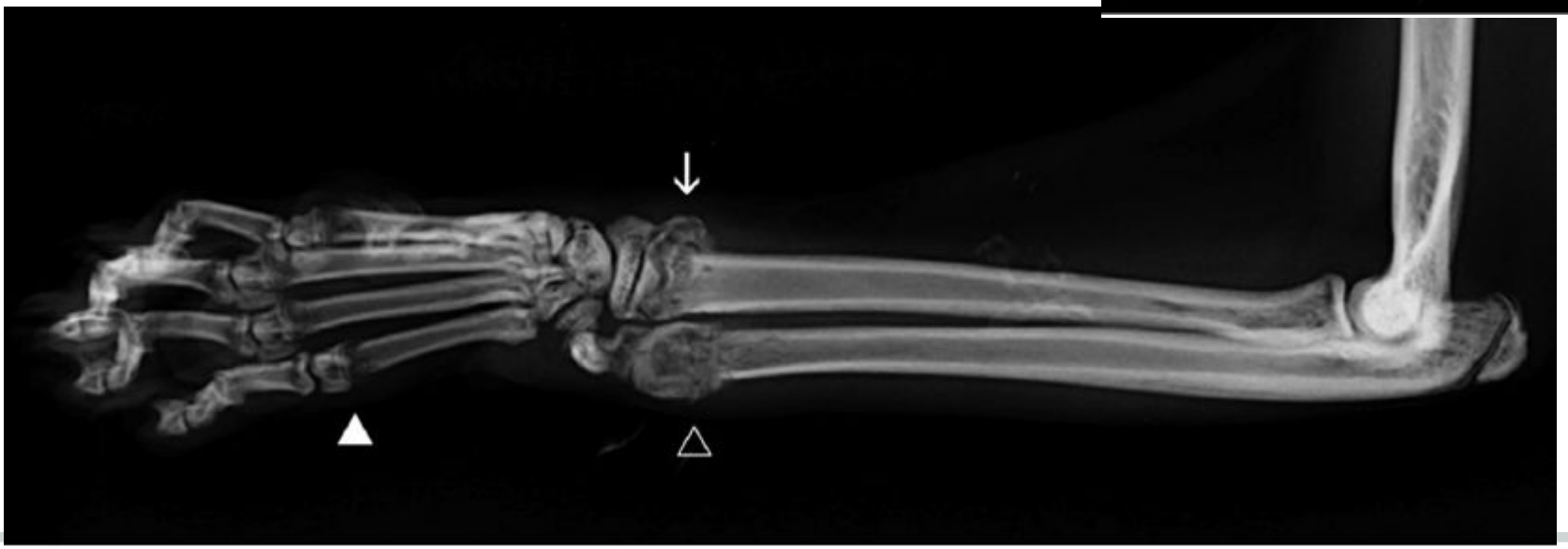
Andere lymfomen: bot

Polyostotic lymphoma with multiple pathological fractures in a six-month-old cat

Journal of Feline Medicine ar
14(4) 285–291

DOI: 10.1177/1098612X1243
jfms.com
SAGE

Laura K Brockley[1], Kathryn L Heading[2], John E Jardine[3], Peter F Moore[4] and Peter F Bennett[2]



Andere: perifeer zenuwstelsel

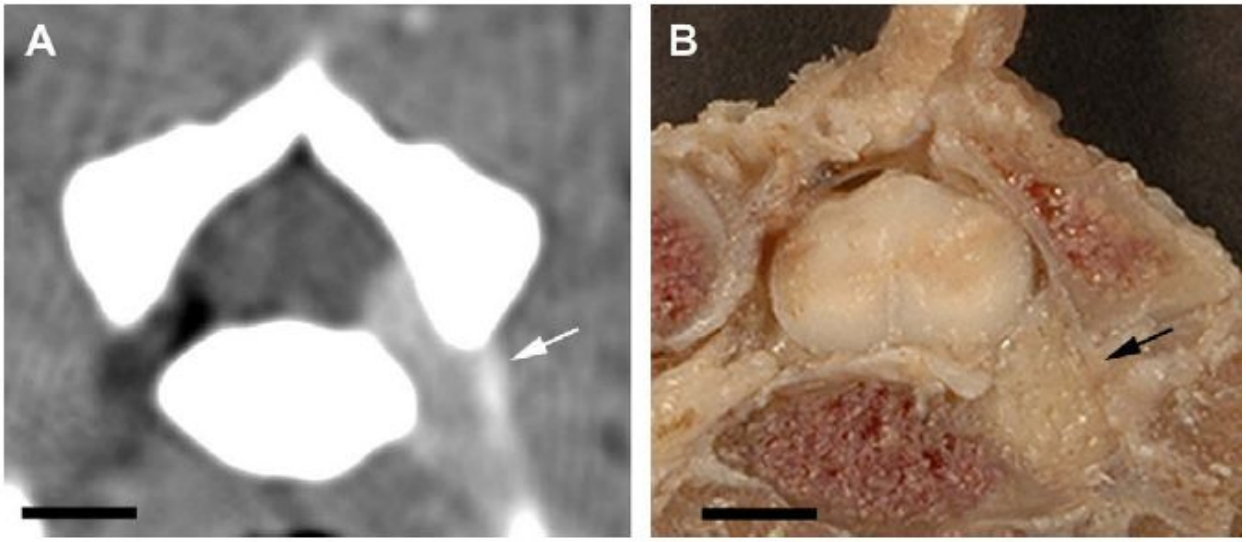
Journal of Feline Medicine and Surgery (2009) **11**, 522–524
doi:10.1016/j.jfms.2008.09.007

ELSEVIER

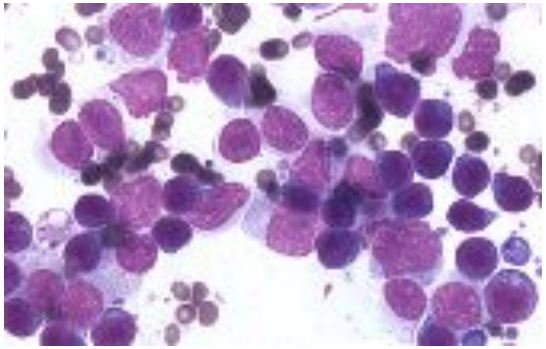
jfms

SHORT COMMUNICATION
A neurotropic lymphoma in the brachial plexus of a cat

Helge Linzmann DVM[1], **Leo Brunnberg** Prof, Dr Med Vet[1], **Achim D Gruber** Prof, Dr Med Vet, PhD, DECVP[2], **Robert Klopfleisch** Dr Med Vet, DACVP[2*]

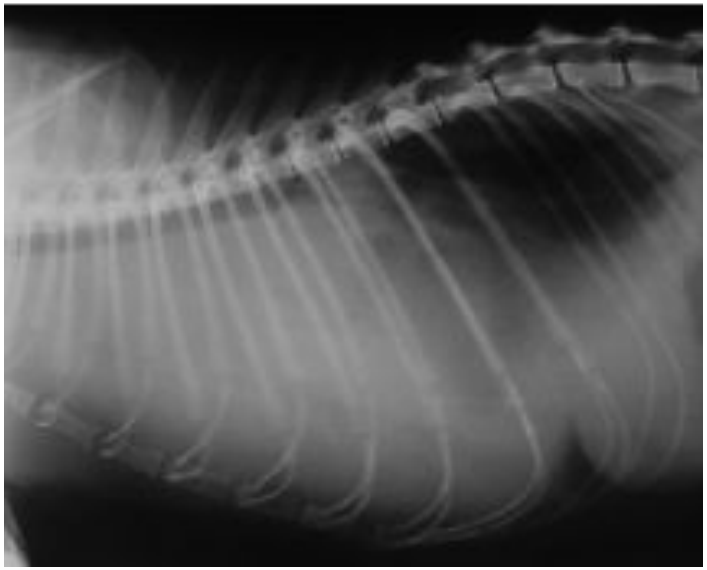


Andere: pericard



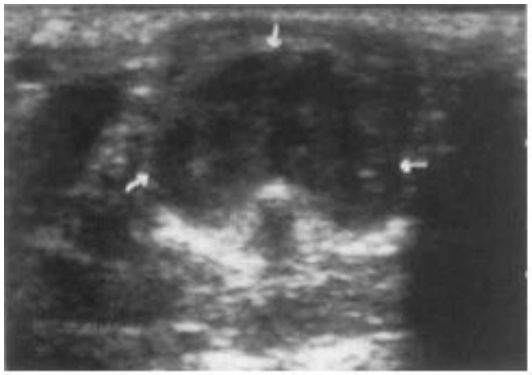
Pericardial lymphoma in seven cats

Maria Amati[1], Luigi Venco[1], Paola Roccabianca[2],
Sara Francesca Santagostino[2] and Walter Bertazzolo[1]

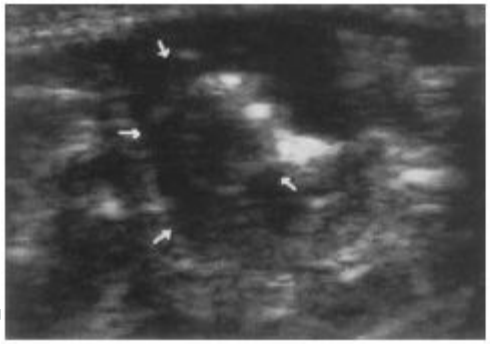


Laryngeaal Lymfoom

- Zelden (extra-nodaal 11/110 katten)
  - veralgemeende zwelling
  - massa in lumen



- Meestal Stage 1
  - 25% locale lnn.
- Reageert goed op chemo!!!
  - >70% CR (sommige studies 100%)
  - 3-19 maanden
- Rol radiotherapie??



Pulmonair Lymfoom

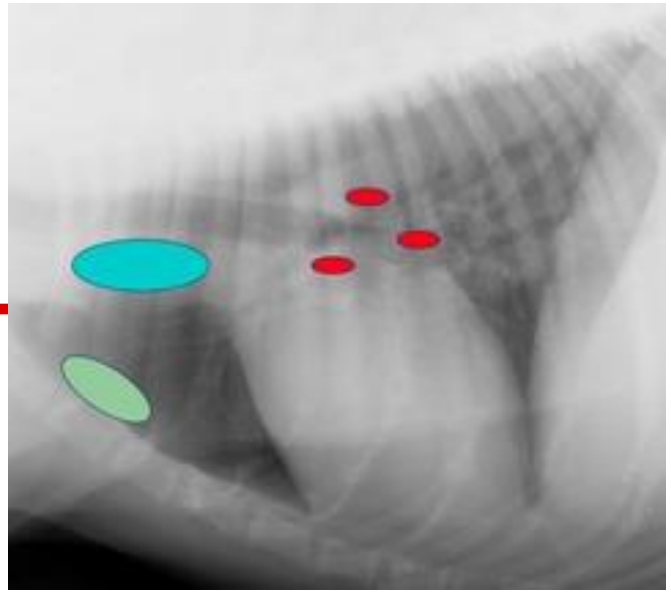
RADIOGRAPHIC APPEARANCE OF CONFIRMED PULMONARY LYMPHOMA IN CATS AND DOGS

Nicole E. Geyer, Jean K. Reichle, Alejandro Valdés-Martínez, Jamie Williams, Justin M. Goggin, Lesley Leach, Jennifer Hanson, Steve Hill, Tasha Axam

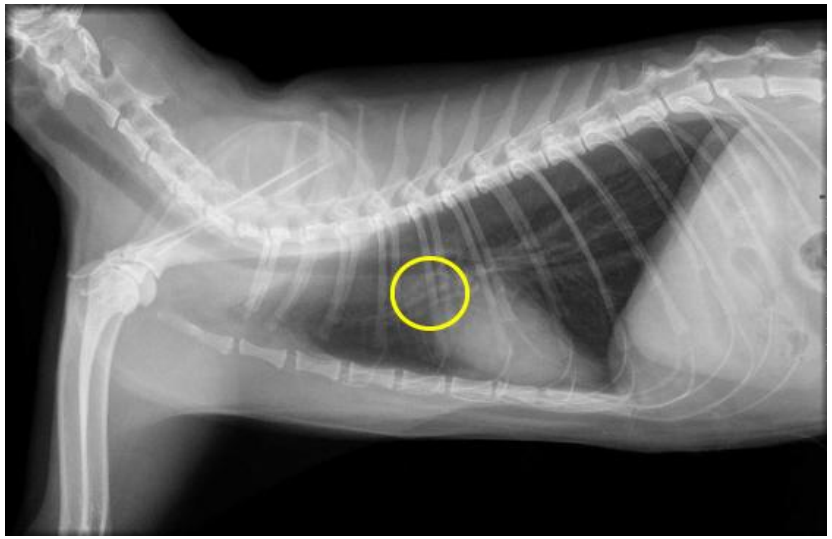
- Zeer variabel
  - Massa (>4cm) of nodules
    - 1 tot meerdere
  - Alveolair infiltraat
  - Metastatische nodules
    - mogelijks solitair!
  - COMBINATIE van patronen

- Distributie
  - symmetrisch en diffuus
  - assymmetrisch en diffuus
  - focaal

Pulmonair Lymfoom



- Thoracale effusie
  - meestal symmetrisch, bilateraal
  - mogelijks vrij uitgesproken



- Lymphadenopathie
  - Hilair
  - Sternaal
  - Craniaal mediastinaal

Pulmonair Lymfoom

- Primair
  - BALT
  - Peribronchovasculair : alveolair
    - destructie alveoli
    - dilatatie luchtwegen
- Secundair
  - lymfoom op andere lokalisatie
  - belang RX thorax bij staging

DEEL 12
Prognostische factoren

Response op behandeling

- Belangrijke prognostische factor
  - PR sterk negatieve factor

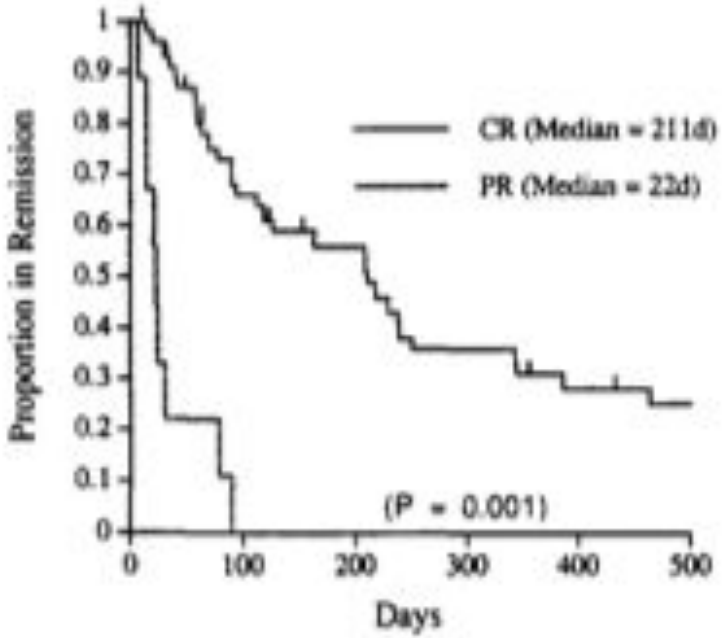


Fig 1. Kaplan–Meier 1st remission duration estimates stratified by response to therapy. Tick marks represent censored observations.

FeLV status

Positieve FeLV test : negatieve prognostische factor : remissie

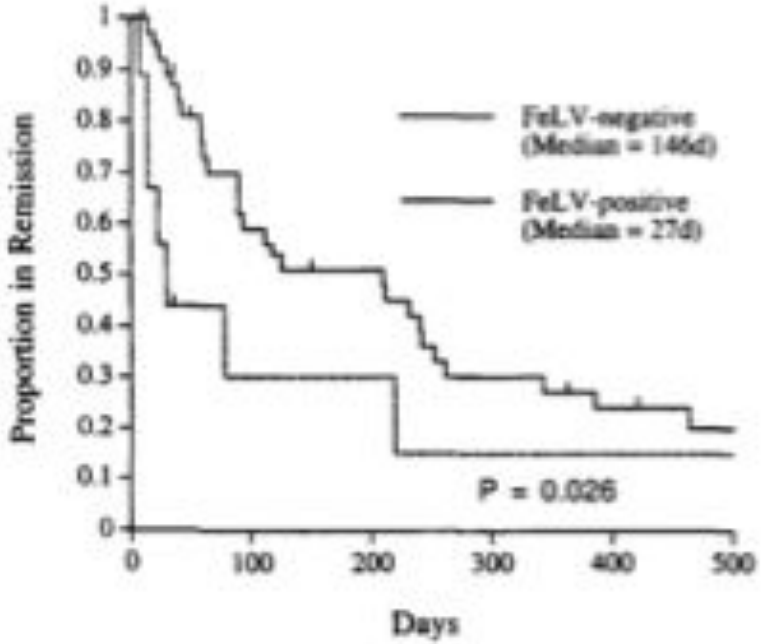


Fig 2. Kaplan–Meier 1st remission duration estimates stratified by feline leukemia virus enzyme-linked immunosorbent assay result. Tick marks represent censored observations.

FeLV status

Positieve FeLV test : negatieve prognostische factor : overleving

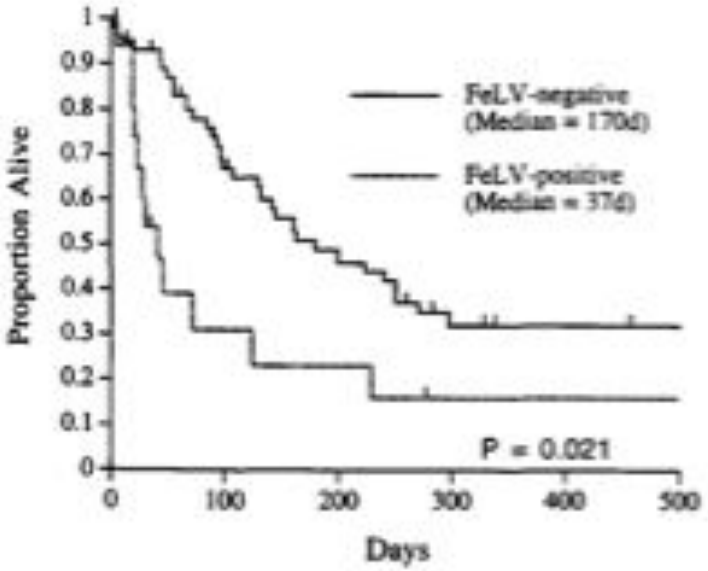


Fig 5. Kaplan–Meier survival time estimates stratified by feline leukemia virus enzyme-linked immunosorbent assay result. Tick marks represent censored observations.

Staging

- Stage
  - 1/2/3 188 dagen remissie 197 dagen overleving
    - Stage 1 beste prognose (93% CR)
  - 4/5 32 dagen remissie 54 dagen overleving

- Substage a>b
  - a : 230d/282d
  - b : 90d/102d

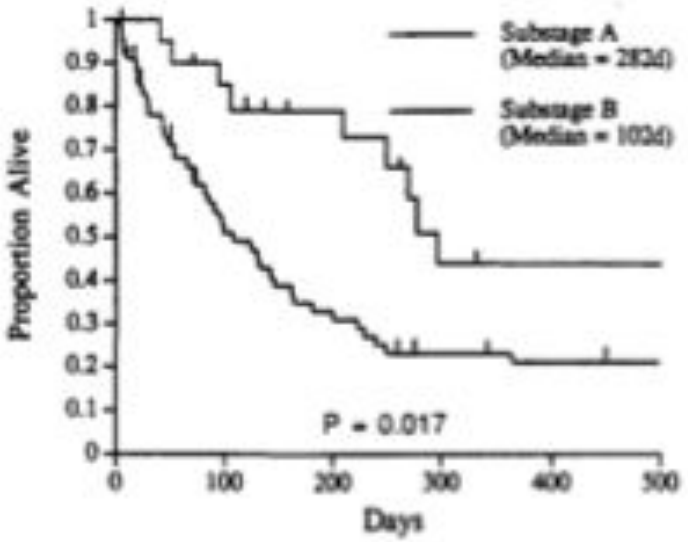


Fig 4. Kaplan–Meier survival time estimates stratified by substage. Tick marks represent censored observations.

Anatomische locatie

	Remissie	Overleving
Alimentair	277	213
Multicentrisch	112	143
Mediastinaal	60	69
Nasaal	380	465
Renaal	94	145
Hepatisch	14	26
Andere extra-nodale	172	145

Graad

- Laaggradig veel betere prognose
  - GI : laaggradig = mucosaal (kleine lymfocyten)
    - 29maanden mediaan overleving
  - GI : hooggradig = transmuraal (grote lymfocyten)
    - korte overleving
  - GI : LGL : zeer korte overleving

- B versus T
  - nasaal : B lymfoom : langste overleving
  - andere bv. renaal : niet onderzocht ngl. B of T

Doxorubicin

- Positieve invloed op remissie-duur
  - 273 dagen vs. 90
- Overleving niet significant
  - 225 dagen vs. 107

DEEL 13
BEHANDELING

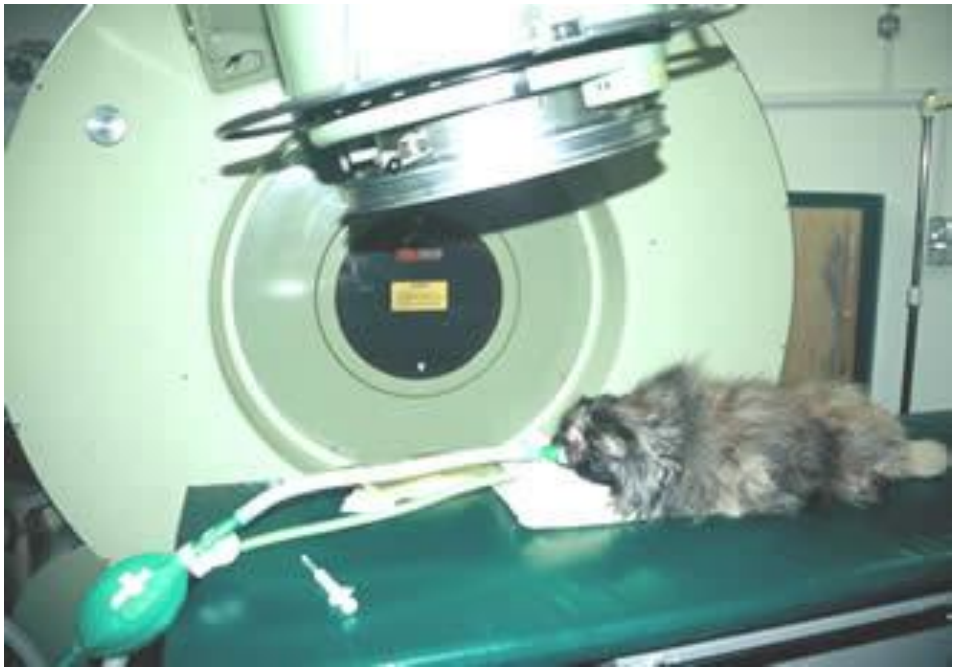
Behandeling

- !!! Vormen onderkennen met gunstige en ongunstige prognose

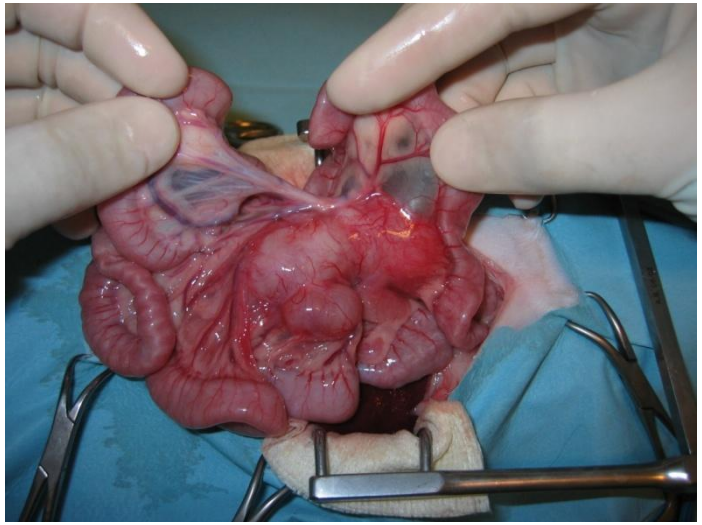
- Meest geschikte behandeling voorstellen in functie van
  - Type lymfoom
  - Eigenaar

Lokale Behandeling

- **Nasaal lymfoom**
  - Gelocaliseerde vorm
  - Gunstige prognose
  - MST RadioTx alleen 12-18 maanden



Lokale Behandeling



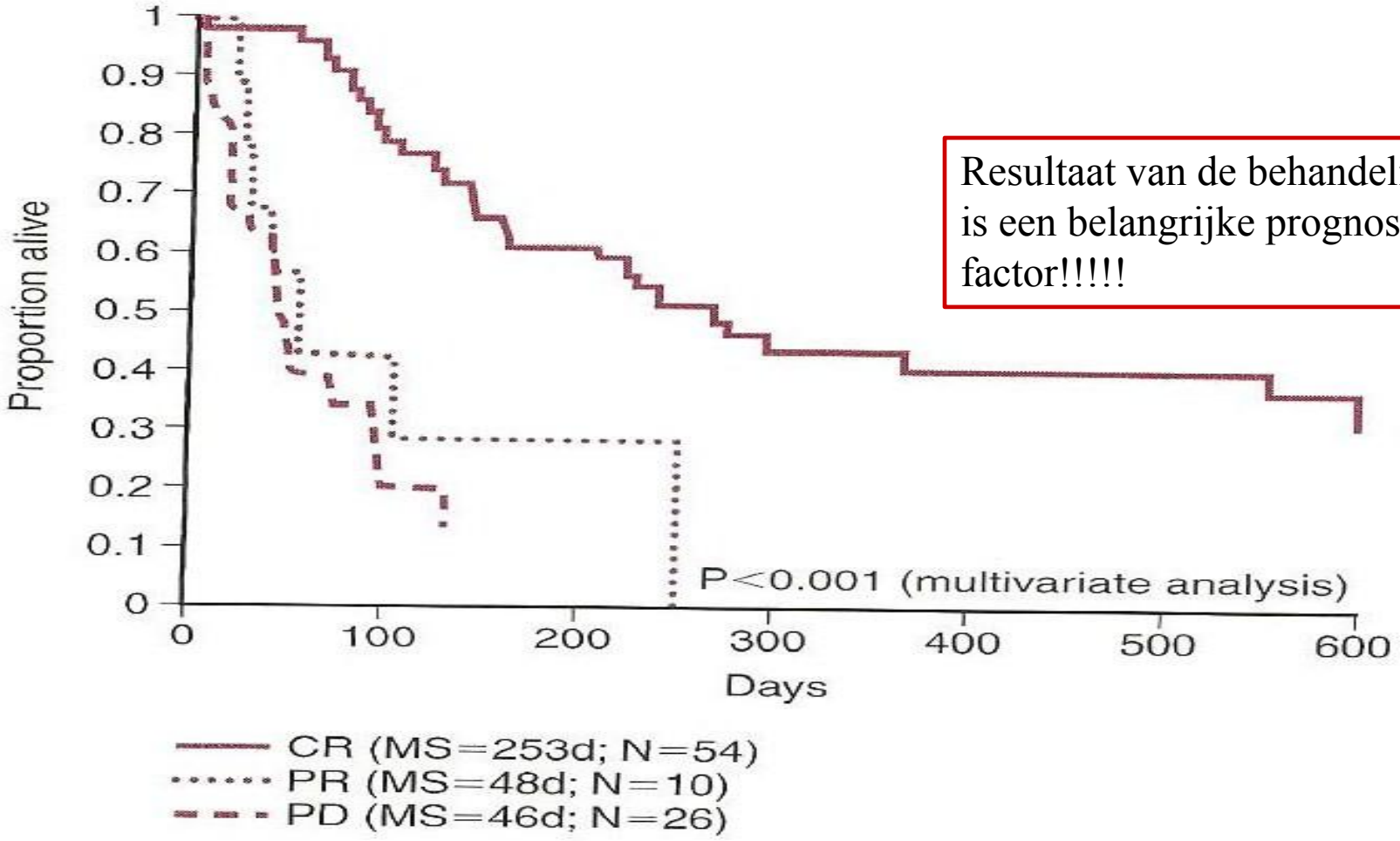
- **Chirurgie GI-lymfoom**
  - Gelokaliseerde vorm!!!!
  - Enterectomie
  - Diagnostisch
  - Beperkt risico
  - Gevolgd door chemo
  - Chirurgisch + chemo: soms lange overleving

- **Ileocecaal en colon**
  - alleen chirurgie
  - lange overleving

Chemotherapie

- Hoge graad COP of CHOP
- Lage graad: prednisolone + alkylerende agentia
  - Chlorambucil (Leukeran)
- Resultaten
  - GI: 7-10 maanden
  - LGL: 2 maanden
  - Renaal: 4 maanden
  - Mediastinaal jonge katten FeLV+: 2-3 maanden
  - Mediastinaal oudere katten FeLV -: +++
  - Nasaal: 12 maanden zonder RadioTx
    - Met radiotx: langer
  - Lage graad: 18 maanden

Chemotherapie



Resultaat van de behandeling is een belangrijke prognostische factor!!!!!

Chemotherapie

- Follow-up zeer belangrijk om prognose te bepalen
  - Remissie of niet!!
  - Goede staging belangrijk voor start behandeling
  - Volledig onderzoek na inductie periode

Nevenwerkingen

- Frequent 87%
- Braken
  - Maroptitant (Cerenia)
  - Metoclopramide
- Anorexie
  - Predni
  - Periactin
- Voeding
  - Indien nodig: voedingsonde
- Opletten met sommige orale medicaties

Table 2. Adverse effects reported during COP chemotherapy for feline lymphoma in 31 cats

Adverse effect reported	Number of owners reporting effect (%)
Hair loss	11 (35)
Loss of appetite	9 (29)
Lethargy	8 (26)
Vomiting	7 (23)
Whisker loss	5 (16)
Sleepiness	5 (16)
Weight loss	4 (13)
Stress	1 (3)
Breathing difficulties	1 (3)
Scared	1 (3)
Constipation	1 (3)
Incontinence	1 (3)
Falling over	1 (3)
Miserable	1 (3)
Diarrhoea	1 (3)
Urinary tract infection	1 (3)

COP

	S1	S2	S3	S4	S5	S6	S7
Vincristine 0,5 à 0.7 mg/m2 IV	X	X	X	X			X
Cyclophosphamide 200 mg/m2 PO	(X)			X			
Prednisolone 1 mg/kg/j	X	X	X	X	X	X	X

- MS de 6 à 8 mois

L-COPA

	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14
Vincristine 0.5 à 0,7 mg/m2 IV		X	X	X	X						X			X
Cyclophosphamide 200 mg/m2 PO					X						X			X
L-asparaginase 400 UI/kg IM	X													
Doxorubicine 20 à 25 mg/m2								X						
Prednisolone 1 mg/kg/j PO	X	X	X	X	X	X	X	X	X	X	X	X	X	X

- MS à 9 mois

S1	Vincristine 0,5 à 0.7 mg/m2 IV
	Kidrolase 400 UI/kg IM ou SC
	Prednisone 2 mg/kg/j
S2	Cyclophosphamide 200 mg/m2 IV (ou PO) une seule fois
	Prednisone 2 mg/kg/j
S3	Vincristine 0,5 à 0.7 mg/m2 IV
	Prednisone 1 mg/kg/j
S4	Doxorubicine 20 à 25 mg/m2 ou 1 mg/kg IV (20 minutes)
	Prednisone 1 mg/kg 1 jour sur 2
S5	REPOS
S6	Vincristine 0,5 à 0.7 mg/m2 IV
S7*	Cyclophosphamide 200 mg/m2 IV (ou PO) une seule fois
S8	Vincristine 0,5 à 0.7 mg/m2 IV
S9	Doxorubicine 20 à 25 mg/m2 ou 1 mg/kg IV (20 minutes)
S10	REPOS
S11	Vincristine 0,5 à 0.7 mg/m2 IV
S12	REPOS
S13*	Cyclophosphamide 200 mg/m2 IV (ou PO) une seule fois
S14	REPOS
S15	Vincristine 0,5 à 0.7 mg/m2 IV
S16	REPOS
S17	Doxorubicine 20 à 25 mg/m2 ou 1 mg/kg IV (20 minutes)
S18	REPOS
S19	Vincristine 0.7 mg/m2 IV
S20	REPOS
S21*	Cyclophosphamide 200 mg/m2 IV (ou PO) une seule fois
S22	REPOS
S23	Vincristine 0,5 à 0.7 mg/m2 IV
S24	REPOS
S25	Doxorubicine 20 à 25 mg/m2 ou 1 mg/kg IV (20 minutes)

Owners 'perception of their cats' quality of life during COP chemotherapy for lymphoma

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Table 1. QoL ratings for cats by owners, rated on a scale of 1 (worst possible) to 10 (best possible)

Rating of cats' QoL	Mean (SD)	Median	Minimum–maximum
Before cancer	9.5 (0.99)	10	6–10
After diagnosis, pre-treatment	3.9 (2.4)	4	1–9.4
During treatment	6.3 (2.4)	7	1–10
Owners' perceptions of cats' own rating during treatment	6 (2.4)	7	1–9

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