

CRP在骨關節疾病的臨床應用

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CRP在骨關節疾病的臨床應用

跛行診斷 – 如何發現關節疾病

除了DJD之外還有什麼？

- 什麼是多發性關節炎

如何運用CRP幫助關節炎的診斷與監控



步態視診

頭部上下擺動 Head bobbing



步態視診

頭部上下擺動 Head bobbing

身體理學檢查

神經學檢查

區別神經疾病 / 骨關節疾病
定位

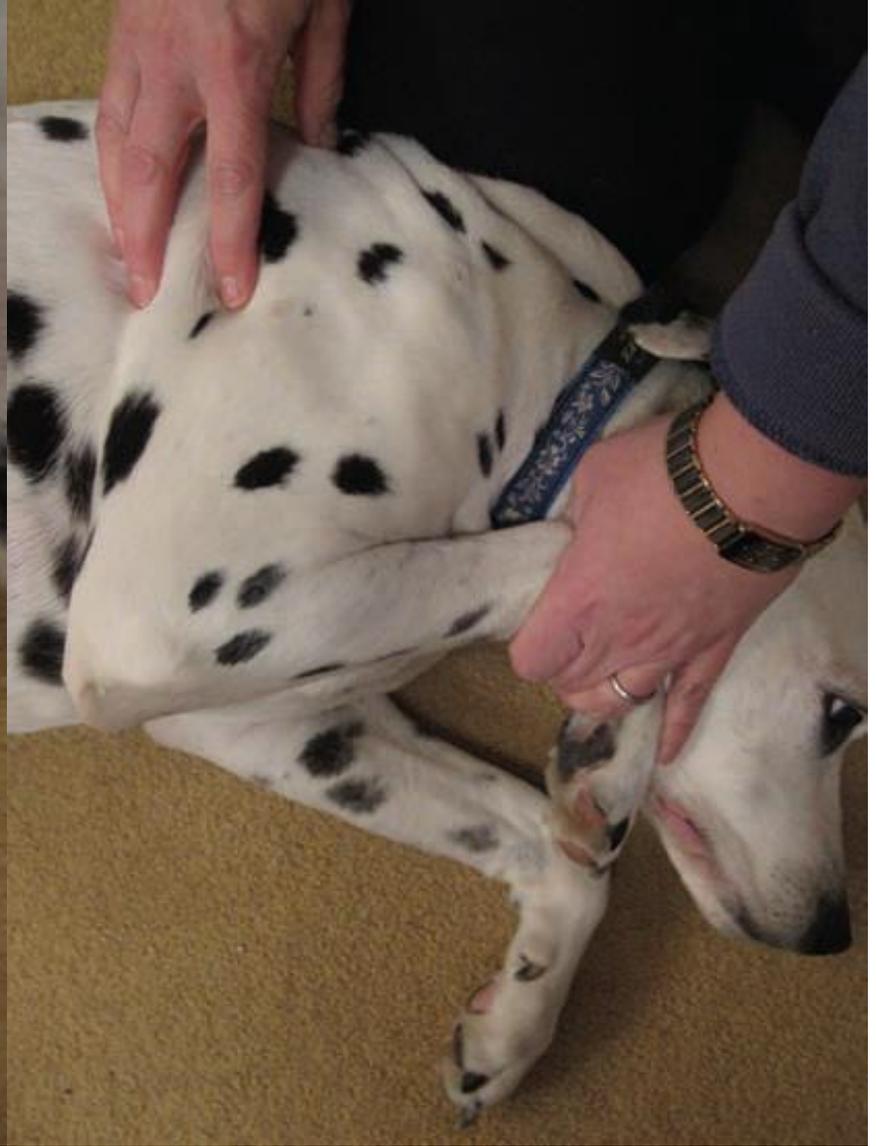
骨關節檢查

四肢骨觸診 / 關節活動範圍 / 關節觸診
哪裡痛

腳痛也要看全身



站立檢查



側躺檢查

鎮靜骨關節檢查，X光

血檢，尿檢

進階影像檢查

找到疼痛位置之後

如何發現

關節疾病

7y, NM, 臘腸

8個月前開始

不太愛走

食慾/排尿/排便 正常



1-2級癱瘓 (?)



CT ?

血檢 ?

X光 ?

止痛藥 ?

腳痛也要看全身

身體理學檢查

神經學檢查

區別神經疾病 / 骨關節疾病
定位

骨關節檢查

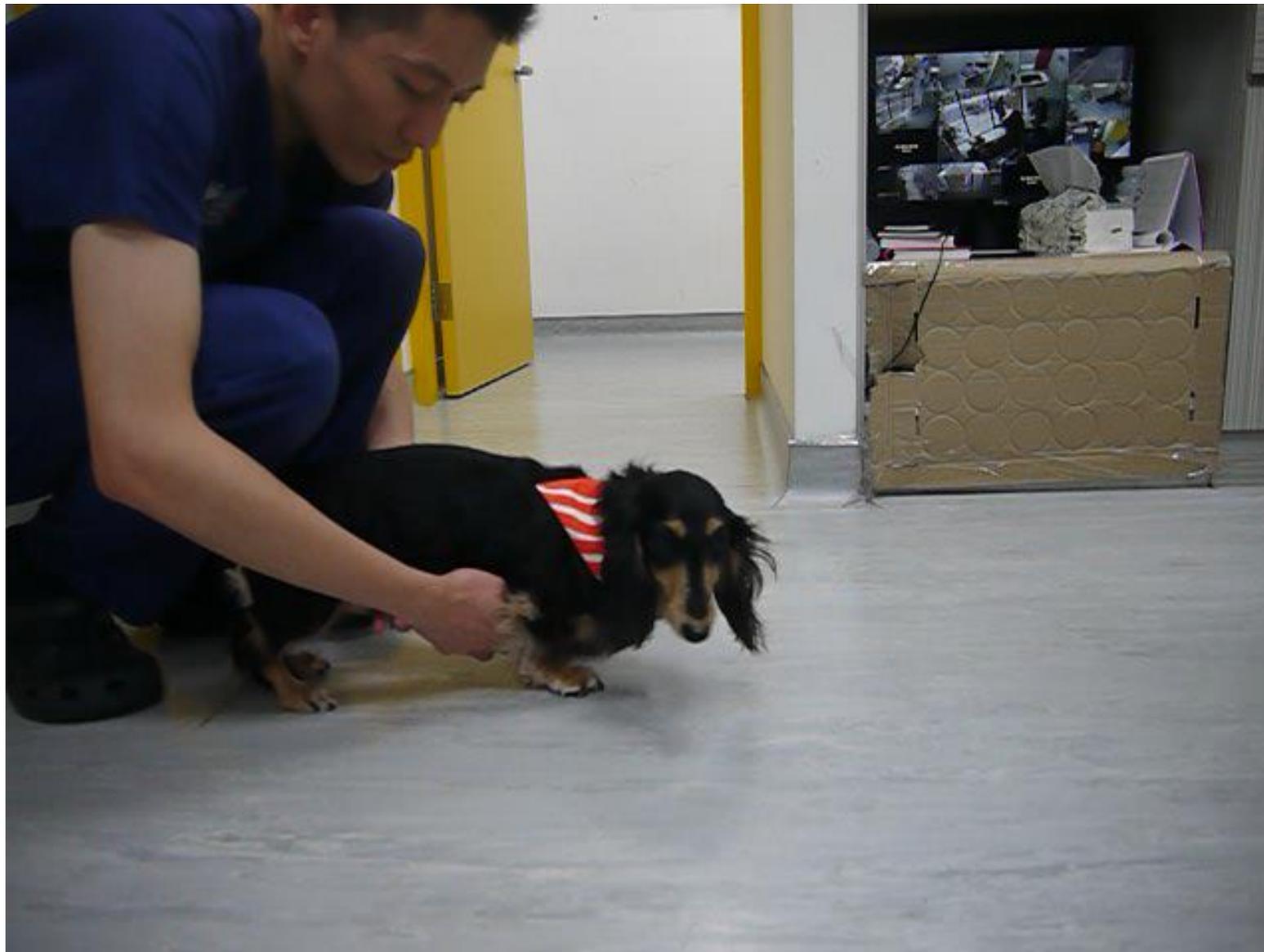
四肢骨觸診 / 關節活動範圍 / 關節觸診
哪裡痛

腳痛也要看全身

身體理學檢查

沈鬱，不願行走，僵硬，坐姿
黏膜 / CRT / 聽診 / 腹腔觸診





視診 運動能力



神經學檢查

本體知覺

Conscious Proprioception



骨關節檢查

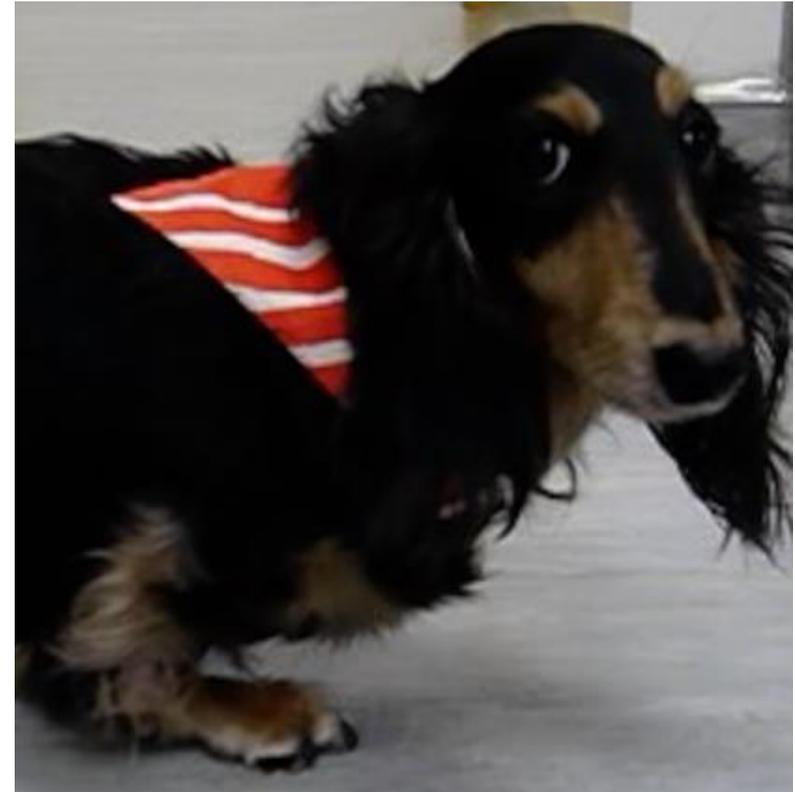
骨觸診/關節活動範圍/關節觸診

初步評估

慢性疼痛，僵硬不願行走

神經功能正常

多發關節腫脹疼痛



免疫媒介性 多發性關節炎？

Immune-mediated polyarthritis (IMPA)

關節炎 Arthritis

非發炎性 Non-inflammatory

發炎性 Inflammatory

退化性關節炎
DJD

創傷性

凝血異常性

免疫媒介性 多發性關節炎
Immune-Mediated Poly-Arthritis
IMPA

感染性
Infectious arthritis

非糜爛性
Non-erosive IMPA

糜爛性
Erosive IMPA

非 糜爛性 Non-erosive IMPA

特發性 Idiopathic

紅斑性狼瘡 SLE

疫苗/藥品誘發

Breed specific

Polyarthrititis/polymyositis syndrome

非 糜爛性 Non-erosive IMPA

特發性 Idiopathic

Type I 無潛在疾病 50-65%

單純性

Type II 遠端感染或發炎 13-25%

Type III 腸胃或肝臟疾病 4%

反應性

Type IV 關節外腫瘤 2%

糜爛性 Erosive IMPA

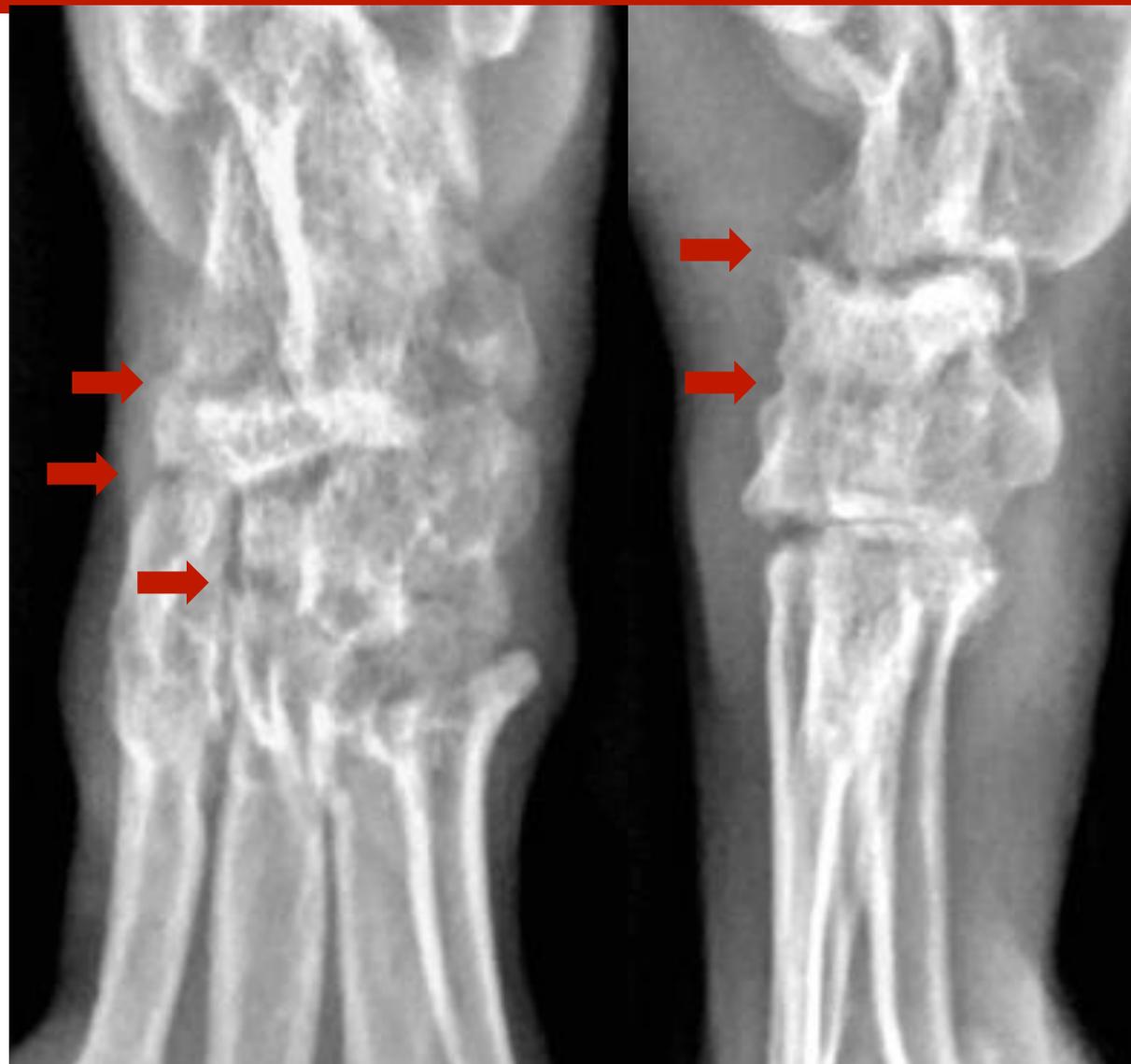
軟骨下骨破壞

Subchondral bone destruction

關節表面不規則

關節表面打洞

Punched-out lesion



免疫媒介性 多發性關節炎

Immune-mediated polyarthritis (IMPA)

步態僵硬 (38/38)

不明原因發燒 (22/38)

腕 (31), 踝 (28), 膝 (28), 肘 (17)

J Am Vet Med Assoc. 2004 Apr 15;224(8):1323-7.

Type I immune-mediated polyarthritis in dogs: 39 cases (1997-2002).

如何診斷IMPA

關節囊液分析

至少2個關節

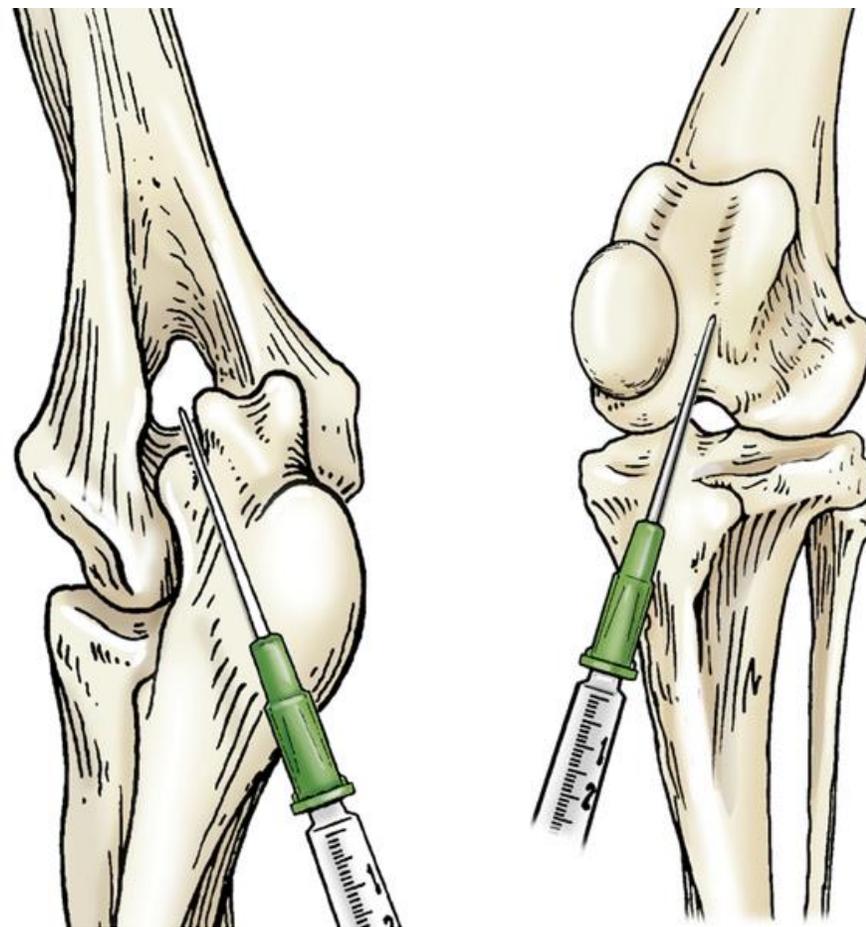
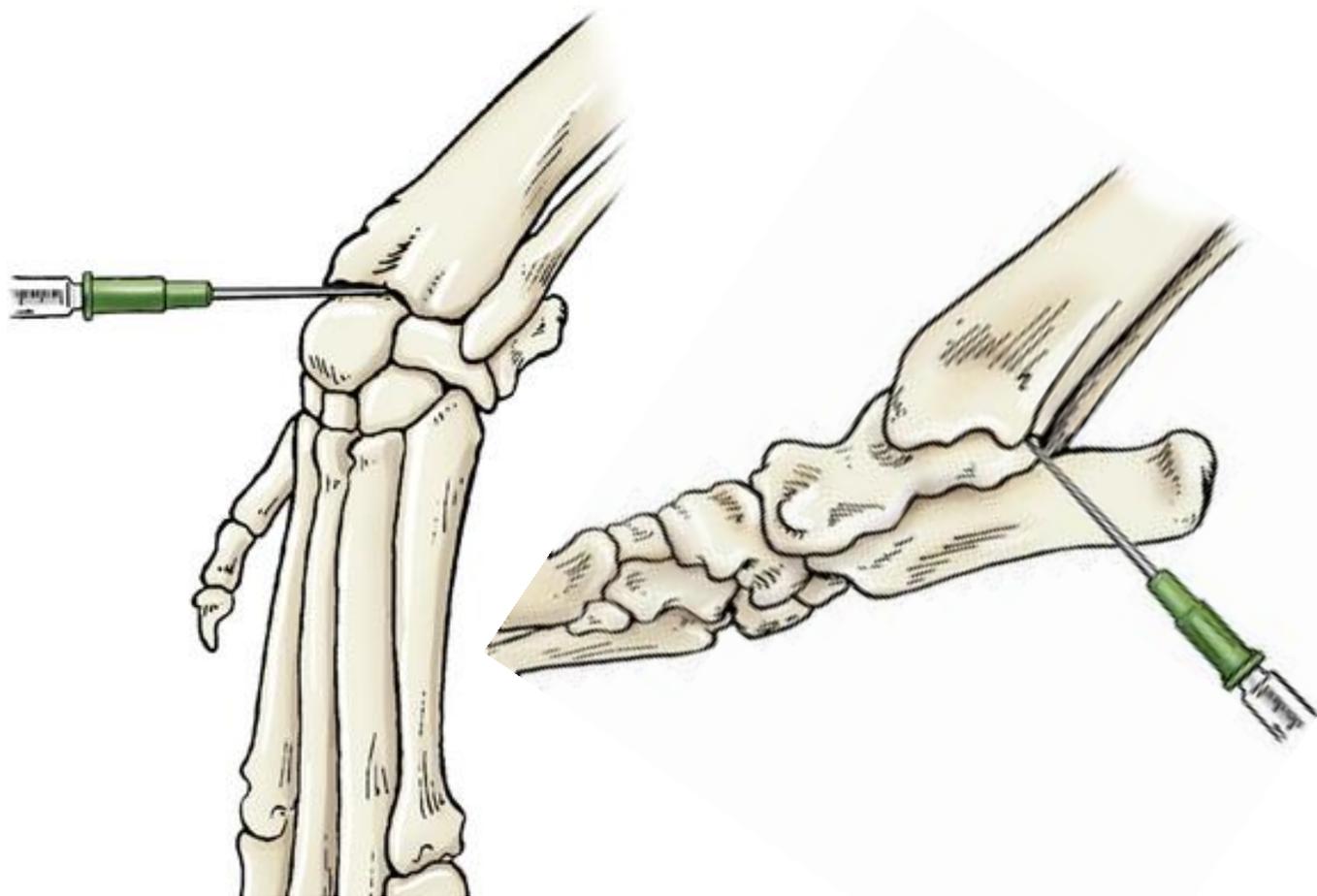
關節液有核細胞數增加

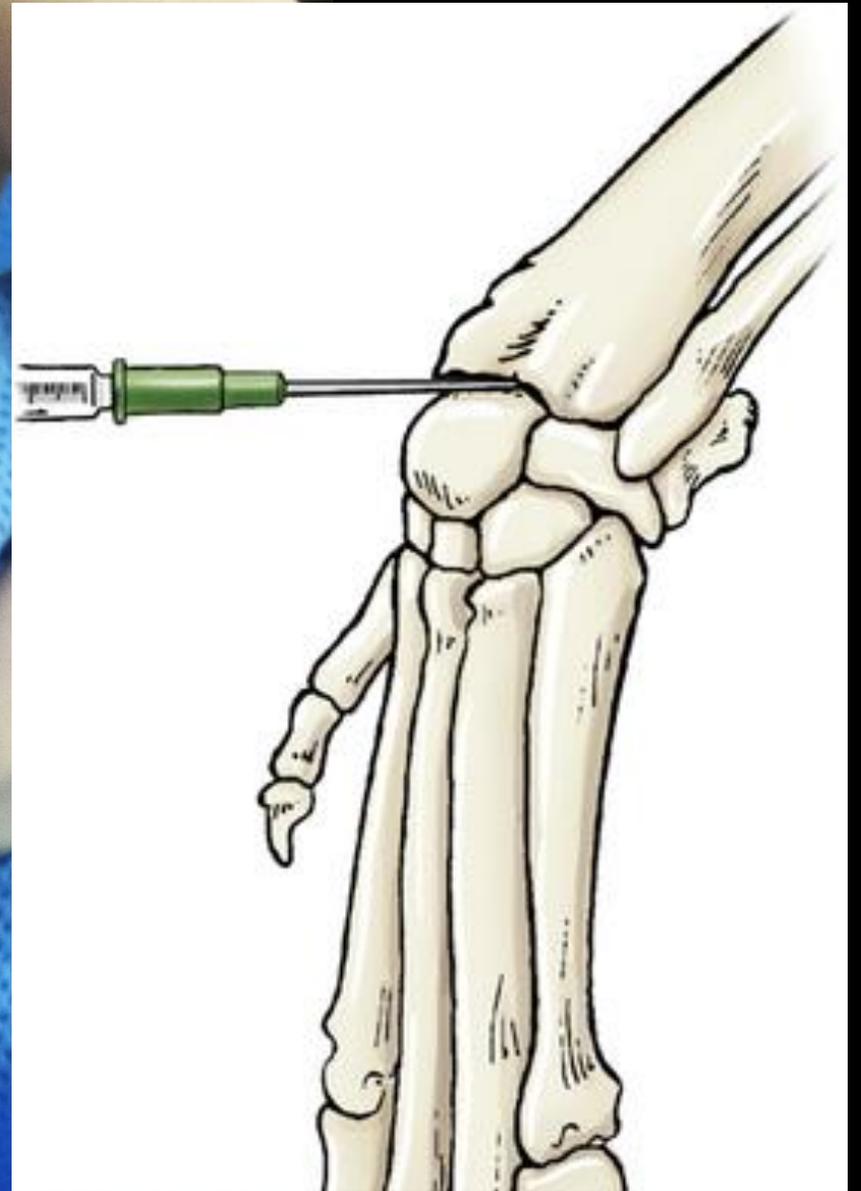
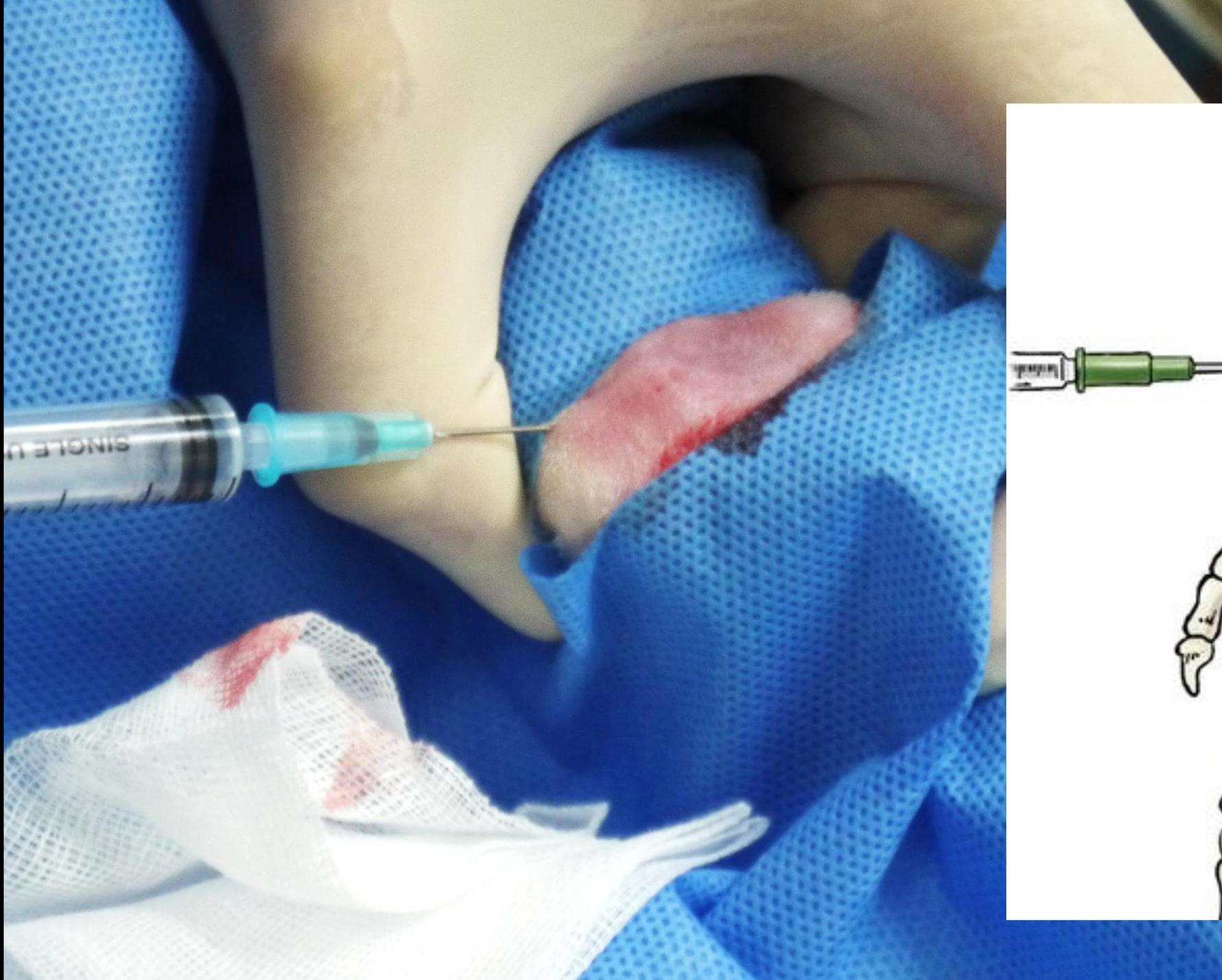
> 10% 嗜中性球

無感染

CONFIRMED

關節囊液分析





關節囊液分析

量 Volume **<1 ml**

顏色 Color **淡黃色**

混濁 Turbidity **清澈**

黏稠度 Viscosity **牽絲 2.5cm**



關節囊液分析

細胞計數

有核細胞數 TNCC

細胞學

單核球 mononuclear cell

中性球 Neutrophil

細菌培養

血液培養基

		Total cell count	Mononuclear %	Neutrophil %
	正常關節	<3 × K/uL	>90	<10
非發炎性	退化性關節炎 DJD	<5 × K/uL	>90	<10
發炎性	免疫性關節炎 IMPA	>3 × K/uL 可高達150	通常<20	通常>80
	感染性關節炎 Infectious	>3 × K/uL 可高達250	通常<10	通常> 90





白血球測試

有核細胞數明顯增加

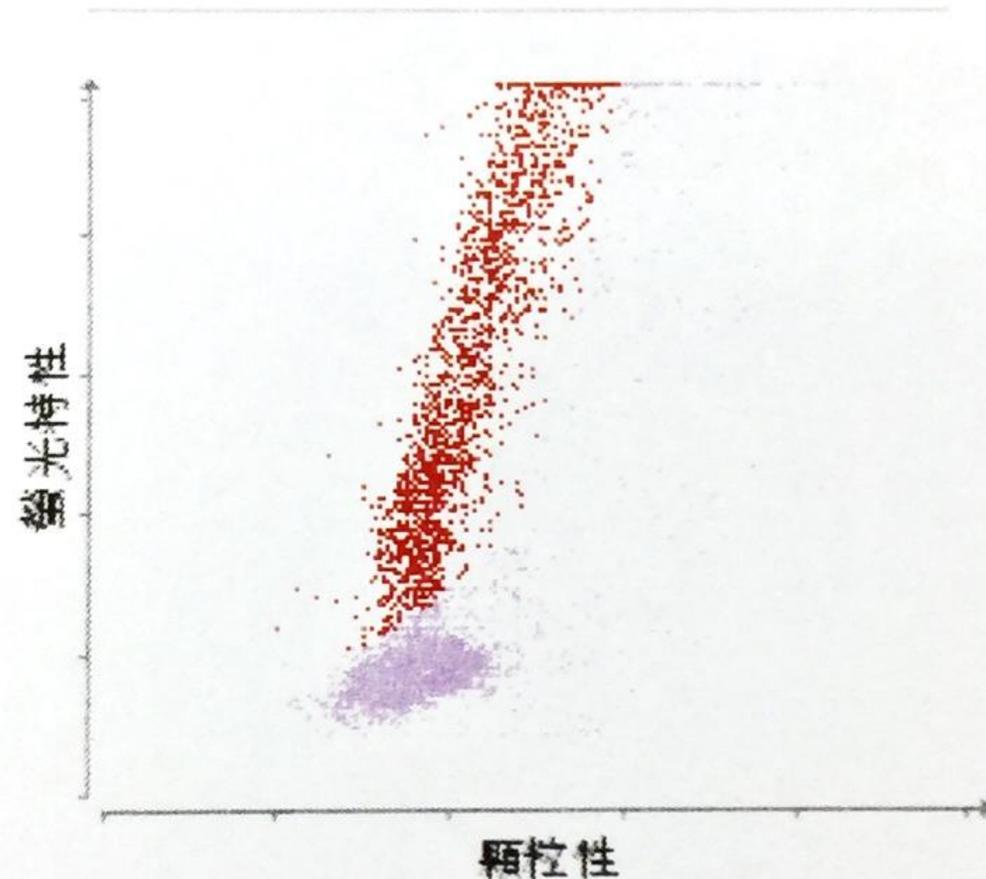
Nucleated Cell Count	19.72	M/ μ L K/ μ L
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Granulocytes	17.82	K/ μ L
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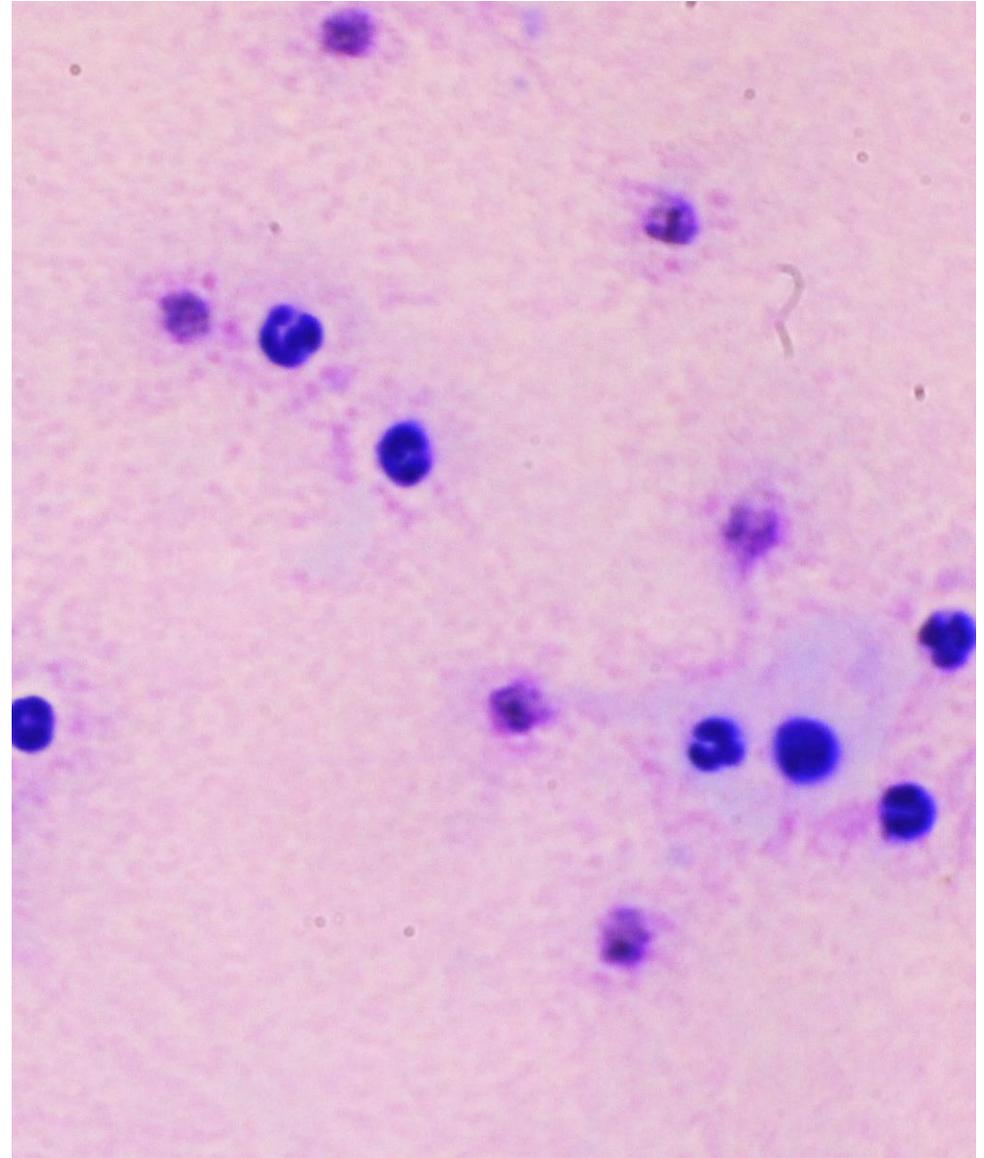
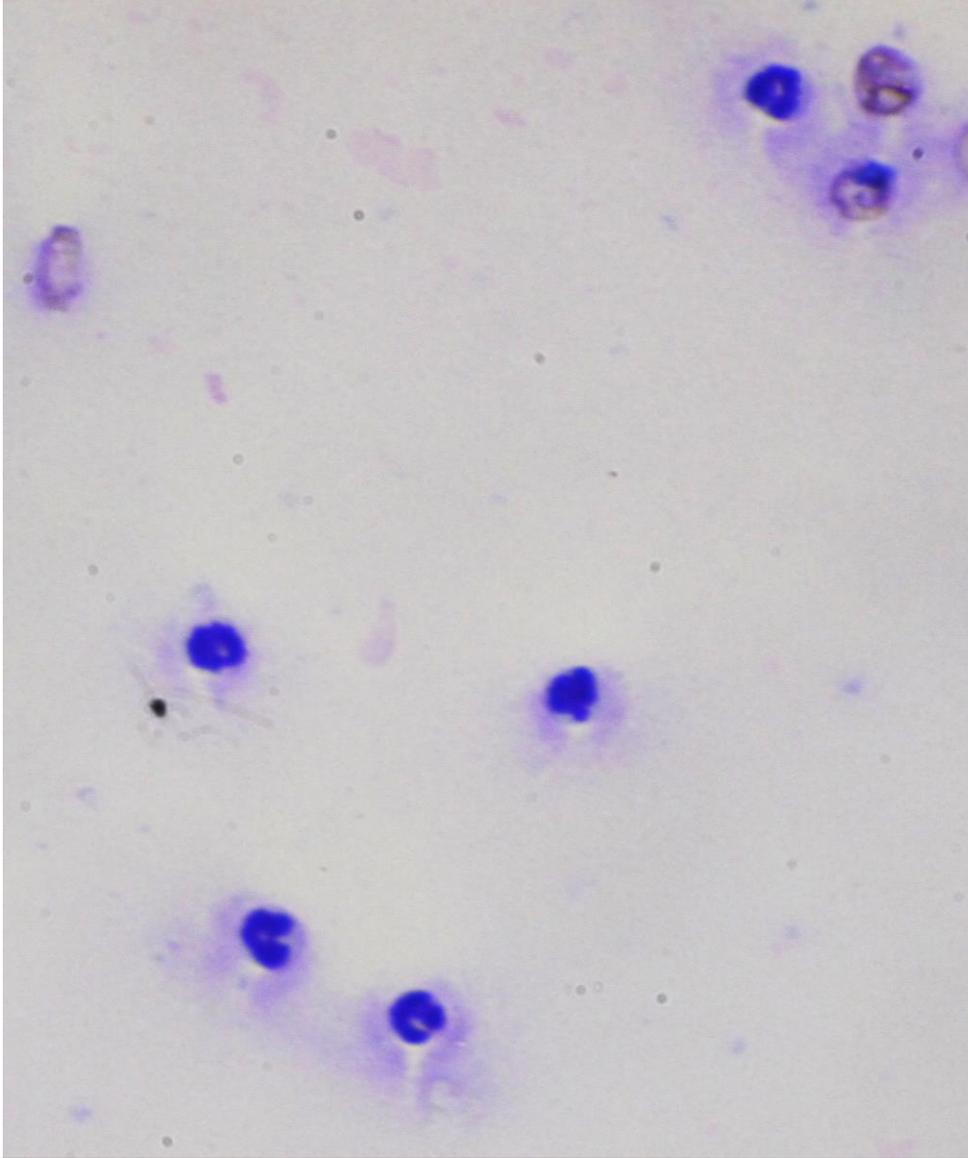
% Granulocytes	90.4	%
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顆粒球為主

% Agranulocytes	9.6	%
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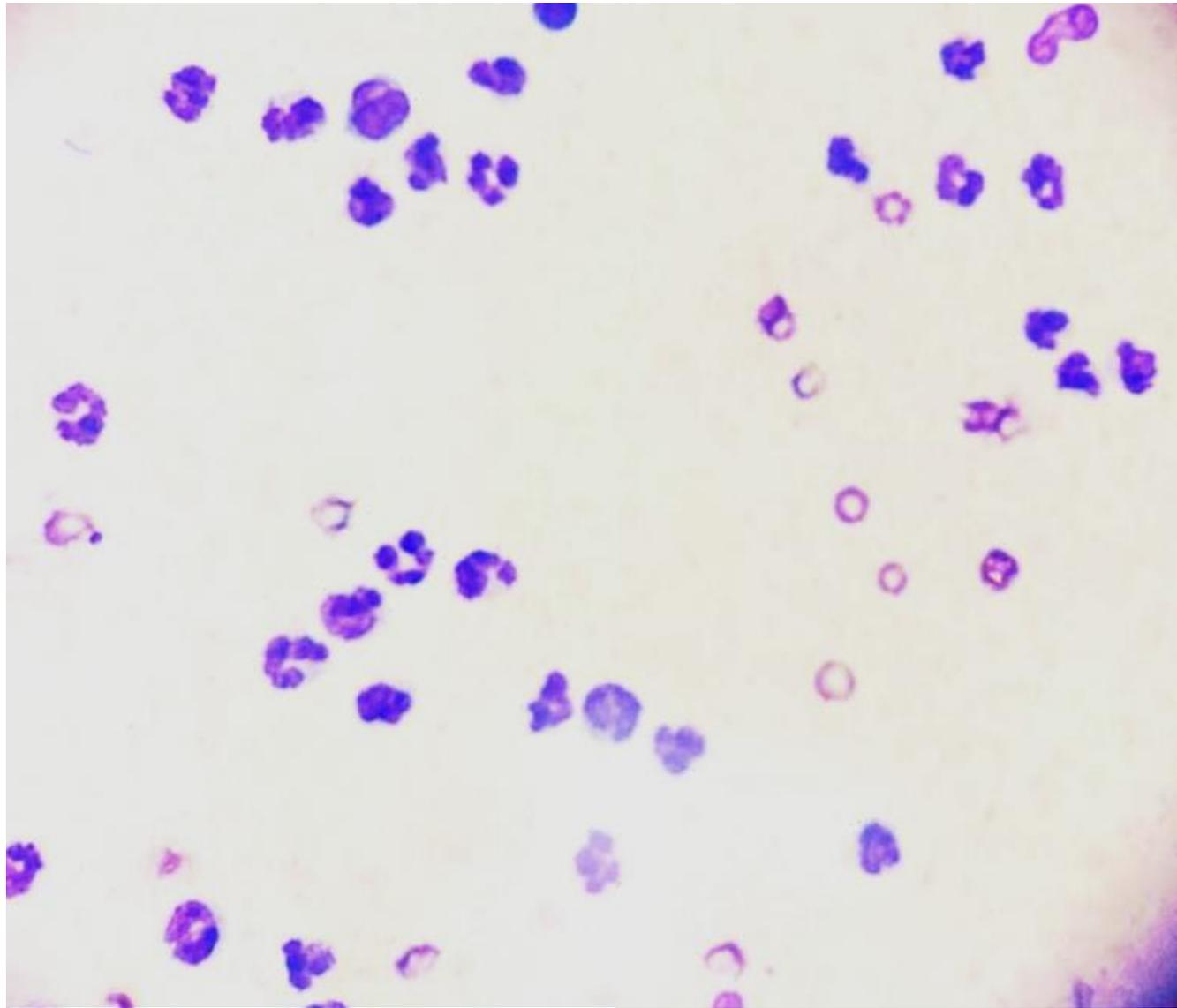


- 顆粒性白血球 (GRANS)
- 非顆粒白血球 (AGRANS)

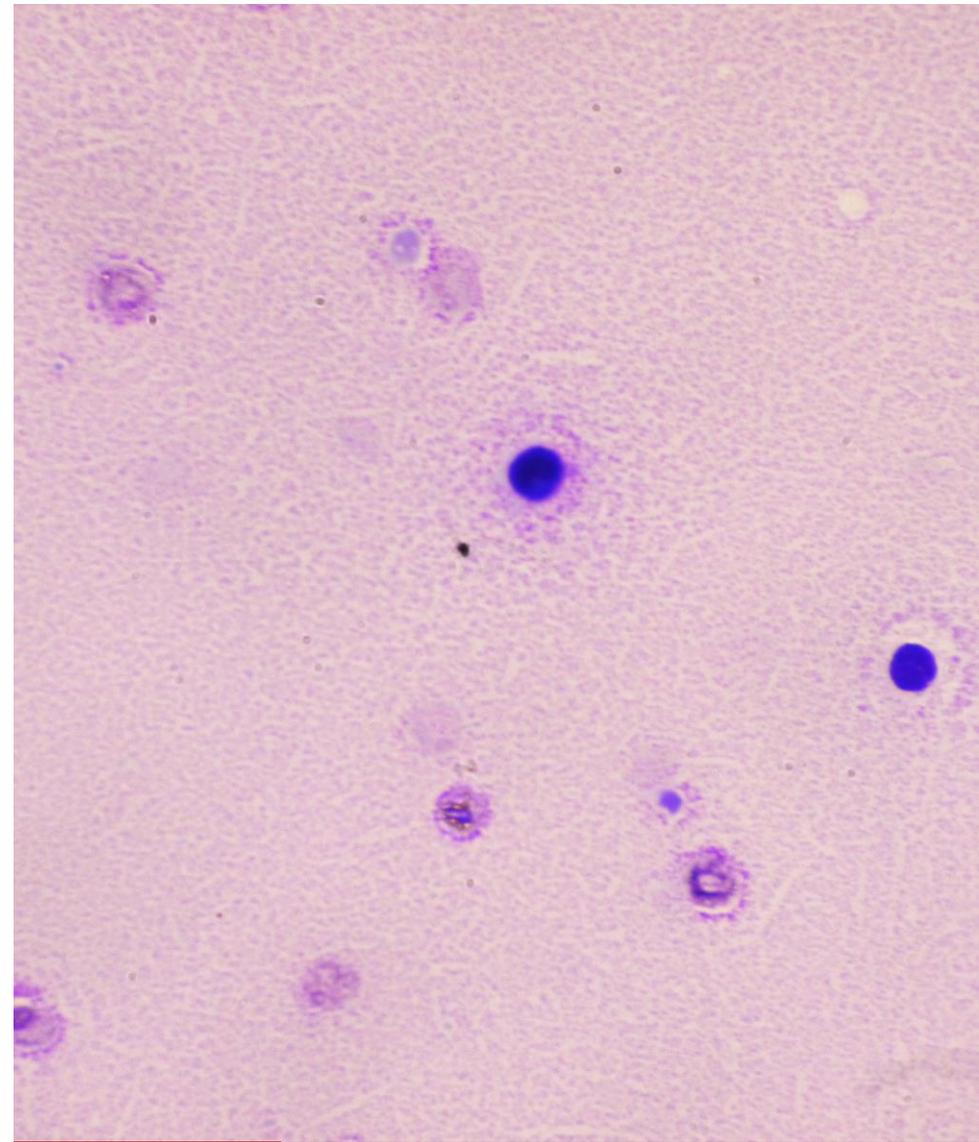


IMPA關節液

TNCC↑↑ 非退行性嗜中性球



感染性關節炎 退行性嗜中性球



DJD 單核球

區別單純性或反應性IMPA

確認有無遠端感染、發炎疾病、腫瘤

血檢，尿檢，尿液培養

全身感染性疾病，血液寄生蟲

關節X光

胸腔腹腔X光，超音波

關節囊液分析的困難

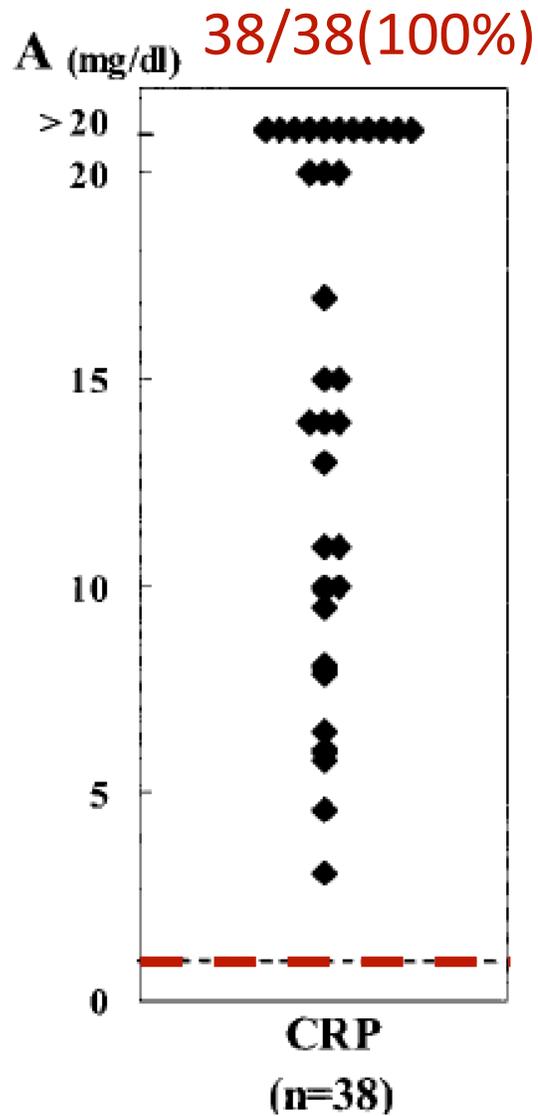
侵入性

鎮靜麻醉

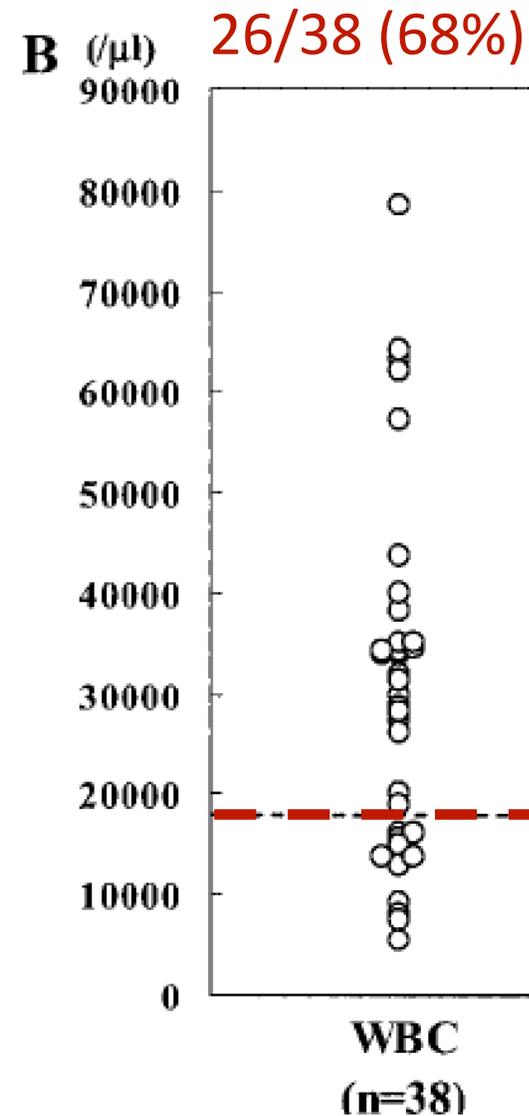
費用

技術性

除了關節囊液之外？



每個病患
CRP都顯著
上升

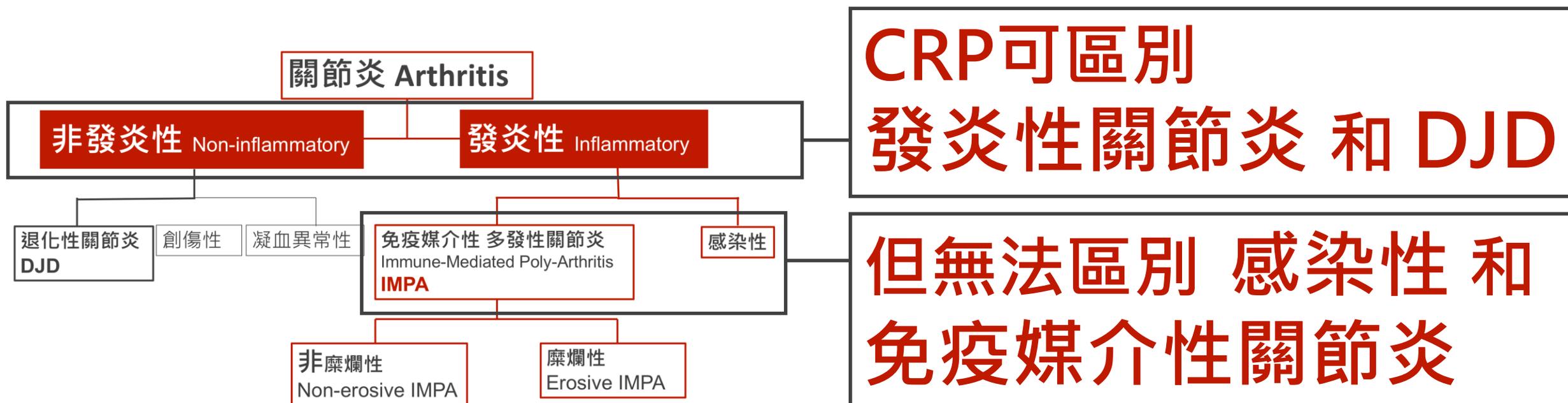


只有68%病患
WBC 上升



Measurement of serum C-reactive protein concentration for discriminating between suppurative arthritis and osteoarthritis in dogs

Hillström *et al. BMC Veterinary Research* (2016) 12:240



IMPA治療後CRP明顯下降

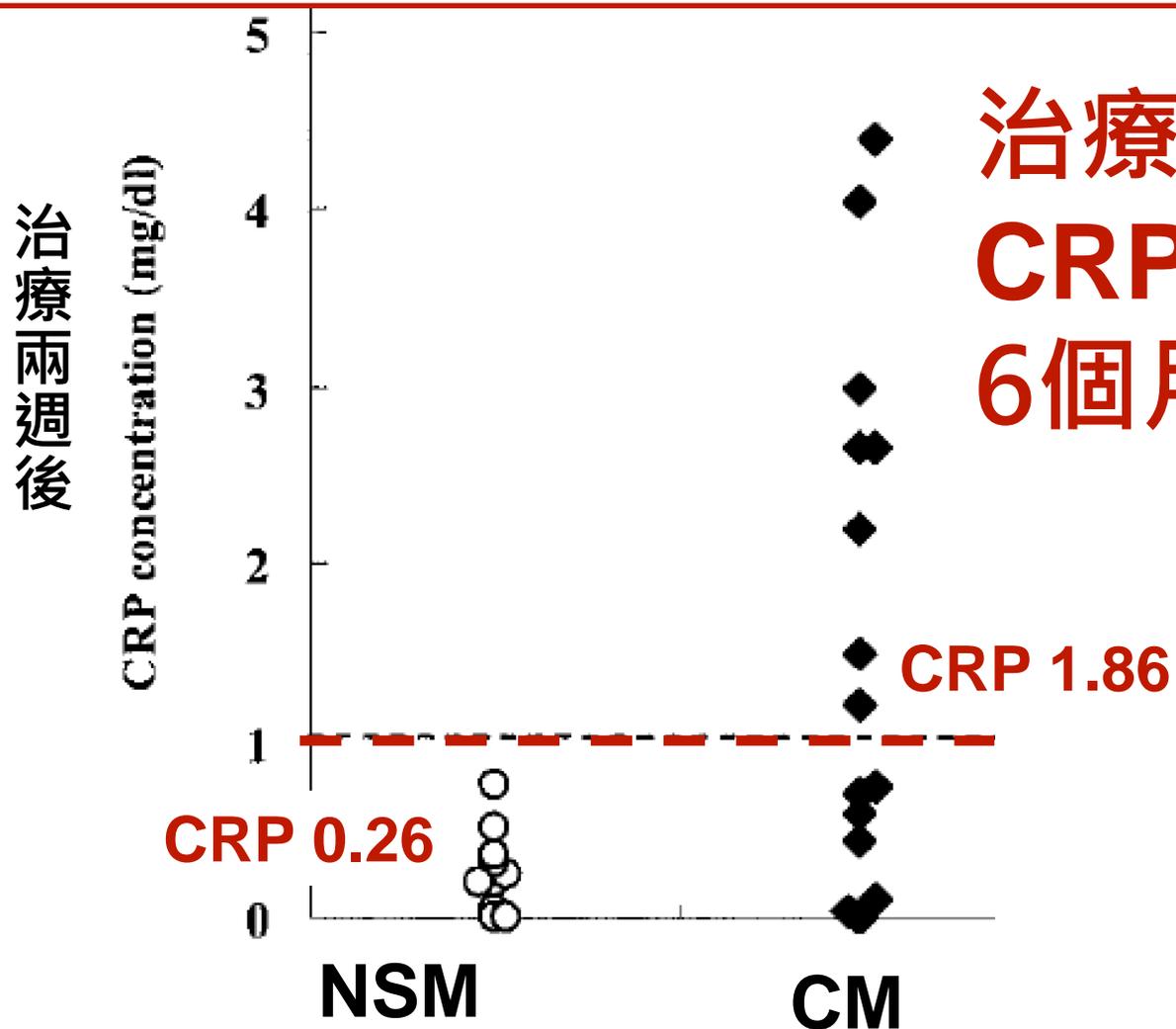
與 疼痛評估、關節液細胞數、運動量變化相符

**CRP可作為 關節發炎 和 IMPA 疾病變化的
代理標記**

J Vet Intern Med 2014;28:905–911

**Serum Biomarkers of Clinical and Cytologic Response in Dogs with
Idiopathic Immune-Mediated Polyarthropathy**

C-reactive protein concentration in canine idiopathic polyarthritis.



治療兩週後
CRP可回到正常的病患，
6個月時幾乎不再需要藥物

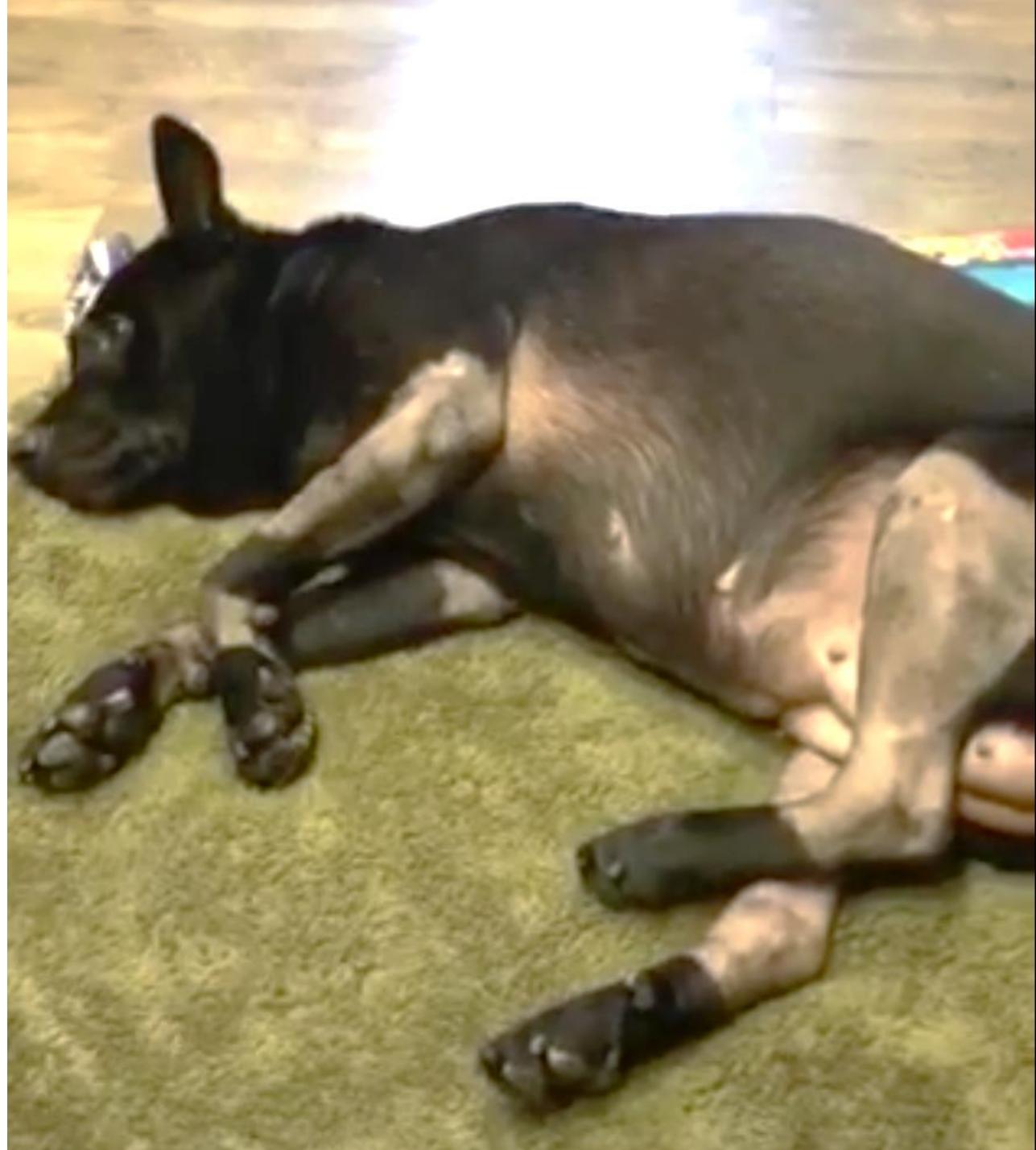
治療6個月後

NSM
不再或偶爾
需要藥物

CM
經常
需要藥物

6y, SF, Mix

LF, RH, LH 交替跛行



雙側腕關節及膝關節腫脹且疼痛

十字韌帶及膝蓋骨正常

止痛藥治療後僅部分改善

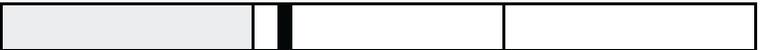


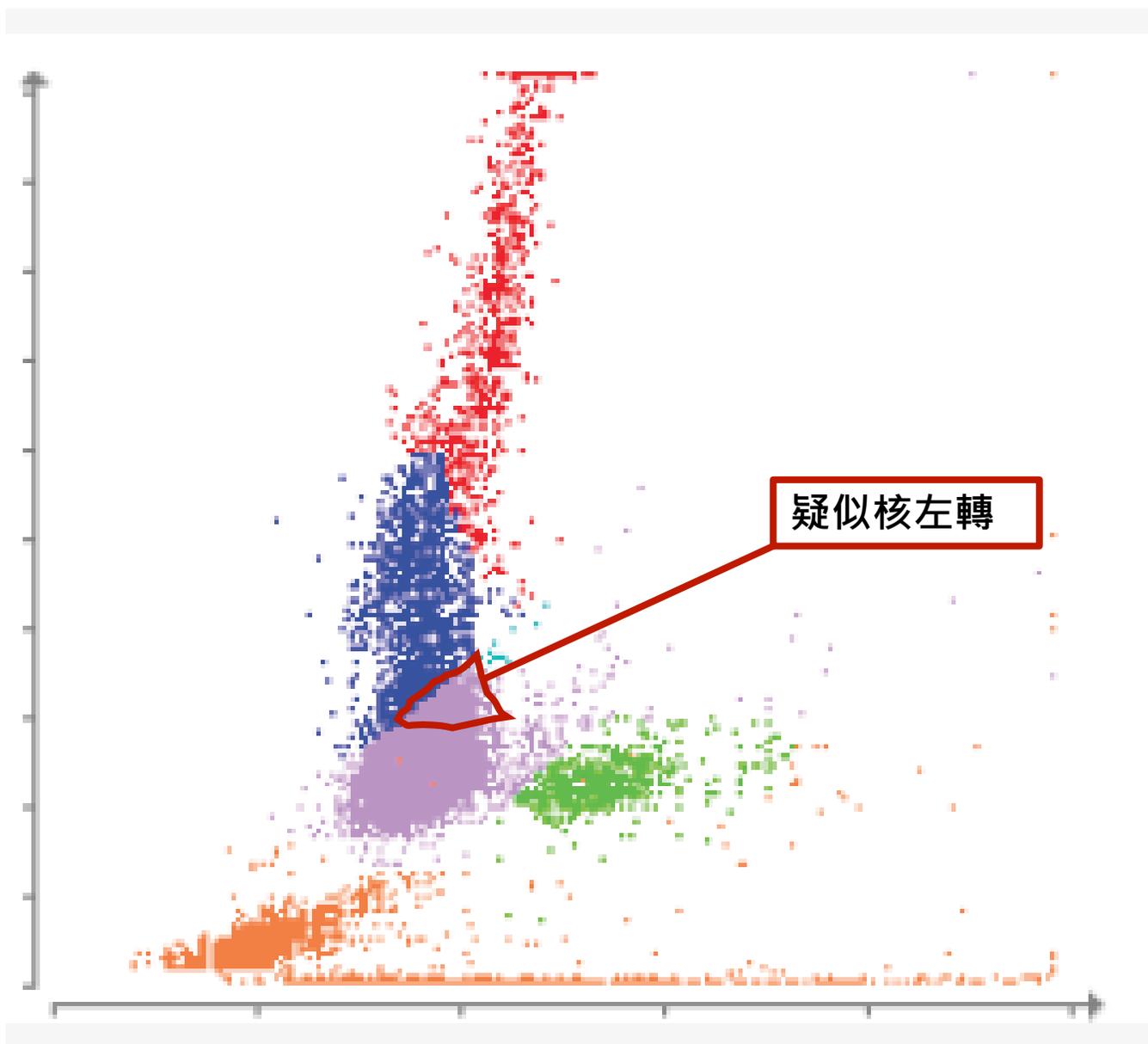


RESULT

REFERENCE VALUE

RBC	6.95	5.65 - 8.87 M/ μ L	
Hematocrit	39.8	37.3 - 61.7 %	
Hemoglobin	14.7	13.1 - 20.5 g/dL	
MCV	57.3	61.6 - 73.5 fL	L
MCH	21.2	21.2 - 25.9 pg	
MCHC	36.9	32.0 - 37.9 g/dL	
RDW	20.3	13.6 - 21.7 %	
% Reticulocyte	0.6	%	
Reticulocytes	38.2	10 - 110 K/ μ L	
Platelets	243	148 - 484 K/ μ L	
PDW	15.4	9.1 - 19.4 fL	
MPV	11.0	8.7 - 13.2 fL	
Plateletcrit	0.27	0.14 - 0.46 %	

WBC	23.59	5.05 - 16.76 K/μL	H 
% Neutrophils	* 85.9	%	
% Lymphocytes	* 7.7	%	
% Monocytes	* 3.4	%	
% Eosinophils	3.0	%	
% Basophils	0.0	%	
Neutrophils	* 20.26	2.95 - 11.64 K/μL	H 
Bands	* Suspected		
Lymphocytes	* 1.81	1.05 - 5.1 K/ μ L	
Monocytes	* 0.81	0.16 - 1.12 K/ μ L	
Eosinophils	0.7	0.06 - 1.23 K/ μ L	
Basophils	0.01	0 - 0.1 K/ μ L	



- URBC
- EOS
- LYM
- NEU
- BASO
- MONO



RESULT

REFERENCE VALUE

	RESULT	REFERENCE VALUE	
Glucose	93	74 - 143 mg/dL	
Creatinine	0.7	0.5 - 1.8 mg/dL	
BUN	9	7 - 27 mg/dL	
BUN: Creatinine Ratio	13		
Total Protein	6.7	5.2 - 8.2 g/dL	
Albumin	2.2	2.3 - 4.0 g/dL	L
Globulin	4.4	2.5 - 4.5 g/dL	
Albumin: Globulin Ratio	0.5		
ALT	52	10 - 125 U/L	
ALP	102	23 - 212 U/L	

IDEXX SNAP 4DX Plus serology

Heartworm
Antigen

Negative

Ehrlichia canis /
ewingii

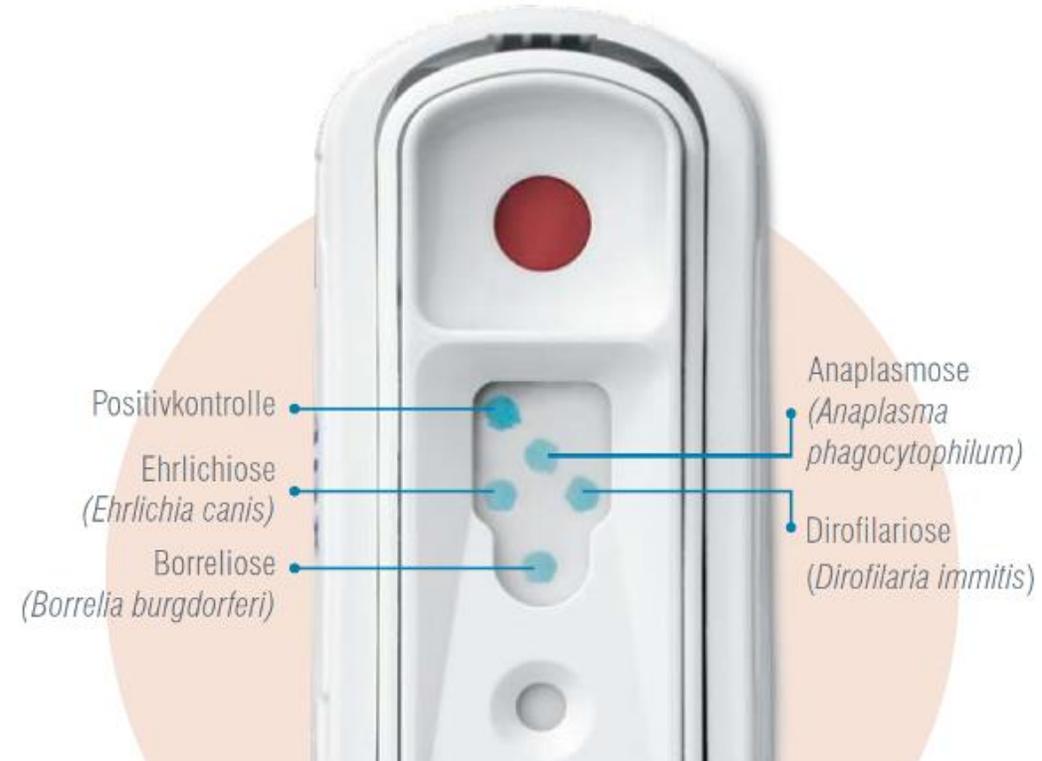
Negative

Lyme (Borrelia
burgdorferi)

Negative

Anaplasma
phagocytophilum
/ platys

Negative





RESULT

SNAP cPL

Normal

Urine Creatinine

24

mg/dL

Urine Protein

54

mg/dL

**Urine Protein:
Creatinine Ratio**

2.24

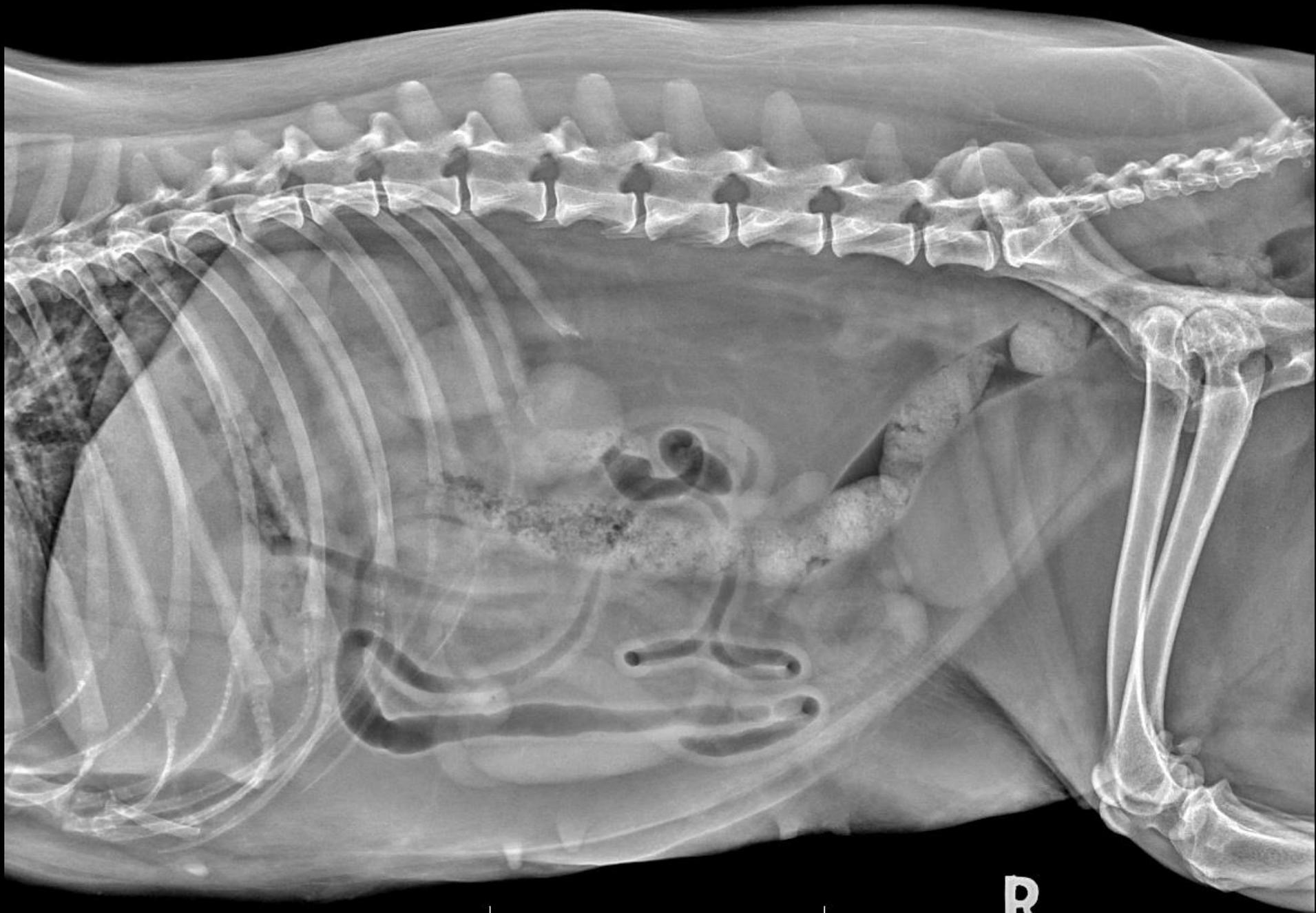
**leu (+/-), nit (-), uro (-), pro (+), pH 8.5-9, blo (-), ket (-), bil (-), glu (-),
S.G 1.012**







age : 6 Years
male



R



雙側肘、腕、膝關節

關節囊液

2個關節以上



有核細胞數增加



非退行性嗜中性球為主



細菌培養陰性



尿液培養

E. Coli,

Pseudomonas aeruginosa

壁蝨套組 PCR

全陰性

泌尿道感染 反應性
特發性 非糜爛性
多發性關節炎

CONFIRMED



治療

疼痛控制

造成免疫反應的根本疾病

免疫控制/抑制

IMPA治療監控

重複關節液檢查

CRP

每3-4週複診，確定關節無發炎

免疫抑制藥物減量25-30%

CRP 監控

2/27 膀胱炎

4/03 尿液培養無生長

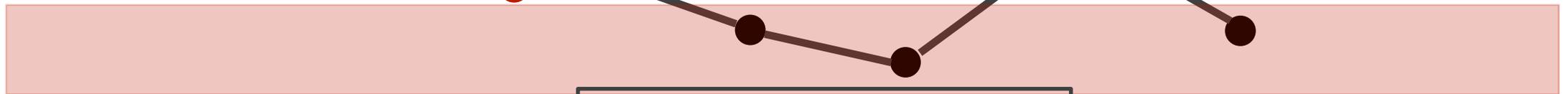
Prednisolone
0.3 mg/kg BID

5/04 膀胱炎 復發

6/11
尿液無細菌生長

9/11
Pred 0.15 mg/kg BID
關節腫痛
UPC 0.25
No growth
恢復劑量

每個月降低Pred 25%



Feb 18

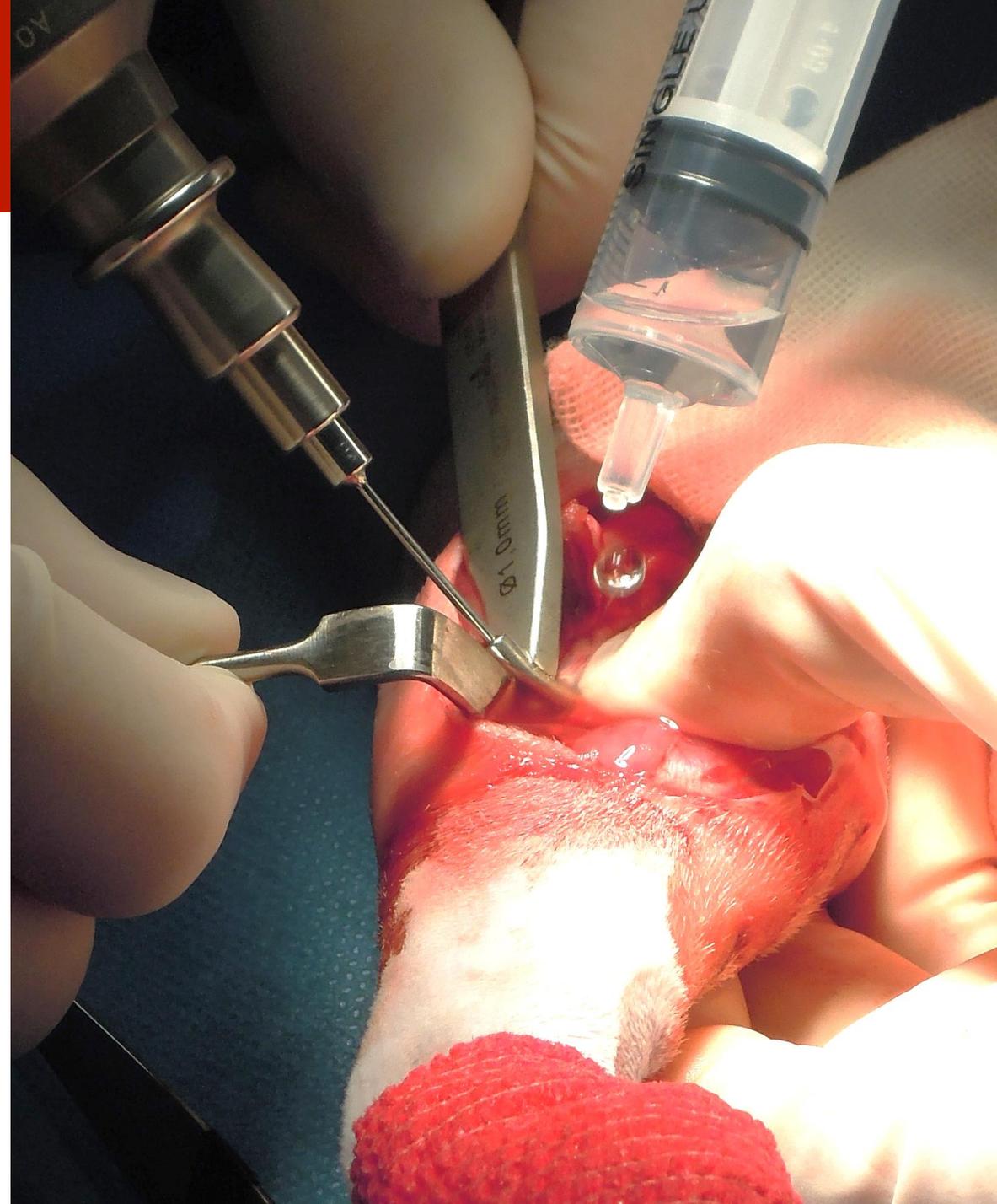
May 18

Sep 18

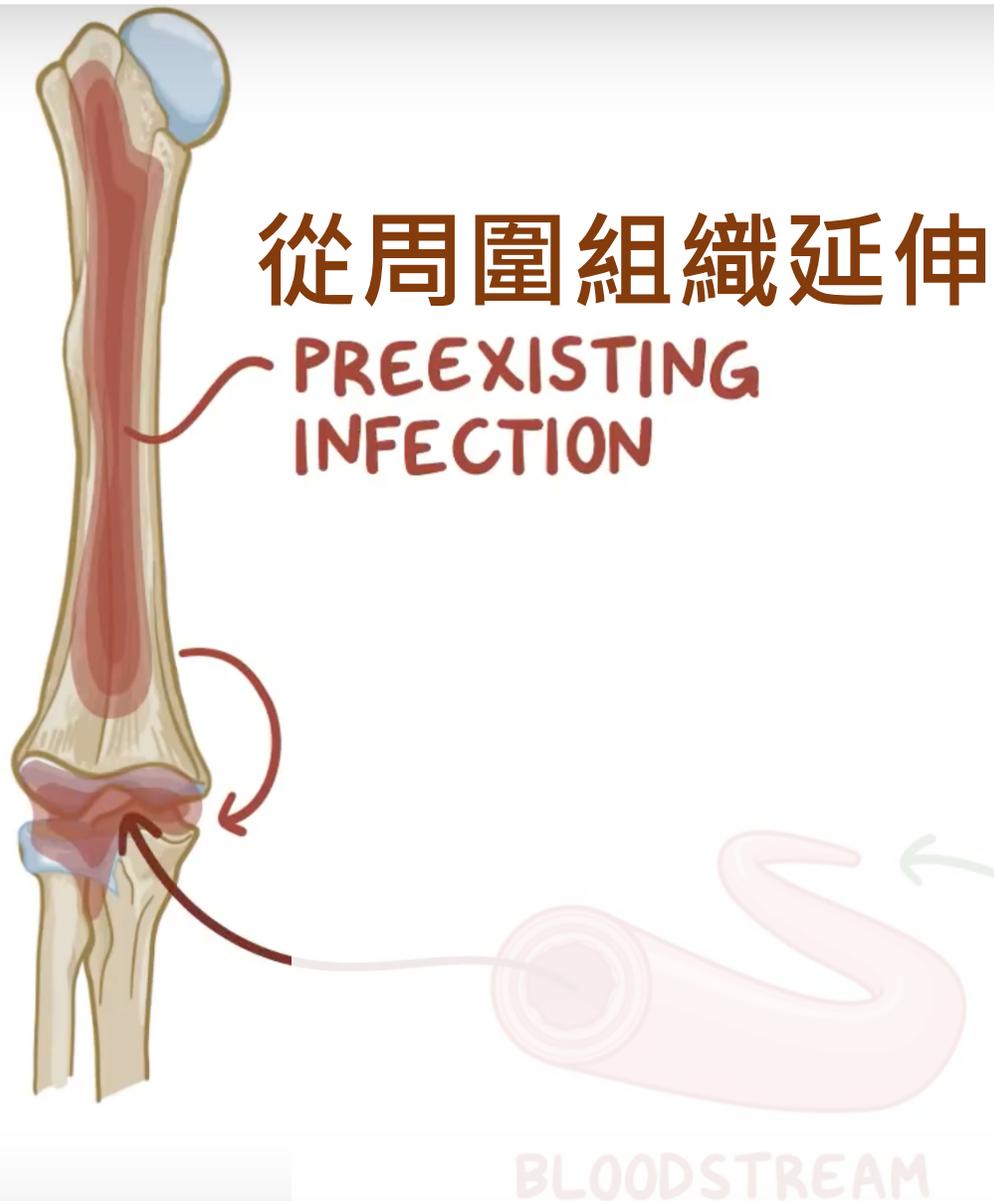
Dec 18

感染性關節炎

穿刺（手術或外傷）

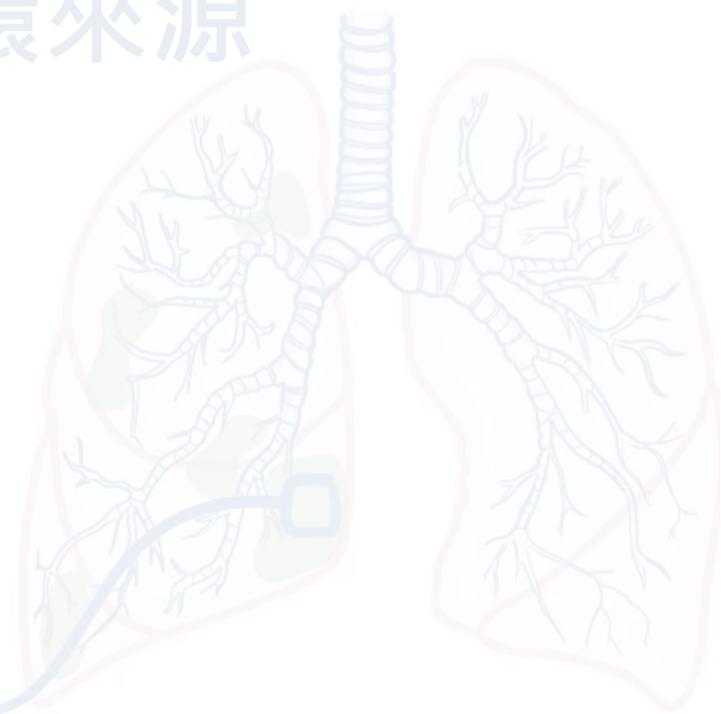


感染性關節炎



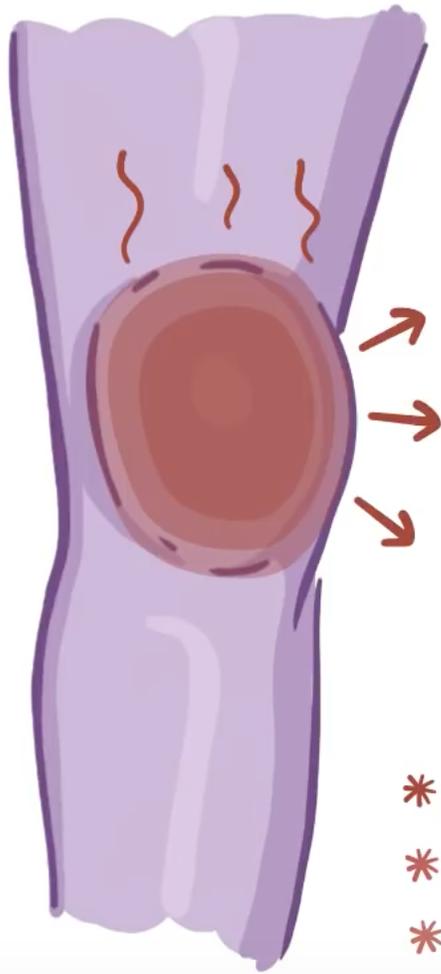
HEMATOGENOUS SPREAD
血液循環來源

BACTERIA



<https://www.youtube.com/watch?v=498Px-BBdOo>

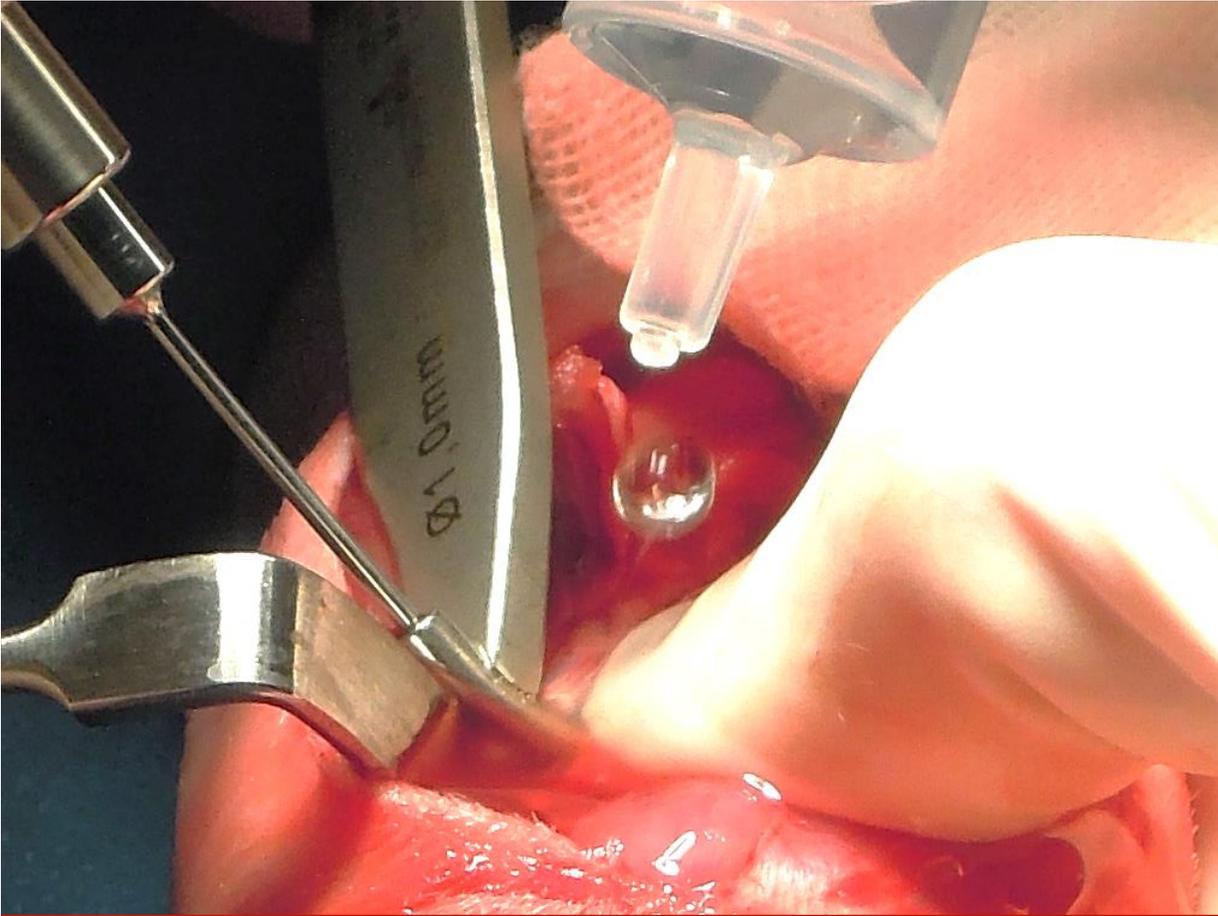
INFLAMMATORY RESPONSE



- * RED
- * SWOLLEN
- * WARM



感染性關節炎 危險因子



關節手術術後感染



原本關節疾病（骨關節炎）

感染性關節炎

急性，單腳跛行

單一關節腫脹，熱，痛

局部淋巴結腫大

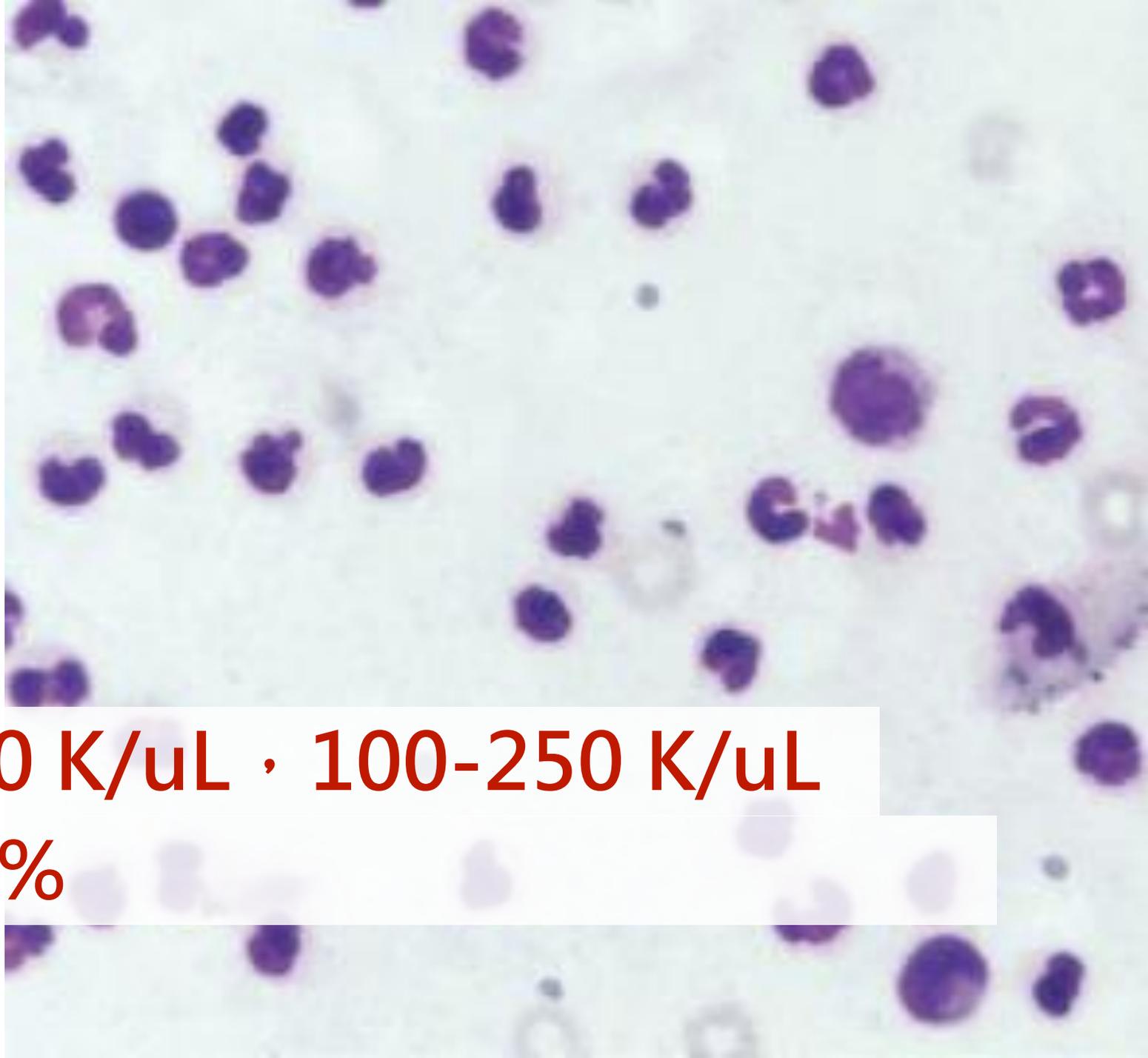


關節囊液分析

關節液增加，混濁

有核細胞數增加 $> 50 \text{ K/uL}$ ， $100-250 \text{ K/uL}$

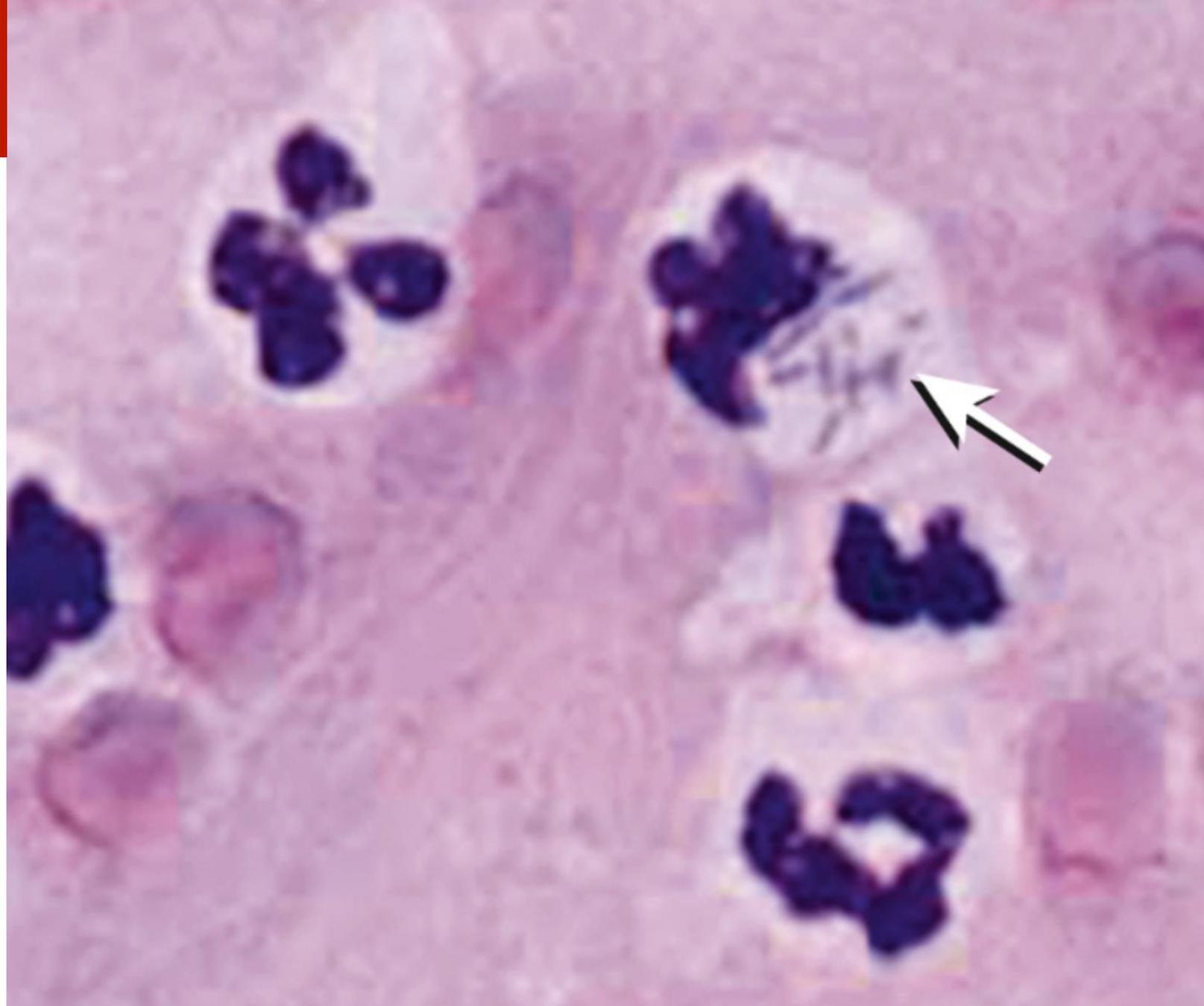
退行性嗜中性球, 98%



關節囊液分析

細胞吞噬細菌

Intracellular bacteria



感染性關節炎

關節囊液細菌培養陽性率低

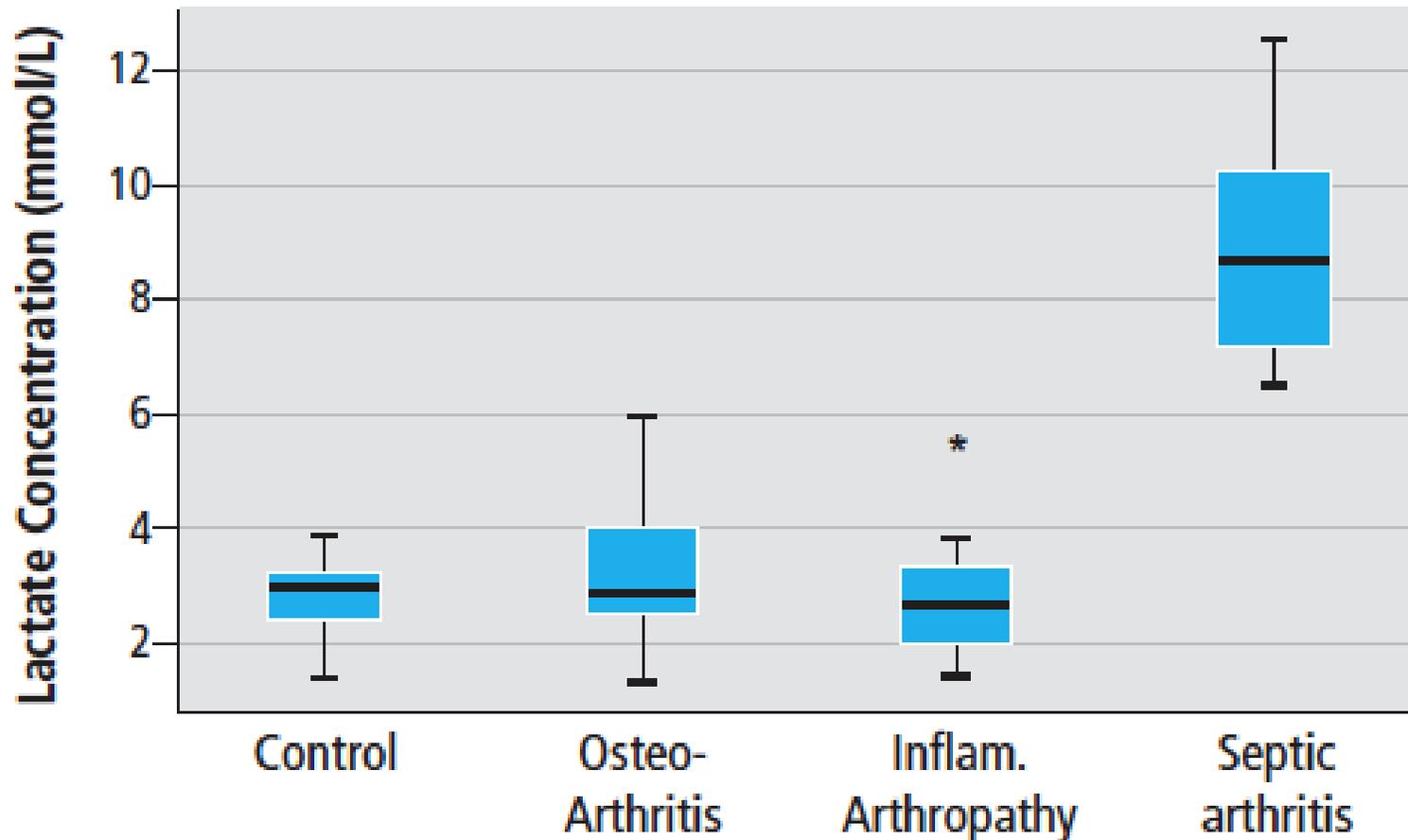
血液培養基液

關節囊組織細菌培養

Analysis of lactate concentrations in canine synovial fluid

Vet Comp Orthop Traumatol 5/2015

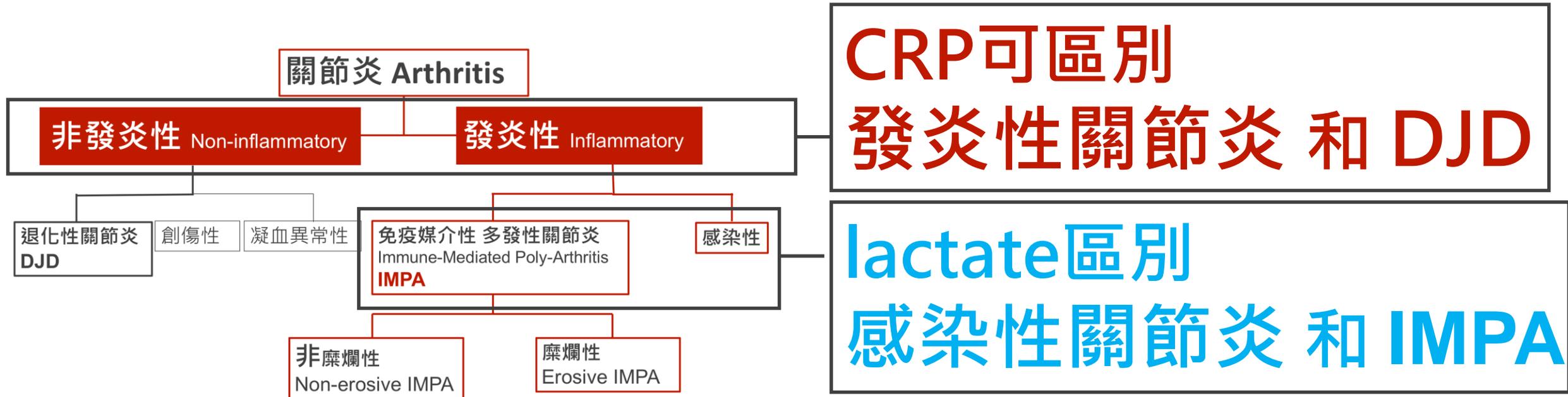
低lactate (<6.5 mmol/L可排除感染性關節炎)



Analysis of lactate concentrations in canine synovial fluid

Vet Comp Orthop Traumatol 5/2015

低lactate (<6.5 mmol/L可排除感染性關節炎)

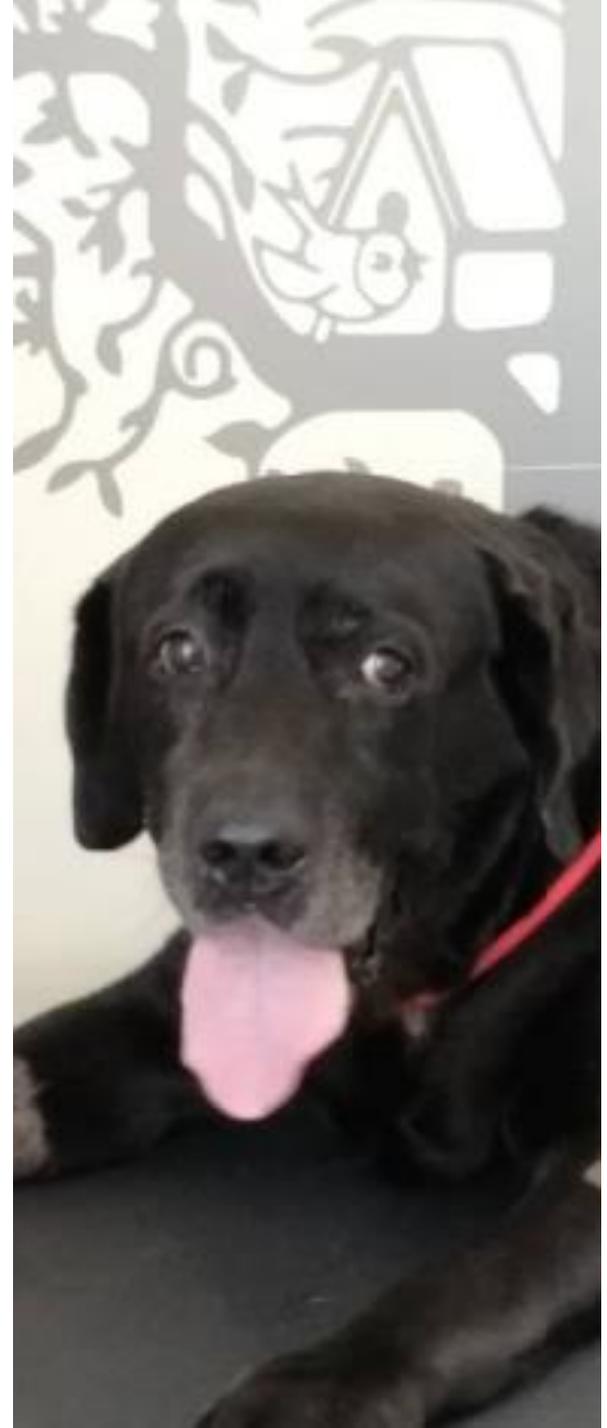


12y, MI, LR, 39kg

BT 39.5, HR 108, RR 64

急性左前肢腫脹，無法站立

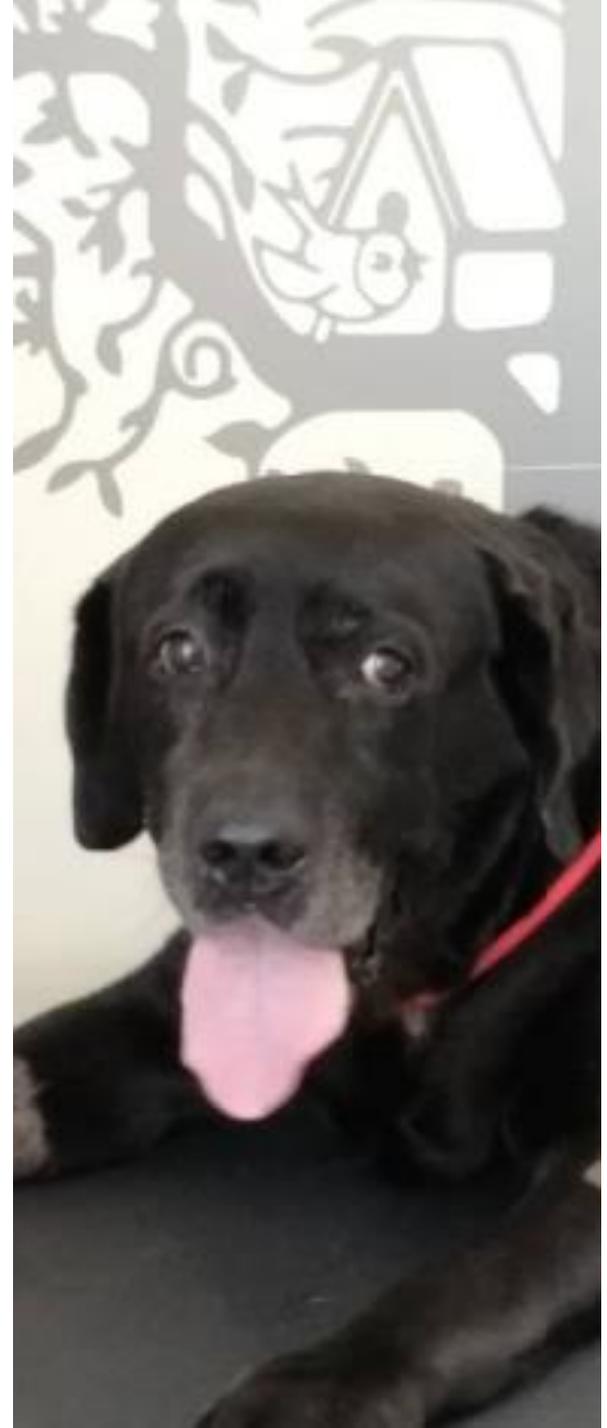
慢性腕關節問題

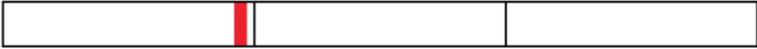
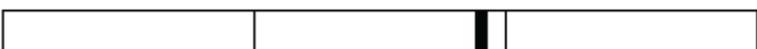


MM pink, tacky, CRT 1.5s

胸腔聽診、腹腔觸診 無異常

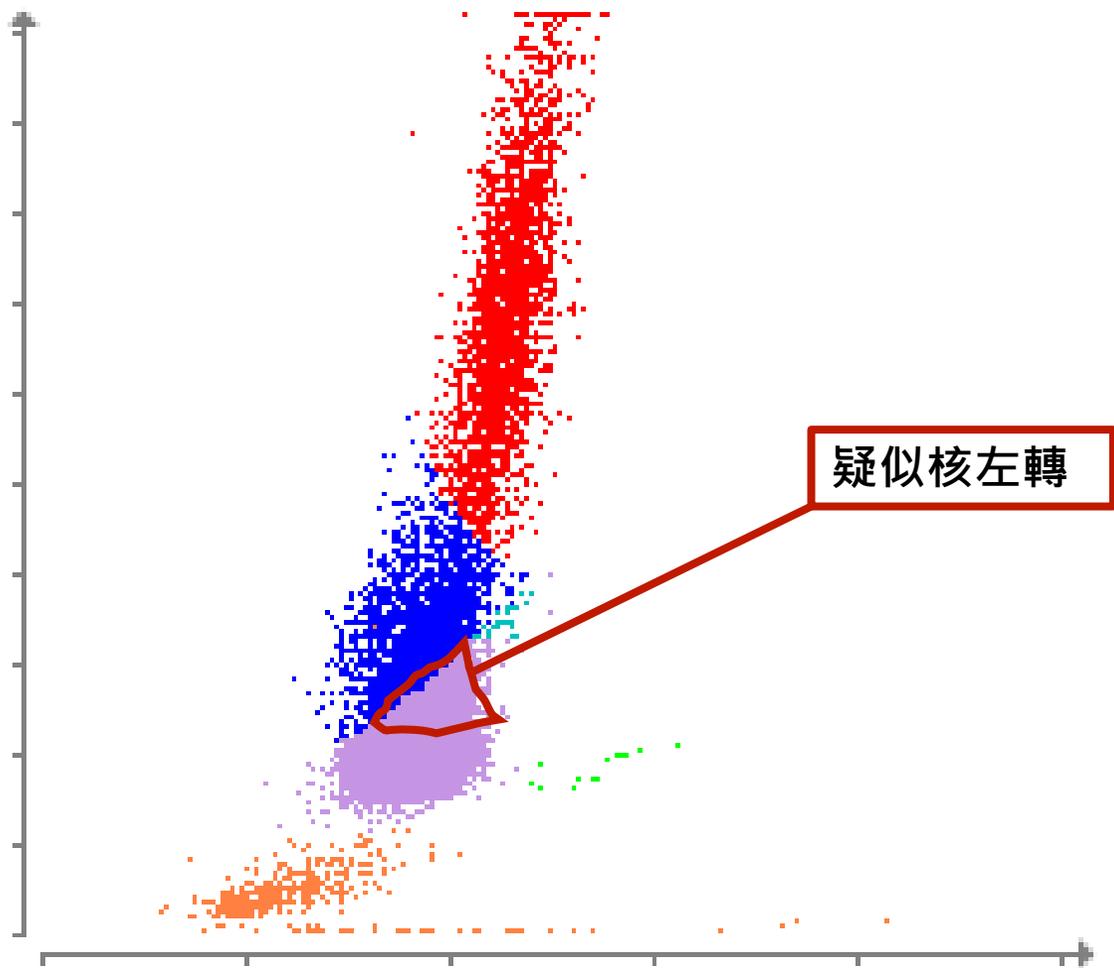
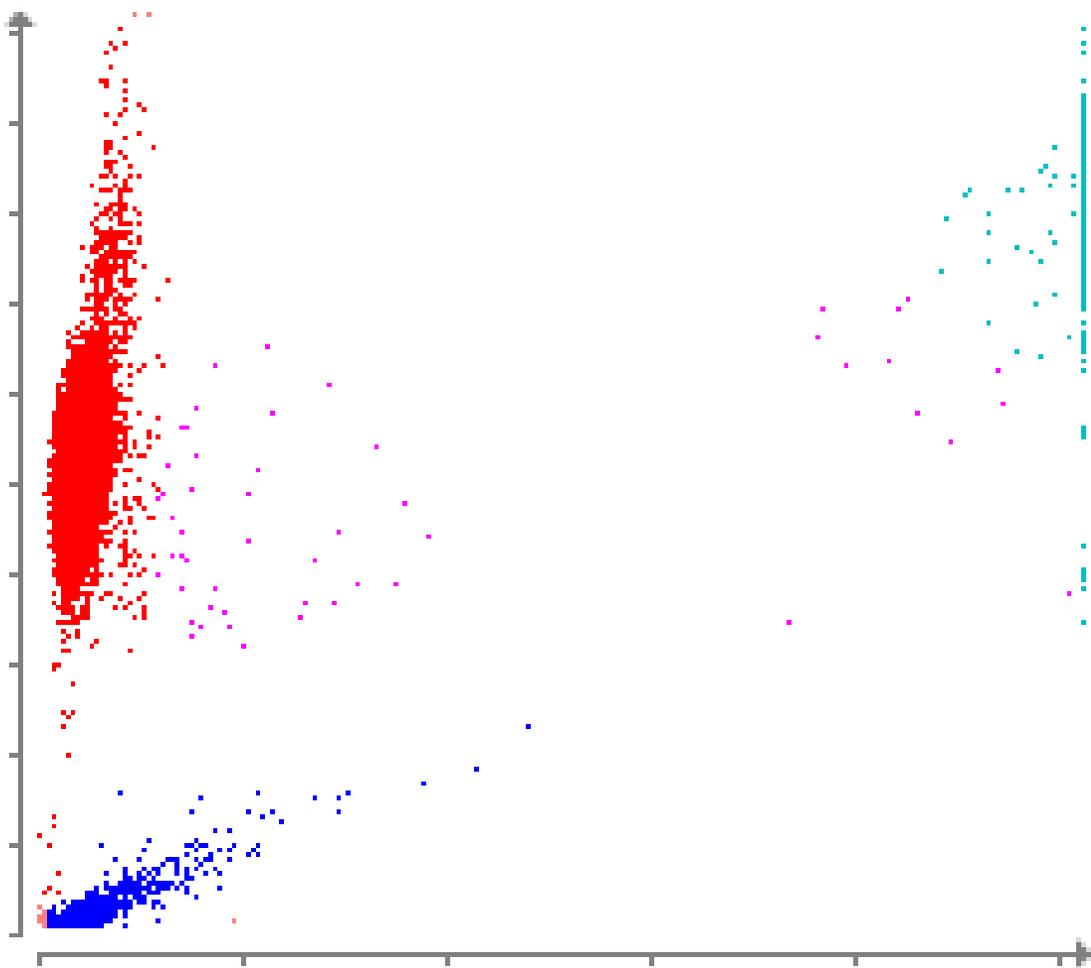
反射：右前減弱、左前無反應



TEST	RESULT	REFERENCE VALUE	
RBC	5.36	5.65 - 8.87 M/μL	L 
Hematocrit	31.7	37.3 - 61.7 %	L 
Hemoglobin	11.8	13.1 - 20.5 g/dL	L 
MCV	59.1	61.6 - 73.5 fL	L 
MCH	22.0	21.2 - 25.9 pg	
MCHC	37.2	32.0 - 37.9 g/dL	
RDW	15.6	13.6 - 21.7 %	
% Reticulocyte	0.2	%	
Reticulocytes	12.9	10 - 110 K/ μ L	

WBC	38.94	5.05 - 16.76 K/μL	H 
% Neutrophils	* 73.8	%	
% Lymphocytes	* 16.1	%	
% Monocytes	* 9.9	%	
% Eosinophils	0.1	%	
% Basophils	0.1	%	
Neutrophils	* 28.78	2.95 - 11.64 K/μL	H 
Bands	* Suspected		
Lymphocytes	* 6.26	1.05 - 5.1 K/μL	H 
Monocytes	* 3.84	0.16 - 1.12 K/μL	H 
Eosinophils	0.02	0.06 - 1.23 K/μL	L 
Basophils	0.04	0 - 0.1 K/ μ L	

Platelets	205	148 - 484 K/ μ L	
PDW	10.3	9.1 - 19.4 fL	
MPV	8.6	8.7 - 13.2 fL	L 
Plateletcrit	0.18	0.14 - 0.46 %	



IDEXX SNAP 4DX Plus serology

Heartworm
Antigen

Negative

Ehrlichia canis /
ewingii

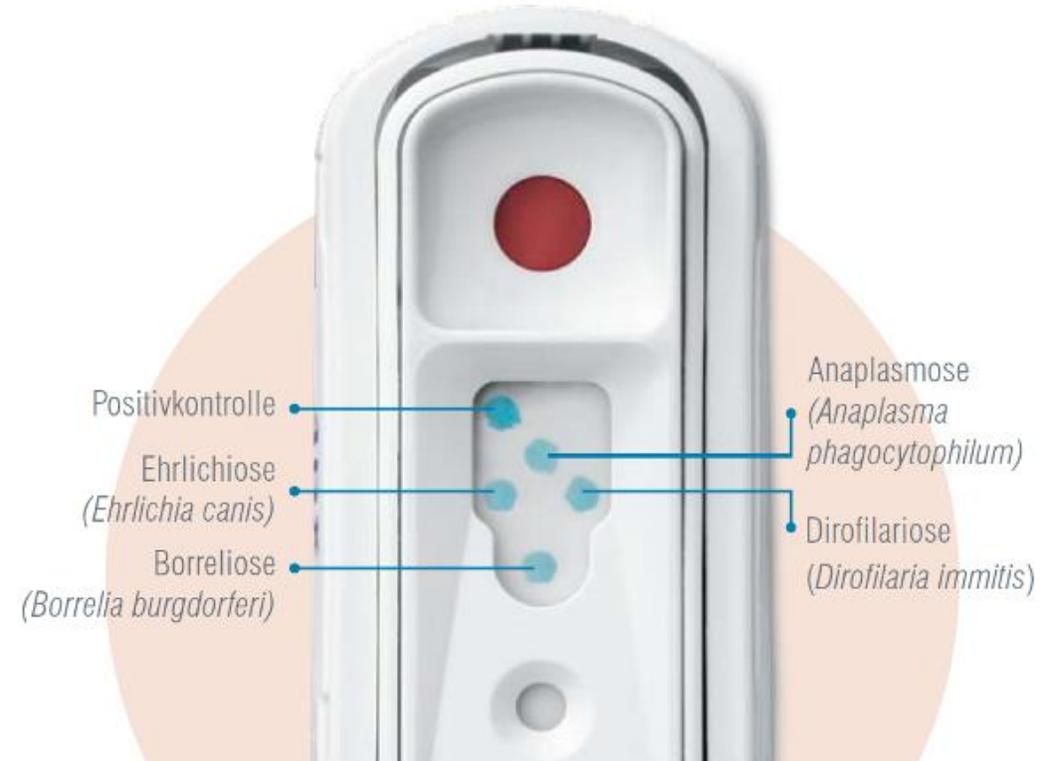
Negative

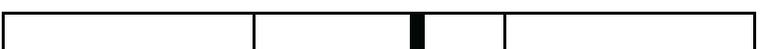
Lyme (Borrelia
burgdorferi)

Negative

Anaplasma
phagocytophilum
/ platys

Negative



Glucose	103	70 - 143 mg/dL	
Creatinine	0.8	0.5 - 1.8 mg/dL	
BUN	9	7 - 27 mg/dL	
BUN: Creatinine Ratio	10		
Phosphorus	5.1	2.5 - 6.8 mg/dL	
Calcium	9.5	7.9 - 12.0 mg/dL	
Sodium	154	144 - 160 mmol/L	
Potassium	3.5	3.5 - 5.8 mmol/L	
Na: K Ratio	44		
Chloride	116	109 - 122 mmol/L	

Total Protein	7.9	5.2 - 8.2 g/dL		
Albumin	2.8	2.2 - 3.9 g/dL		
Globulin	5.1	2.5 - 4.5 g/dL	H	
Albumin: Globulin Ratio	0.6			
ALT	47	10 - 125 U/L		
ALP	336	23 - 212 U/L	H	
GGT	0	0 - 11 U/L		
Bilirubin - Total	0.4	0.0 - 0.9 mg/dL		
Cholesterol	274	110 - 320 mg/dL		

C-Reactive Protein (CRP)

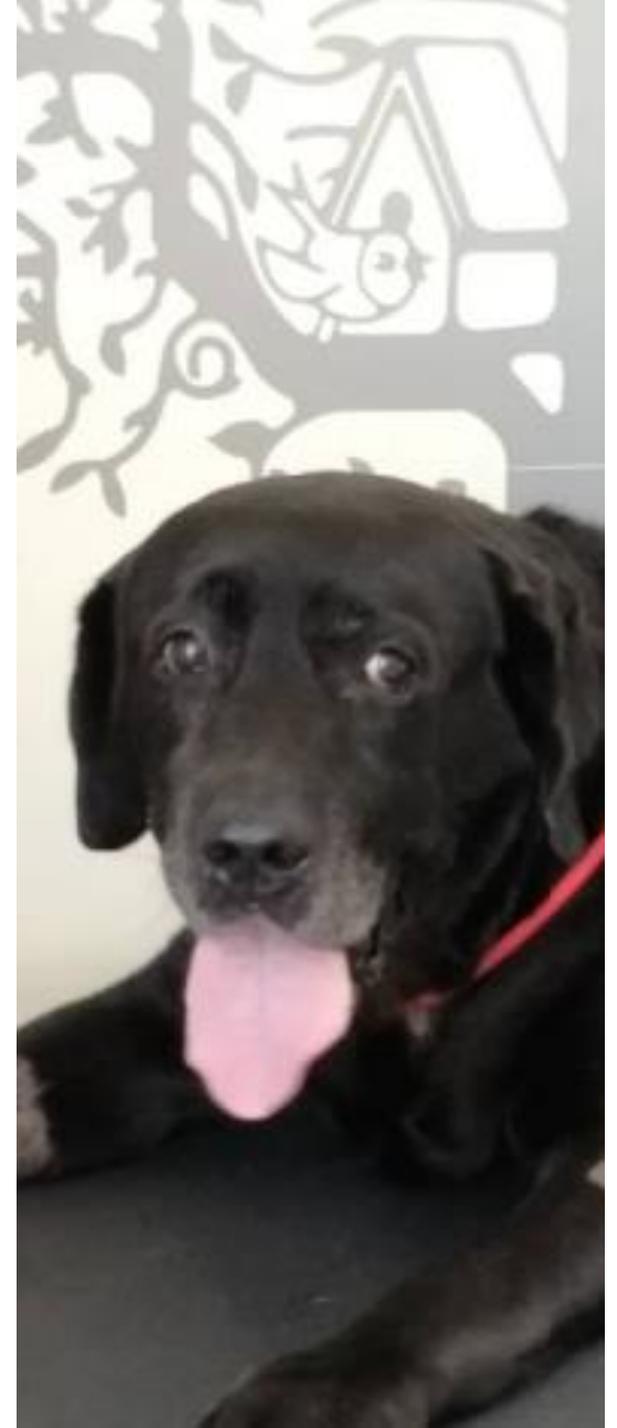
^f > 10.0

0.0 - 1.0 mg/dL



急性左前肢腫脹，無法站立
急性發炎反應

確認發炎的來源





左肘 關節液分析

Pathology

7/10/18

1:11 PM



檢體種類: 滑液

有核細胞數明顯增加

Nucleated Cell
Count

133.68 (<2)

M/ μ L

K/ μ L

Granulocytes

122.80

K/ μ L

% Granulocytes

91.9 (0-6)

%

顆粒球為主

10.88

K/ μ L

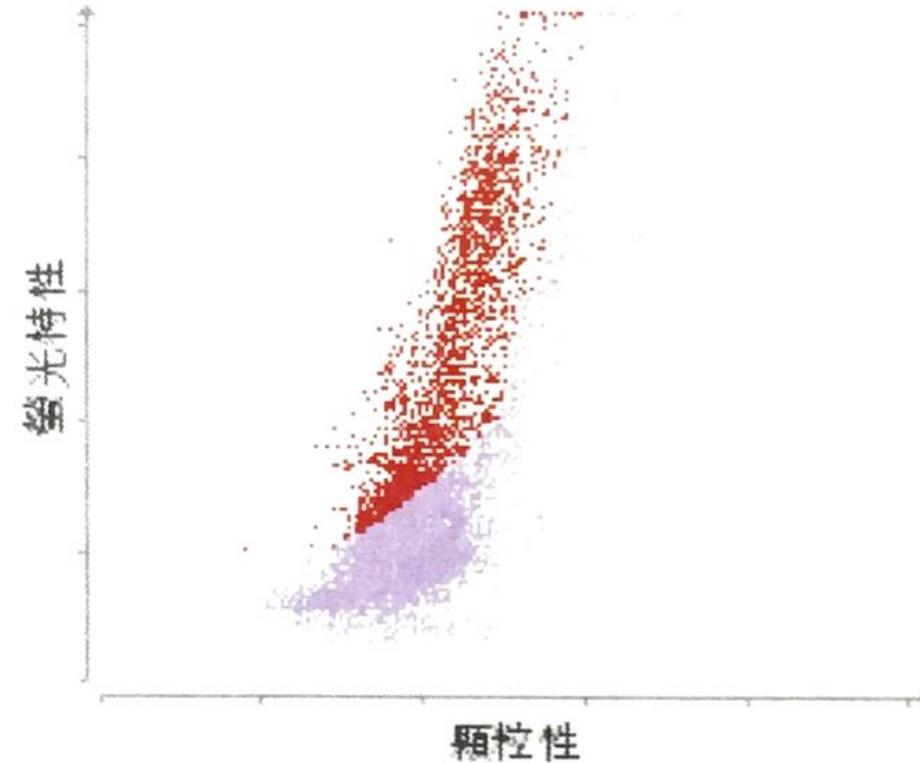
% Agranulocytes

8.1 (94-100)

%

檢體種類: 滑液

白血球測試



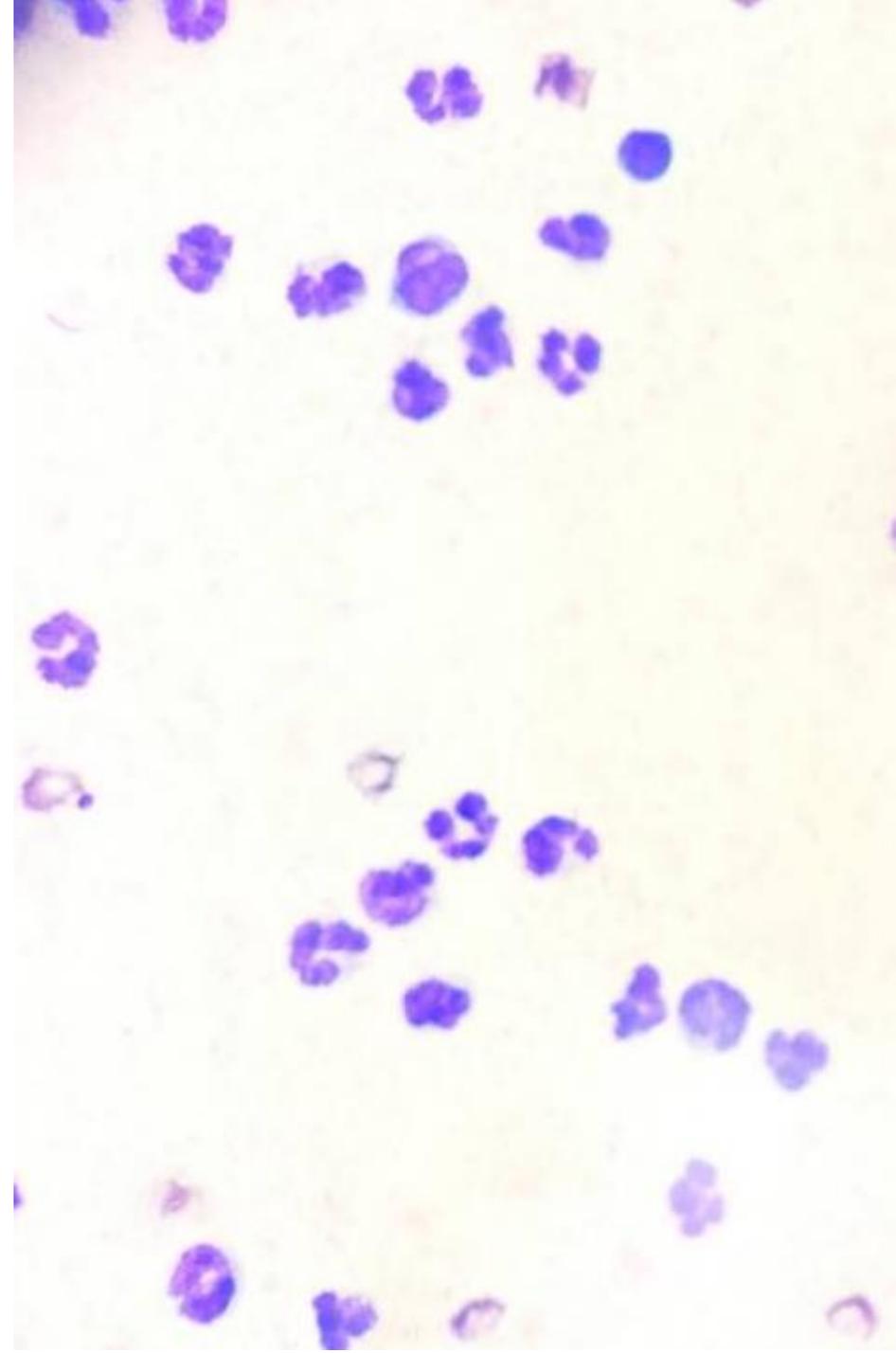
- 顆粒性白血球(GRANS)
- 非顆粒白血球(AGRANS)

左肘 關節液分析

有核細胞數 ↑↑

退行性嗜中性球為主

細菌培養

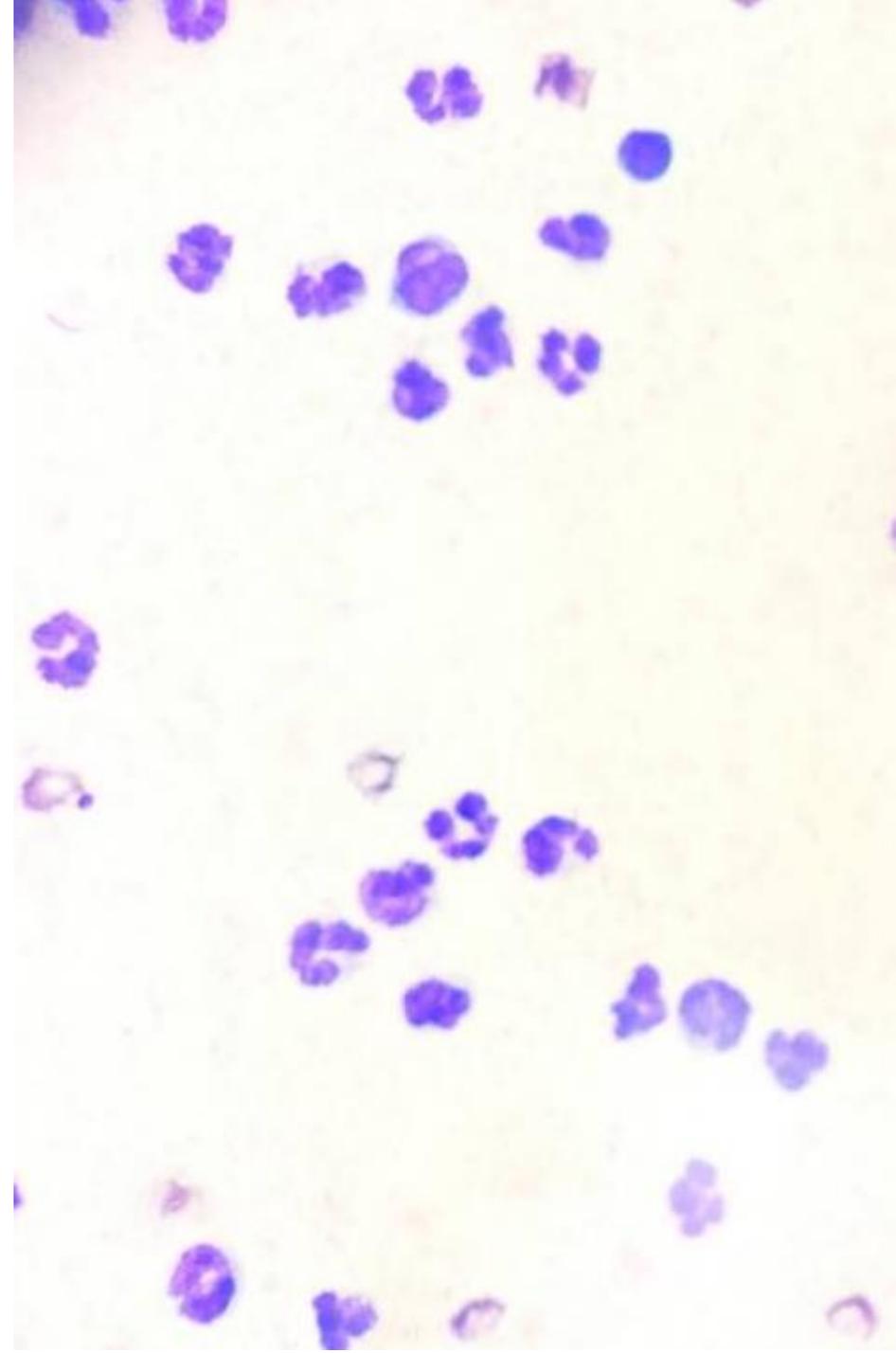


左肘關節感染性關節炎

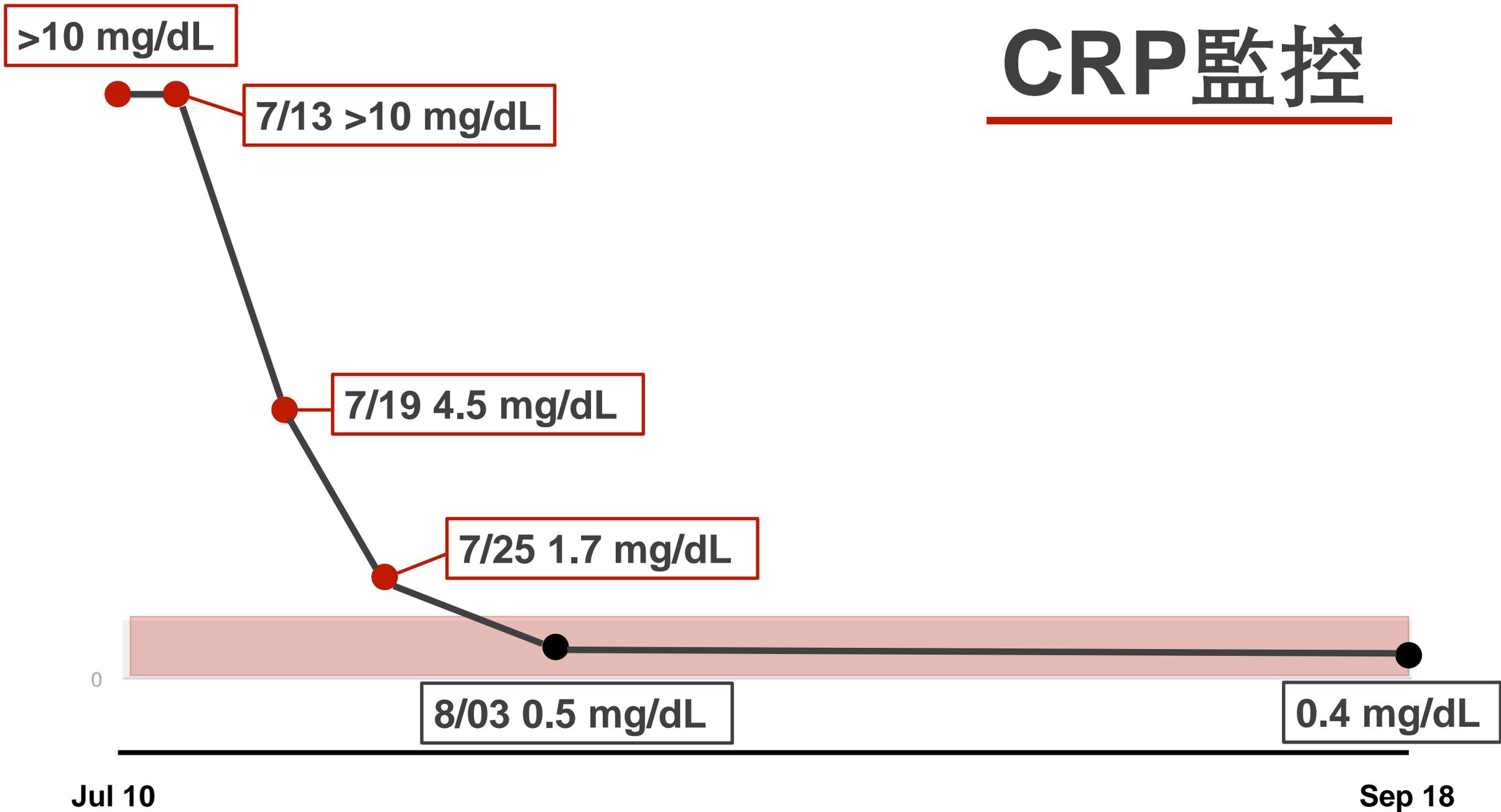
Streptococcus canis

Augumentin

Carprofen, gabapentin



CRP 監控



Pathology

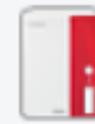
7/10/18

1:11 PM



9/18/18

1:59 PM



RBC

M/ μ L

0.63

0.05

Nucleated Cell
Count

K/ μ L

133.68

1.39

有核細胞數
正常

Granulocytes

K/ μ L

122.80

0.26

% Granulocytes

%

91.9

18.7

Agranulocytes

K/ μ L

10.88

1.13

% Agranulocytes

%

8.1

81.3

單核球為主

檢體種類：滑液

檢體種類：滑液

檢體種類: 滑液

7/10/18

1:11 PM



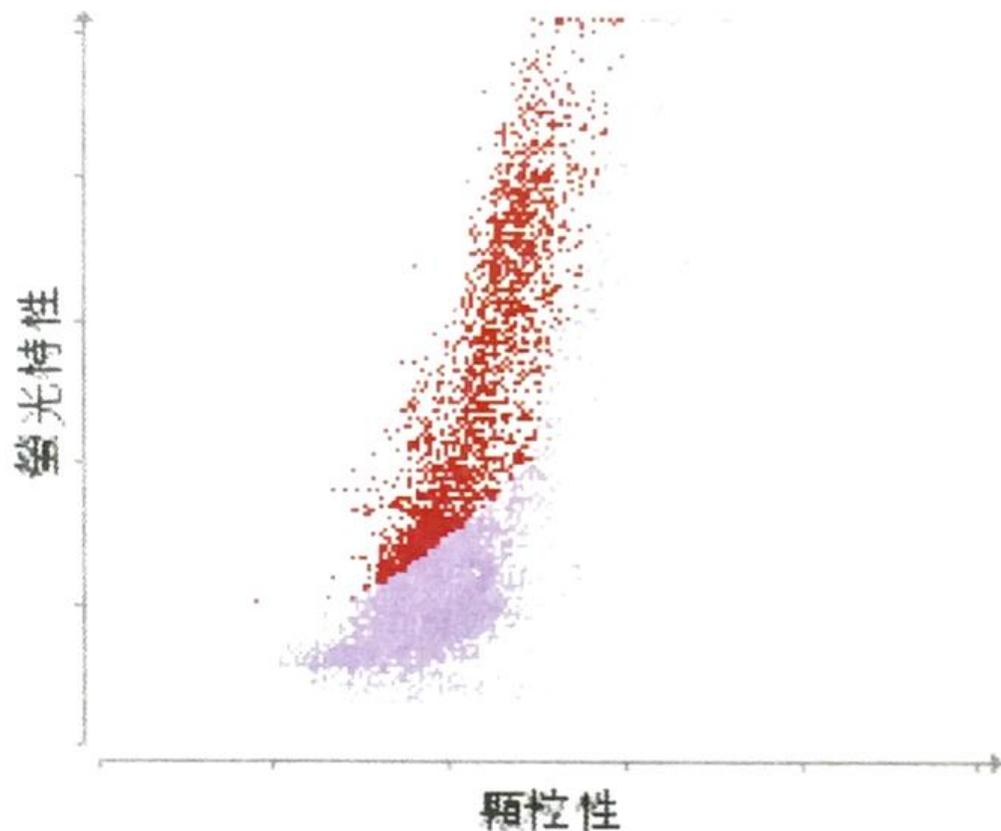
白血球測試

9/18/18

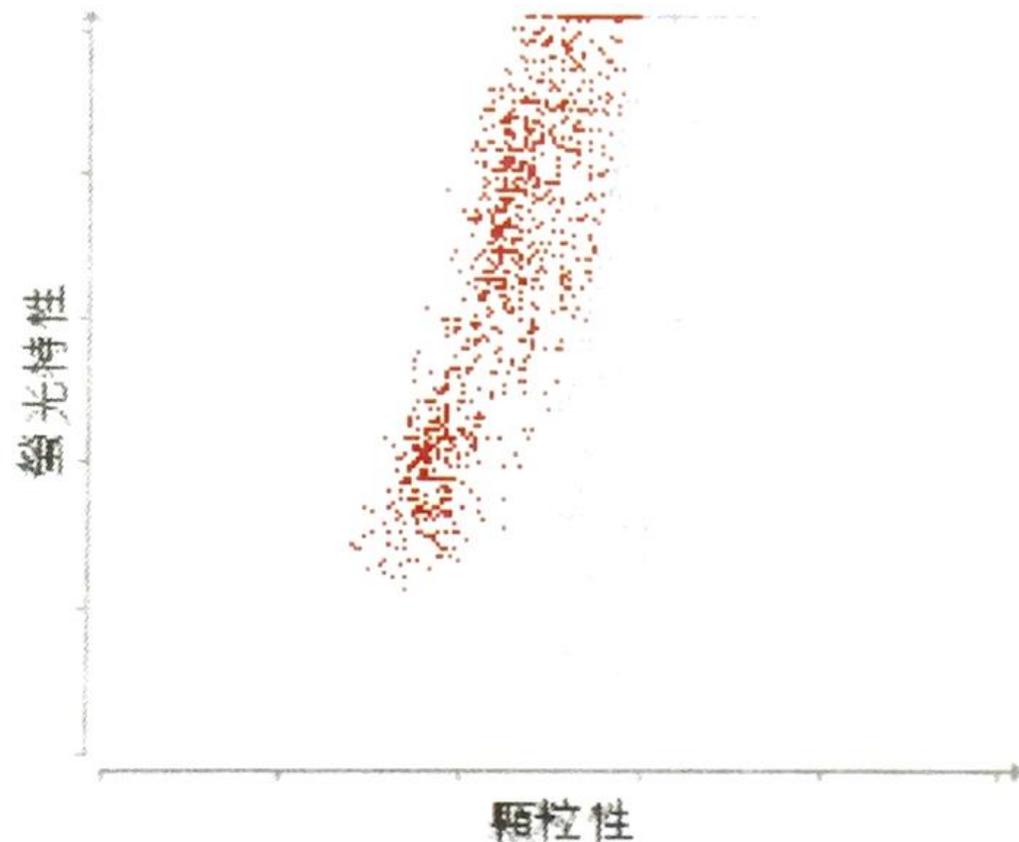
1:59 PM



白血球測試

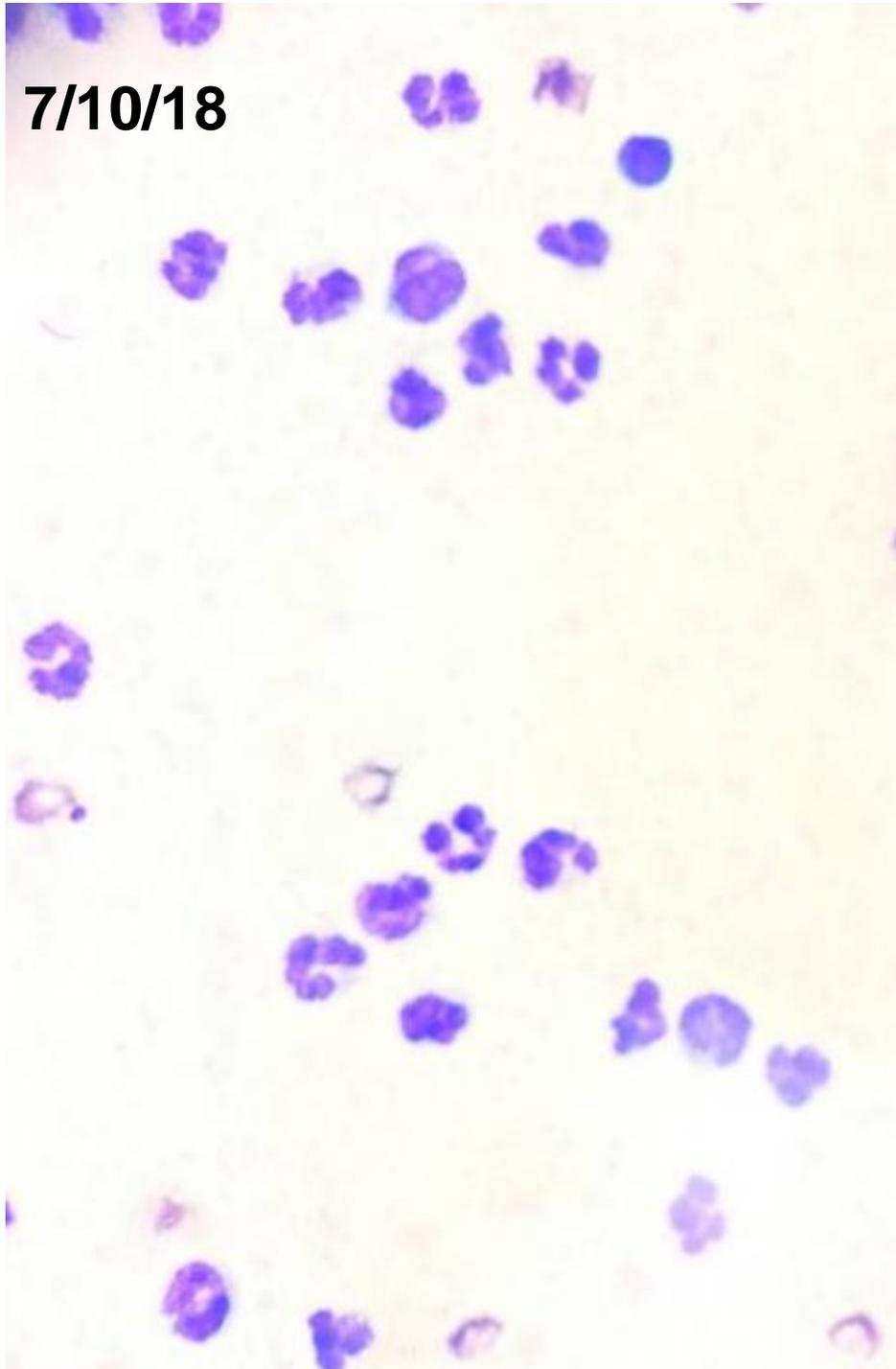


- 顆粒性白血球(GRANS)
- 非顆粒白血球(AGRANS)

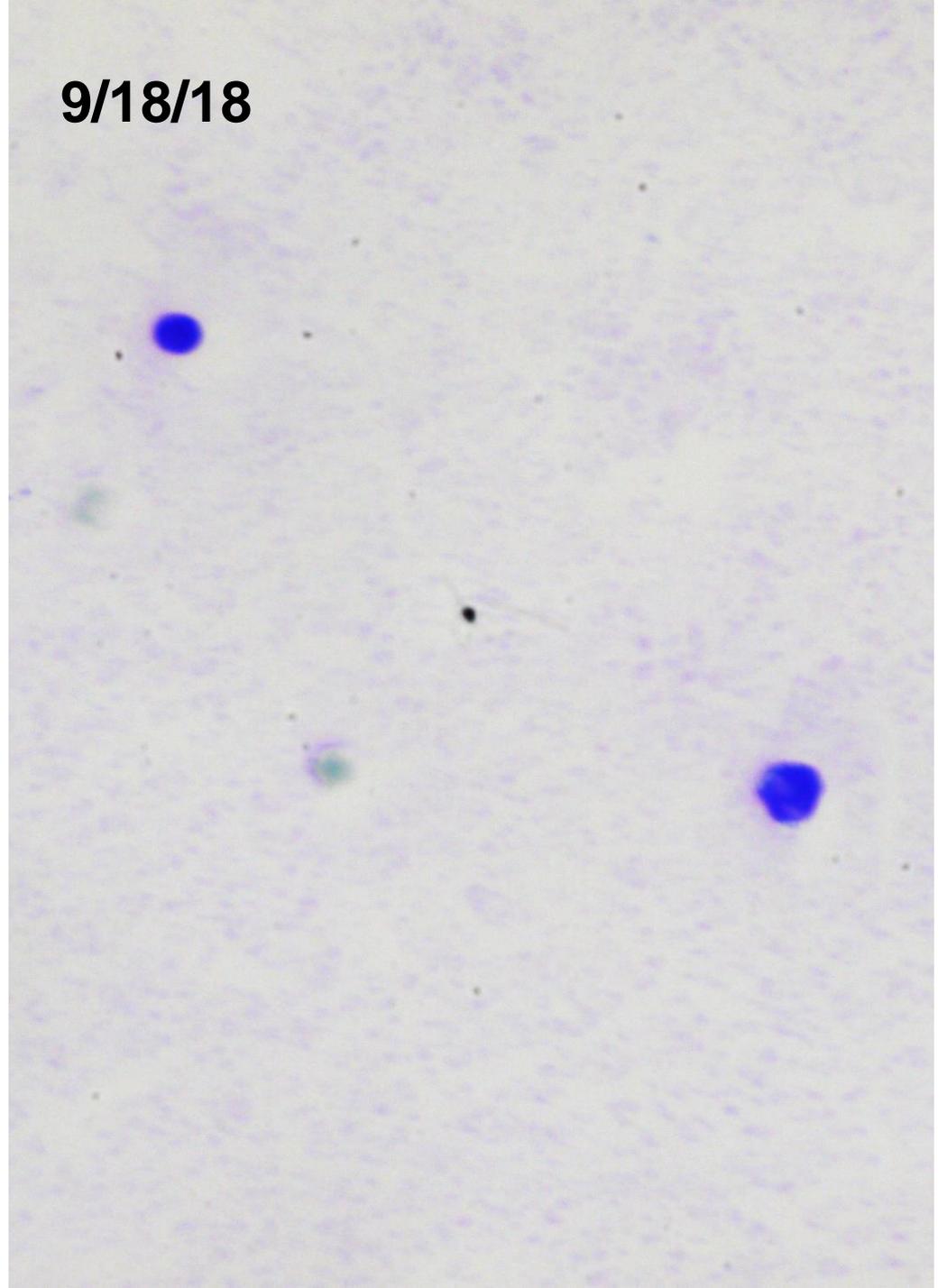


- 顆粒性白血球(GRANS)
- 非顆粒白血球(AGRANS)

7/10/18



9/18/18



左前肢肘關節液

曾經使用/ 使用中/ 採樣後將使用之抗生素：

augmentin

No growth after 2 days

7/10/18



9/18/18



7/1/18



9/18/18



“For every diagnosis missed for not knowing, ten are missed for not looking”

錯失診斷

通常因為沒有檢查，而非不知道

Sharon Kerwin DVM MS DACVS

Take home message

CRP協助 發炎性關節炎 診斷和治療監控

ProCyte 關節囊液分析好幫手

多發性關節炎 – 區別單純性或反應性

感染性關節炎 – 危險因子(OA, surgery)