



IDEXX

貧血病因的調查與追蹤---網織球的臨床運用分享

張黎文 獸醫師/博士 | 愛德士醫療事務顧問經理 | Nov 4 2020

貧血是一種症狀

貧血是一種因為生理異常導致的現象

不是最終診斷

了解這個現象可以幫助我們找到真正的病因

Case: 豆豆

- 雪納瑞
- 5.5 Kg
- 8月齡
- 雌性
- 三個月前有焦蟲感染，已治癒。
- 早上被車撞到，無明顯外傷。
- 診斷：右大腿骨骨折及右側骨盆骨折。

Case: 豆豆

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx (2020年9月27日 下午3:39)					
RBC	2.33 M/ μ L	5.65 - 8.87	LOW		
HCT	17.3 %	37.3 - 61.7	LOW		
HGB	5.3 g/dL	13.1 - 20.5	LOW		
MCV	74.2 fL	61.6 - 73.5	HIGH		
MCH	22.7 pg	21.2 - 25.9			
MCHC	30.6 g/dL	32.0 - 37.9	LOW		
RDW	-- %	13.6 - 21.7			
%RETIC	* 35.3 %				
RETIC	821.6 K/ μ L	10.0 - 110.0	HIGH		
RETIC-HGB	21.9 pg	22.3 - 29.6	LOW		
WBC	16.88 K/ μ L	5.05 - 16.76	HIGH		
%NEU	78.2 %				
%LYM	16.7 %				
%MONO	4.6 %				
%EOS	0.3 %				
%BASO	0.2 %				
NEU	13.20 K/ μ L	2.95 - 11.64	HIGH		
LYM	2.82 K/ μ L	1.05 - 5.10			
MONO	0.78 K/ μ L	0.16 - 1.12			
EOS	0.05 K/ μ L	0.06 - 1.23	LOW		
BASO	0.03 K/ μ L	0.00 - 0.10			
PLT	472 K/ μ L	148 - 484			
MPV	14.5 fL	8.7 - 13.2	HIGH		
PDW	17.6 fL	9.1 - 19.4			
PCT	0.68 %	0.14 - 0.46	HIGH		

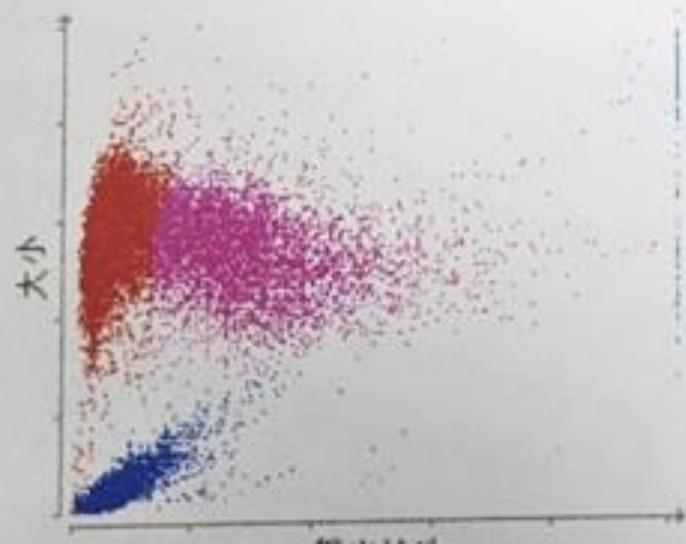
RBC

WBC

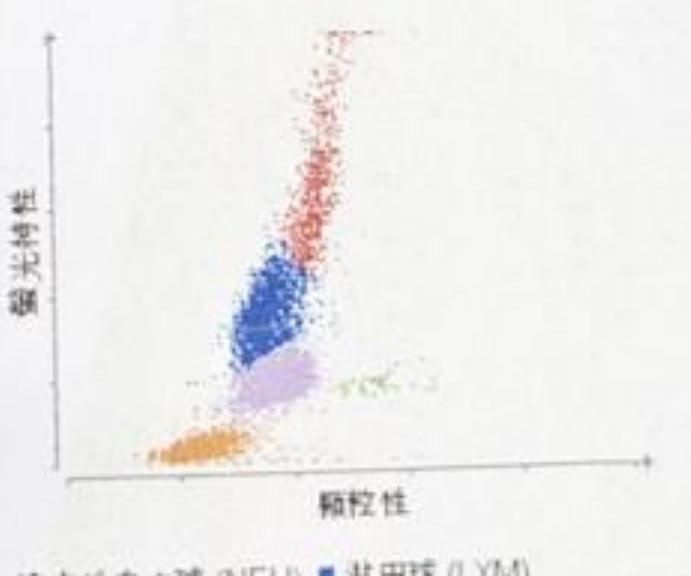
PLT

DEXX

紅血球測試



白血球測試



1.您認為豆豆貧血的原因是什麼？

- a. 先前焦蟲的感染，還在恢復中。
- b. 有不明原因的血球破壞。
- c. 車禍導致的出血。
- d. 這是炎症導致骨髓抑制的結果。
- e. 這是生長年齡犬隻的正常現象。

Case: 豆豆

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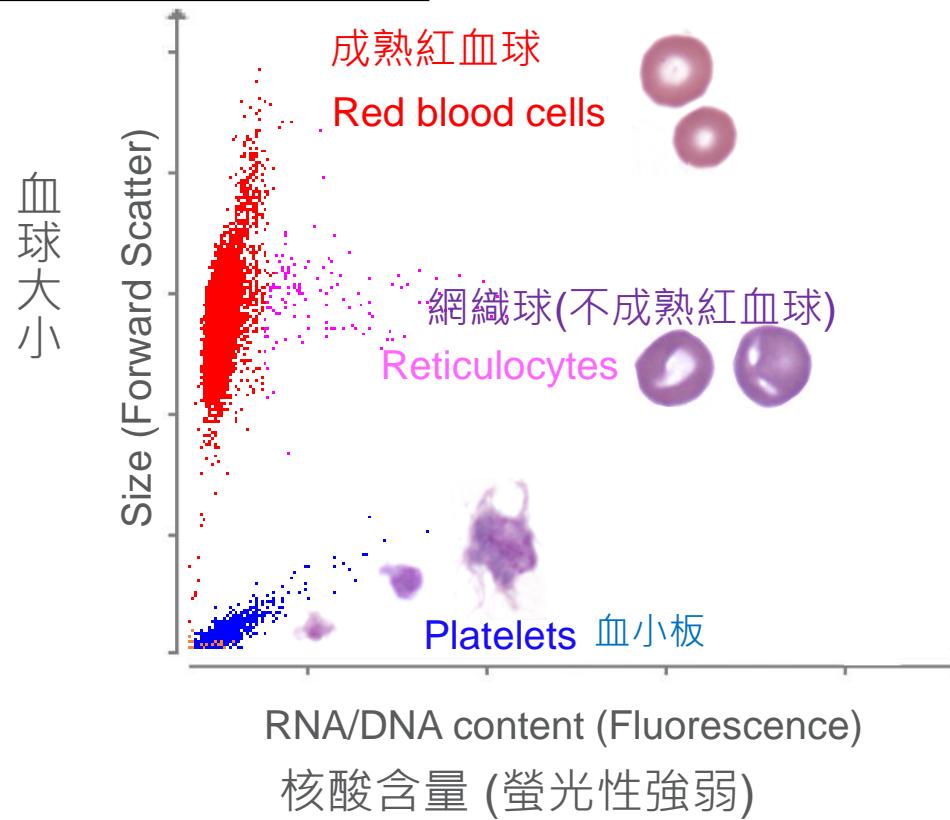
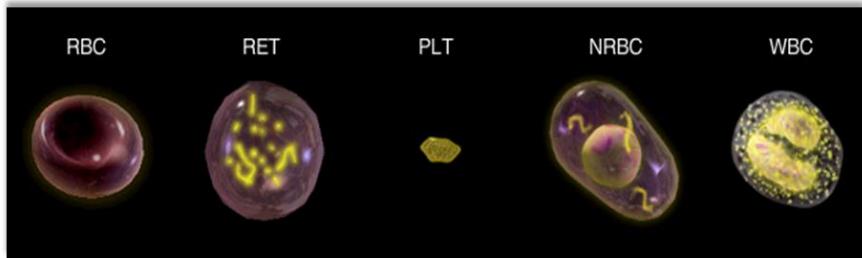
RBC 質量

RBC 品質

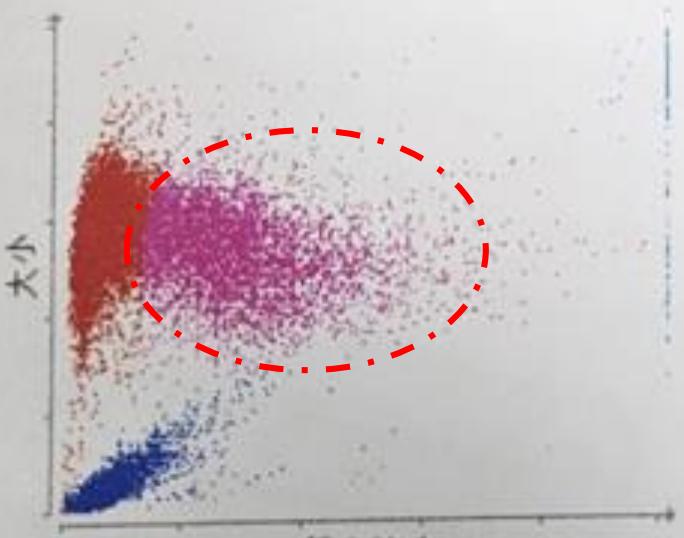
骨髓反應



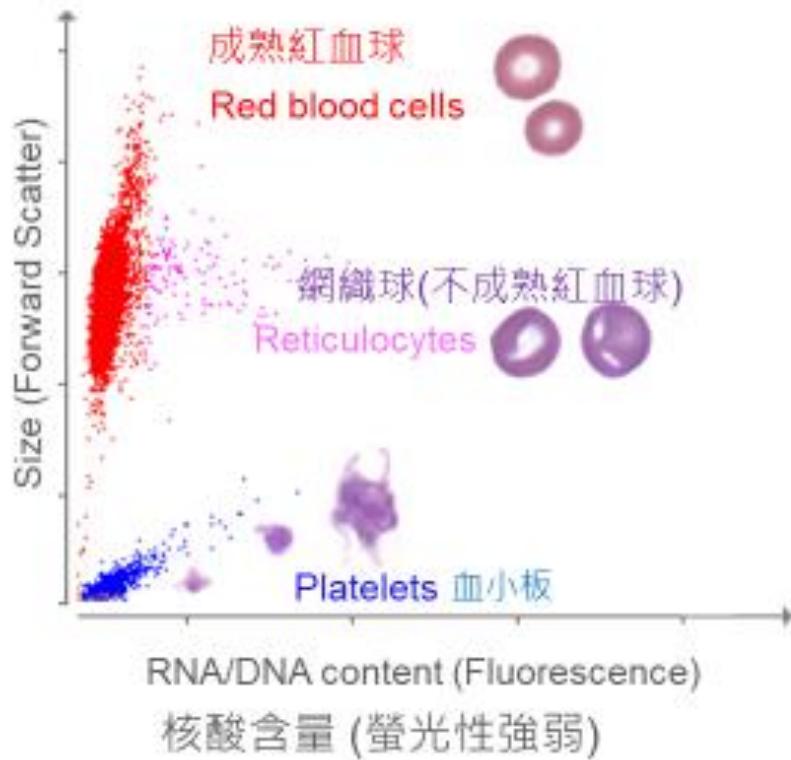
點狀圖下的紅血球 (大數據)



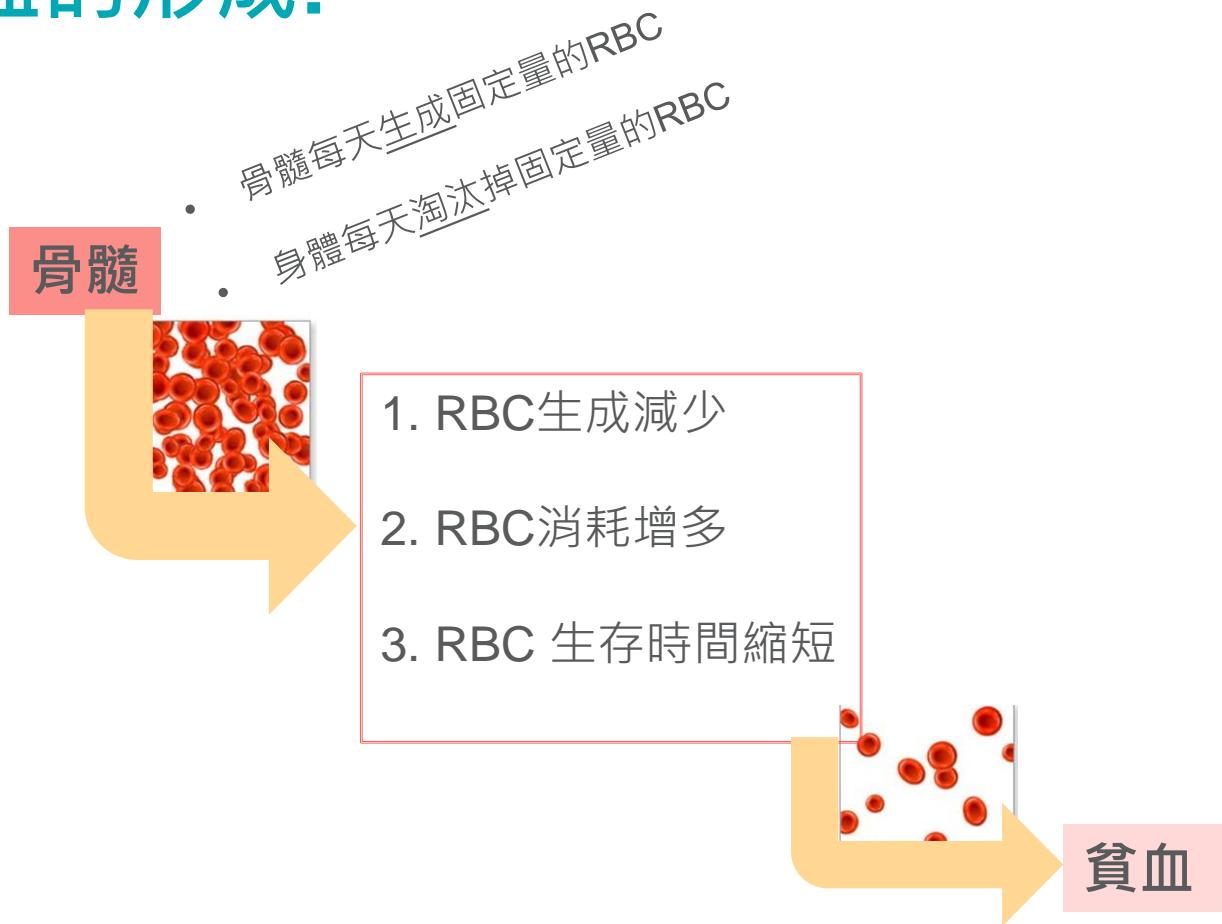
紅血球測試



血球大小



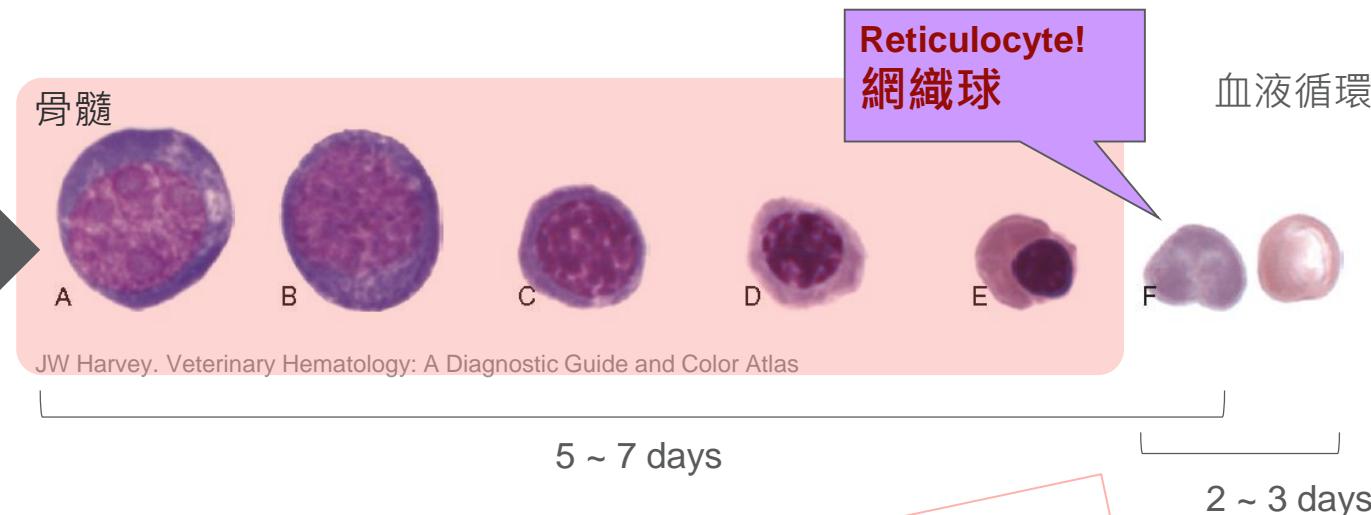
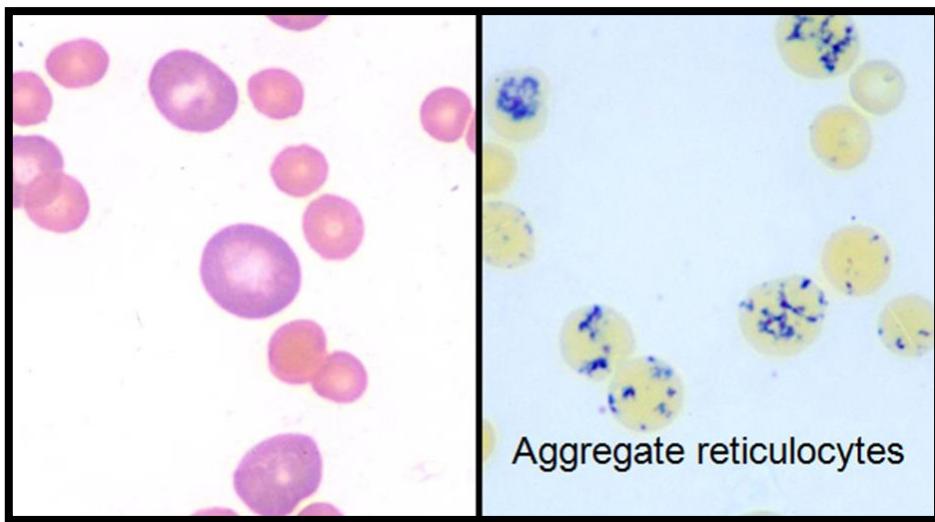
貧血的形成：



2. 您認為網織球升高的原因是什麼？

- a. RBC生成減少 (骨髓抑制或不生成)
- b. RBC消耗增多 (出血、失血)
- c. RBC 生存時間縮短 (溶血、血球破壞、血球生成不良)
- d. 我覺得沒那麼簡單..

網織球的臨床意義



豆豆早上被車撞，
但現在已經滿滿網織球?!

什麼原因造成貧血？



a. RBC生成減少 (骨髓抑制或不生成)

b. RBC消耗增多 (出血、失血)

c. RBC 生存時間縮短 (溶血、血球破壞、血球生成不良)

d. 我覺得沒那麼簡單..

但RBC再生
一定不是
車禍的出血...

焦蟲還在嗎??

還是還有其他 '溶血' 的原因?

骨髓努力產生網織球 (Ret).. 有哪些原因要考慮??

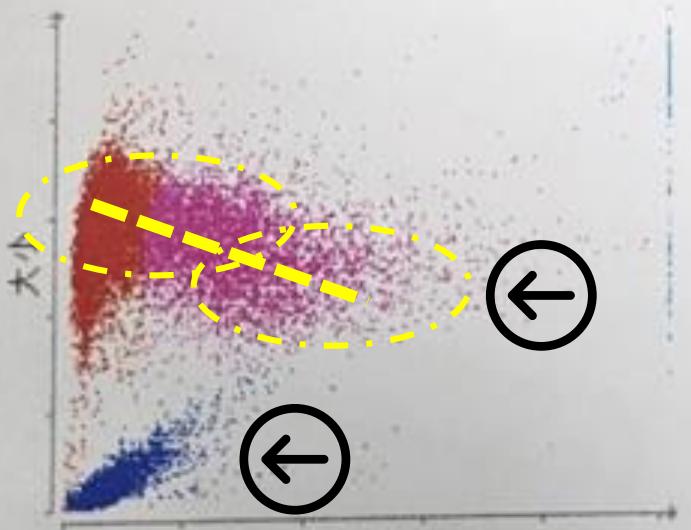
- RBC 耗損增加： **失血類原因**

- 創傷,
- 失血 (Ex. 血便、血尿、牙齦出血),
- 吸血的寄生蟲 (Ex. 跳蚤)

- RBC生存時間縮短: **溶血類原因**

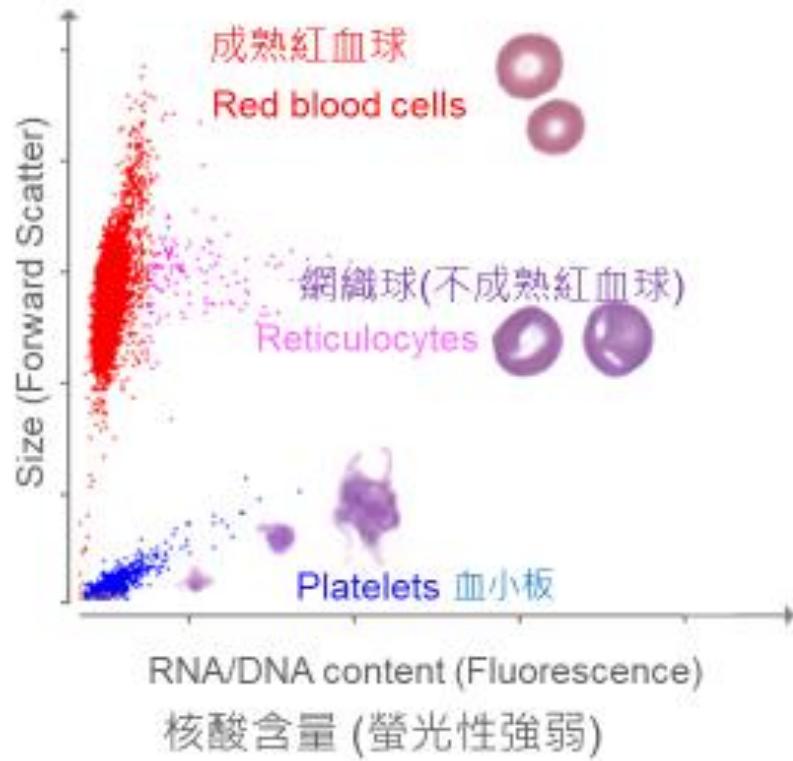
- 血球生成不良(Ex. 細胞膜、RBC形狀不理想),
- 血球被感染 (Ex. 焦蟲、血巴東..etc),
- 自體免疫 (Ex. IMHA),
- 毒素 (Ex. 溶血性細菌毒素)
- 氧化性傷害 (Ex. 吃到洋蔥、毒物..etc)

紅血球測試



失血?! ← 缺鐵的跡象

溶血?!



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RBC 質量

RBC 品質

骨髓反應



調查計畫：

○ 有無進行性RBC破壞？

- 血液寄生蟲確認
- 自體免疫性疾病確認



Fever of Unknown Origin RealPCR™ Panel-Canine 犬不明原因發燒病原偵測套組

- 1. Anaplasma spp. (含分型)
- 2. Babesia spp. (含分型)
- 3. Bartonella spp.
- 4. Blastomyces dermatitidis
- 5. Brucella canis
- 6. Coccidioides spp.
- 7. Cryptococcus spp.
- 8. Ehrlichia spp. (含分型)
- 9. Hepatozoon spp.
- 10. Histoplasma capsulatum,
- 11. Leishmania spp. (含定量)
- 12. Leptospira spp.
- 13. Neospora caninum
- 14. Rocky Mountain spotted fever (*Rickettsia rickettsii*)
- 15. Toxoplasma gondii
- 16. Trypanosoma cruzi

○ 有無未知的出血？

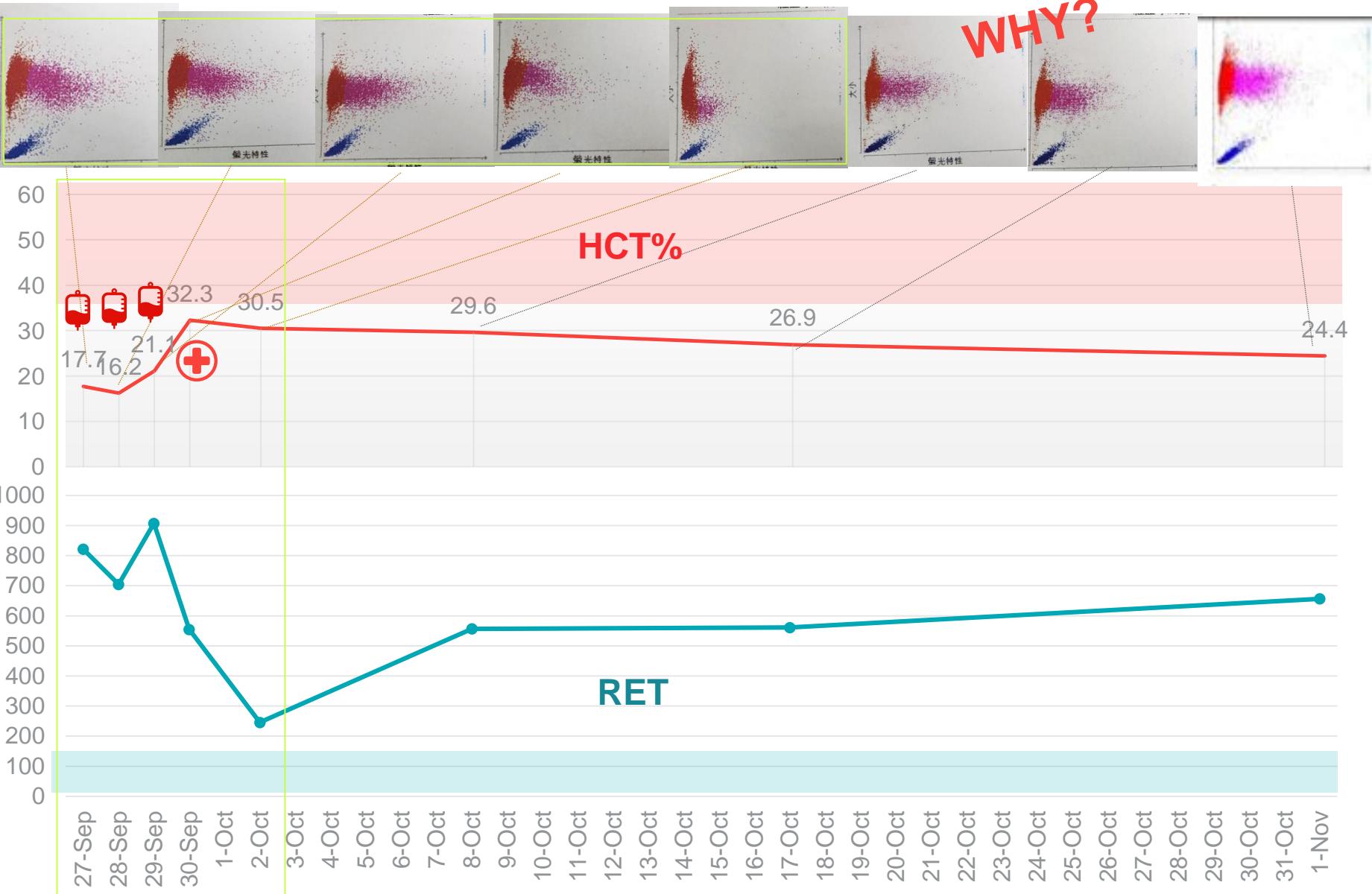
- 外觀檢查 (傷口?)
- 血便? 粪便潛血(+/-)
- 腸道寄生蟲?
- 血尿?



Diarrhea RealPCR™ Panel (Comprehensive) with Fecal Dx® Profile - Canine

- *Campylobacter coli*
- *Campylobacter jejuni*
- canine circovirus
- canine distemper virus (CDV)
- canine enteric coronavirus (CECoV)
- canine parvovirus 2 (CPV-2)
- *Clostridium difficile* toxin A/B gene
- *Clostridium perfringens* alpha toxin (CPA) gene Quant
- *Clostridium perfringens* enterotoxin (CPE) gene Quant
- *Clostridium perfringens* CPnetE/F toxin gene Quant
- *Cryptosporidium* spp.
- *Giardia* spp.
- *Salmonella* spp.
- 粪便浮游法鏡檢
- 免疫抗原檢查: 鉤蟲、蛔蟲、鞭蟲

豆豆 的血液學追蹤變化



調查結果：

○ 有無進行性RBC破壞？

- 血液寄生蟲確認 →
- 自體免疫性疾病確認

Fever of Unknown Origin RealPCR™ Panel-Canine
犬不明原因發燒病原偵測套組

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- 15. Toxoplasma gondii
- 16. Trypanosoma cruzi

皆陰性

○ 有無未知的出血？

- 外觀檢查 (傷口?)
- 血便?糞便潛血(+/-)
- 腸道寄生蟲?
- 血尿?

Diarrhea RealPCR™ Panel (Comprehensive) with Fecal Dx® Profile - Canine

2陽性

- *Campylobacter coli*
- *Campylobacter jejuni*
- **canine circovirus**
- canine distemper virus (CDV)
- canine enteric coronavirus (CECoV)
- canine parvovirus 2 (CPV-2)
- **Clostridium difficile toxin A/B gene**
- *Clostridium perfringens alpha toxin (CPA) gene Quant*
- *Clostridium perfringens enterotoxin (CPE) gene Quant*
- *Clostridium perfringens CPnetE/F toxin gene Quant*
- *Cryptosporidium spp.*
- *Giardia spp.*
- *Salmonella spp.*
- 粪便浮游法鏡檢
- 免疫抗原檢查: 鉤蟲、蛔蟲、鞭蟲

Canine Circovirus 的臨床影響

首次發現在美國加州

Emerg Infect Dis. 2013 Apr; 19(4): 534–541.

RESEARCH

Circovirus in Tissues of Dogs with Vasculitis and Hemorrhage

Linlin Li, Sabrina McGraw, Kevin Zhu, Christian M. Leutenegger, Stanley L. Marks, Steven Kubiski, Patricia Gaffney, Florante N. Dela Cruz Jr, Chunlin Wang, Eric Delwart, and Patricia A. Pesavento

We characterized the complete genome of a novel dog circovirus (DogCV) from the liver of a dog with severe hemorrhagic gastroenteritis, vasculitis, and granulomatous lymphadenitis. DogCV was detected by PCR in fecal samples from 19/168 (11.3%) dogs with diarrhea and 14/204 (6.9%) healthy dogs and in blood from 19/409 (3.3%) of dogs with thrombocytopenia and neutropenia, fever of unknown origin, or past tick bite. Co-infection with other canine pathogens was detected for 13/19 (68%) DogCV-positive dogs with diarrhea. DogCV capsid proteins from different dogs varied by up to 8%. In situ hybridization and transmission electron microscopy detected DogCV in the lymph nodes and spleens of 4 dogs with vascular compromise and histiocytic inflammation. The detection of a circovirus in tissues of dogs expands the known tropism of these viruses to a second mammalian host. Our results indicate that circovirus, alone or in co-infection with other pathogens, might contribute to illness and death in dogs.

Circoviruses are nonenveloped, spherical viruses with a single-stranded circular DNA genome of ≈ 2 kb; they group as a genus within the family *Circoviridae*, together with the proposed genus *Cyclovirus* and the phylogenetically more distinct genus *Gyrovirus* [1]. Most of the known species in the genus *Circovirus* infect birds and cause signs including malformations and necrosis of the integument, lymphoid depletion, and immunosuppression [2].

Before 2012, the only circoviruses reported to infect mammals were the 2 closely related porcine circoviruses (PCVs) [3]. PCV2 is the primary pathogen associated with

Author affiliations: Blood Systems Research Institute, San Francisco, California, USA (L. Li, E. Delwart); University of California, San Francisco (L. Li, E. Delwart); University of California School of

a spectrum of swine diseases called porcine circovirus-associated diseases that have been described in pigs worldwide. PCV2 infection causes severe economic losses because of increased mortality and reduced production, making it one of the most economically important viruses in the global swine industry. Among lesions that have been attributed to PCV2 infection are pneumonia, enteritis, lymphadenitis, vasculitis, nephritis, and reproductive disease [4]. In cases for which PCV2 is considered causative, immunohistochemical and in situ hybridization (ISH) analyses demonstrate large amounts of PCV2 antigen or nucleic acids in the cytoplasm of macrophages and dendritic cells in the depleted follicles in lymphoid tissues [4,5]. Naturally occurring porcine circovirus-associated diseases is often accelerated or exacerbated by concurrent viral or bacterial infections, and secondary infections often occur as a result of immunosuppression [6].

Random nucleic acid amplification with or without prior enrichment for viral particle-associated nucleic acids [7,8], followed by deep sequencing and in silico similarity searches for sequences related to those of known viruses, have been highly productive in the field of animal virus discovery [9–11]. We used this technique to identify virus sequences in affected tissues from companion animals with diseases of unknown cause. We identified a canine circovirus in the liver of a dog that had necrotizing vasculitis and granulomatous lymphadenitis, both of which are described in PCV2-infected pigs [4]. We named this virus dog circovirus (DogCV) rather than canine circovirus to avoid confusion with the CaCV notation used for canary circovirus [12,13], canine calicivirus [14,15], and *Capiticia chlorotis* virus [16]. A closely related variant of DogCV was discovered independently in canine common canines and

屏科大團隊 進行的台灣地區調查

Hsu et al. BMC Veterinary Research (2016) 12:116

Hsu et al. *BMC Veterinary Research* (2016) 12:116
DOI 10.1186/s12917-016-0722-8

BMC Veterinary Research

RESEARCH ARTICLE

Open Access



High detection rate of dog circovirus in diarrheal dogs

Han-Siang Hsu^{1†}, Ting-Han Lin^{1†}, Hung-Yi Wu², Lee-Shuan Lin^{1,3}, Cheng-Shu Chung^{1,3}, Ming-Tang Chiou^{1,4*} and Chao-Nan Lin^{1,4}

Abstract

Background: Diarrhea is one of the most common clinical symptoms reported in companion animal clinics. Dog circovirus (DogCV) is a new mammalian circovirus that is considered to be a cause of alimentary syndromes such as diarrhea, vomiting and hemorrhagic enteritis. DogCV has previously only been identified in the United States, Italy, Germany (GeneBank accession number: KF887949) and China (GeneBank accession number: KT946839). Therefore, the aims of this study were to determine the prevalence of DogCV in Taiwan and to explore the correlation between diarrhea and DogCV infection. Clinical specimens were collected between 2012 and 2014 from 207 dogs suffering from diarrhea and 160 healthy dogs.

Results: In this study, we developed a sensitive and specific SYBR Green-based real-time PCR assays to detected DogCV in naturally infected animals. Of the analyzed fecal samples from diarrheal dogs and health dogs, 58 (28.0 %) and 19 (11.9 %), respectively, were DogCV positive. The difference in DogCV prevalence was highly significant ($P=0.0002755$) in diarrheal dogs.

Conclusions: This is the first study to reveal that DogCV is currently circulating in domestic dogs in Taiwan and to demonstrate its high detection rate in dogs with diarrhea.

Keywords: Dog circovirus, Diarrhea, DogCV, Real-time PCR

Background

Gastrointestinal disorders are one of the most common diseases reported in companion animal clinics. They can be caused by a number of viral, bacterial and parasitic pathogens. The most common viral gastrointestinal pathogens are canine parvovirus [1, 2] and coronavirus. However, other agents, such as dog circovirus (DogCV), have recently been considered to be related to enteric disorders in dogs [3, 4]. DogCV was first identified in dogs with vasculitis and/or hemorrhagic gastroenteritis in the United States in 2012 [4]. DogCV is a non-enveloped, circular, single-stranded DNA virus containing a circular genome approximately 2 kb in length. It belongs to the genus *Circovirus*, together with porcine circovirus type 1 (PCV1), porcine circovirus type 2

(PCV2), canary circovirus, beak and feather disease virus and other viruses of domestic and wild birds [3].

PCV2 causes clinical conditions including systemic, lung, enteric, reproductive and skin diseases [5]. In recent years, a possible association between DogCV and canine enteritis has been suggested [3, 4]. DogCV has also been reported to cause necrotizing lymphadenitis [4] and vasculitis, which are also caused by porcine circovirus type 2 infections in pigs [5]. Previous studies have shown that DogCV is associated with hemorrhagic enteritis in dogs [3, 4], however, limited information is available to determine the direct correlation between the severity of diarrhea and DogCV infections.

DogCV has only been detected in the US [4, 6], Italy [3], Germany (GeneBank accession number: KF887949) and China (GeneBank accession number: KT946839). In the present study, we determined the previously unidentified DogCV and its prevalence in Taiwanese household dogs and clarified the correlation between diarrhea and DogCV infection.

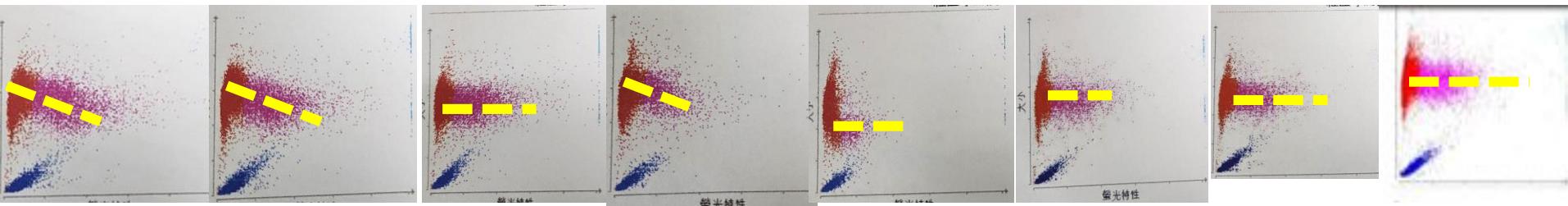
*Correspondence: mthchiou@mail.iupui.edu.tw; chao-n@mai.iupui.edu.tw

†Equal contributors

¹Department of Veterinary Medicine, College of Veterinary Medicine, National Pingtung University of Science and Technology, Nantou, Pingtung, Taiwan
Full list of author information is available at the end of the article

豆豆 的血液學追蹤變化

Sep 27 Sep 28 Sep 29 Sep 30 Oct 2 Oct 8 Oct 17 Nov 1



- 輸血
• 補血能

- 輸血
• 補血能

- 輸血 (pRBC)
• 補血能
• 大便有血腥味
• 手術

- 術後
• 補血能

- 出院

- 粪便潛血 (+/-)

- 補血能
• B12
• 血液、
糞便
PCR

補血能: Liver-Stomach Powder 240mg,Cobalamin Concentrate N.F. Equivalent To Cobalamin 7.5mcg,Ferrous Fumarate 334mg,Ascorbic Acid 75mg,Folic Acid 0.5mg

✓ Circovirus (+)
✓ Clostridium difficile toxin A/B gene (+)

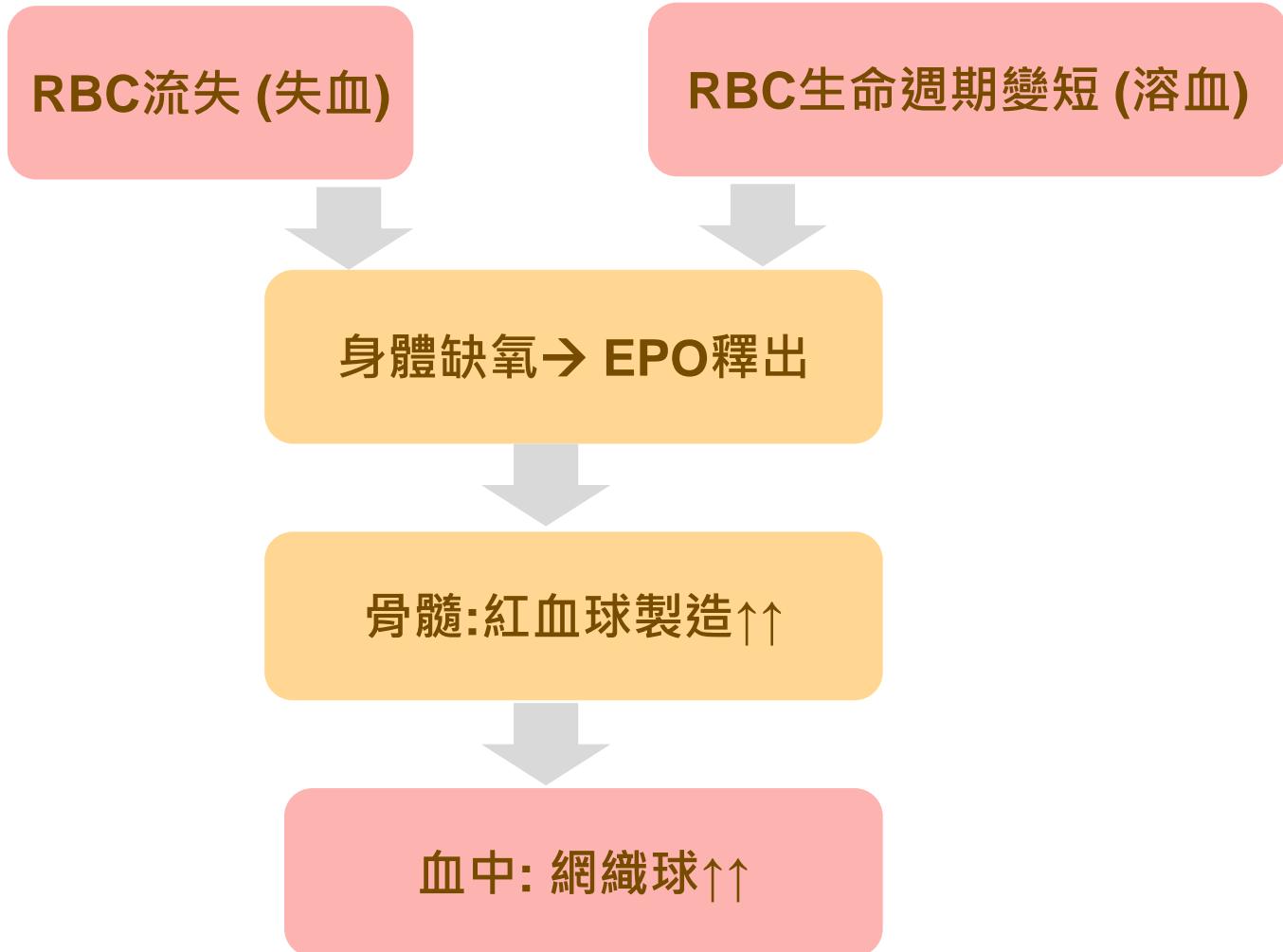
3. 針對豆豆的貧血，理想的治療方案會是什麼？

- a. 施打DPO(紅血球生成素)。
- b. 補充鐵劑、和血紅素生成養分。
- c. 輸血。
- d. 免疫治療。
- e. 換抗生素。
- f. 支持治療，改善消化道環境。
- g. 持續追蹤調查



網織球升高

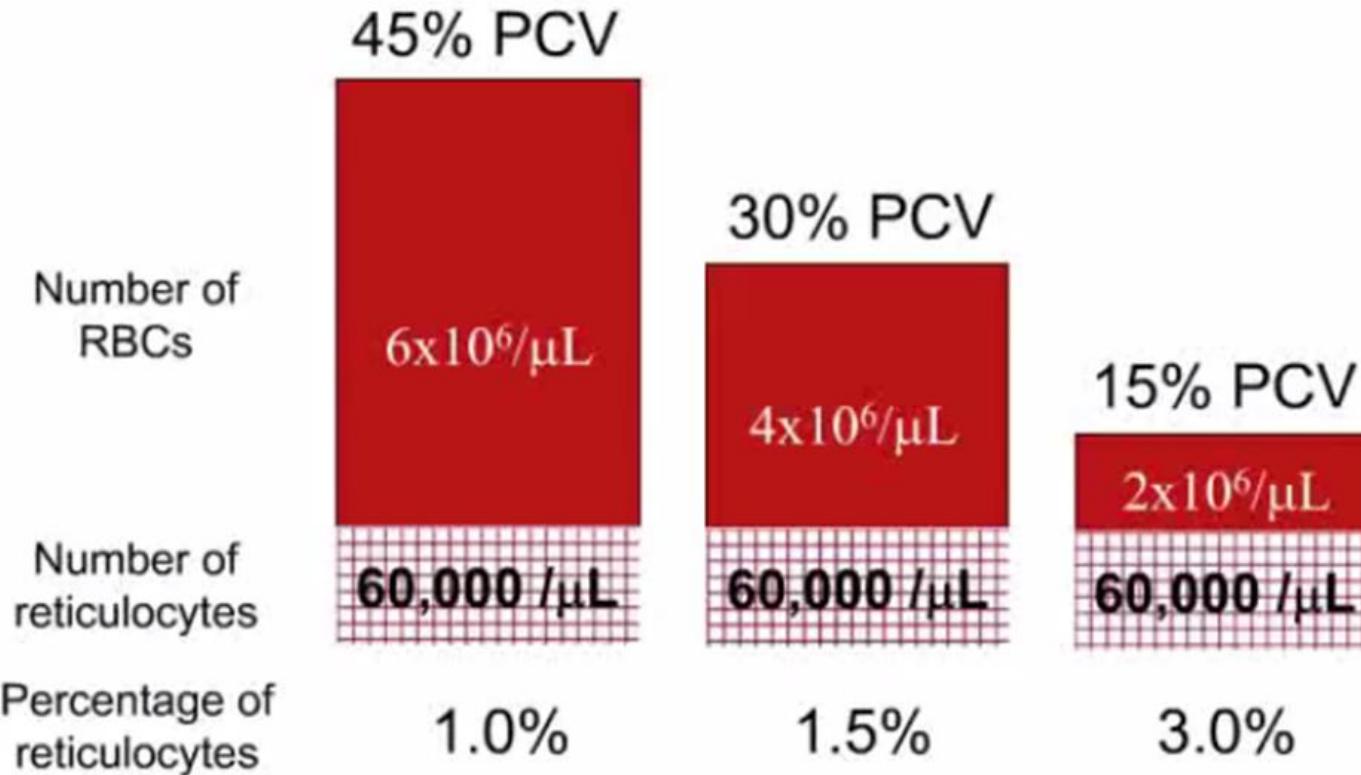
網織球升高的意涵？



怎麼樣的網織球升高有意義？

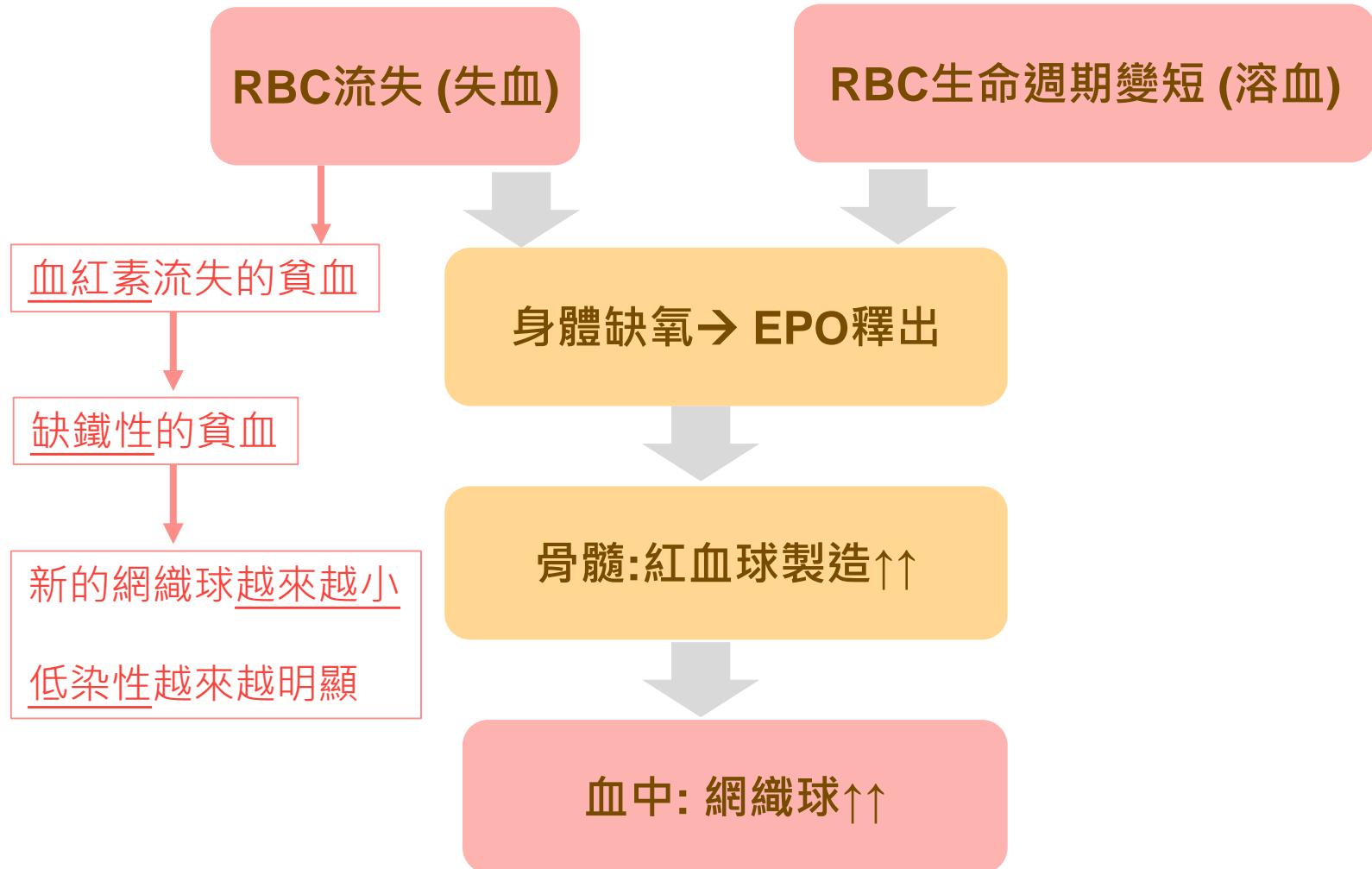
Degree of Stimulation	Dogs	Cats
Normal	1%	0-0.4%
Slight	1-4%	0.5-2.0%
Moderate	5-20%	3-4%
Marked	21-50%	>5%

絕對數量是比較客觀的骨髓反應評估指標!!!



缺鐵的再生性貧血

缺鐵的貧血 (RBC變小的再生性貧血)



Case 小黑

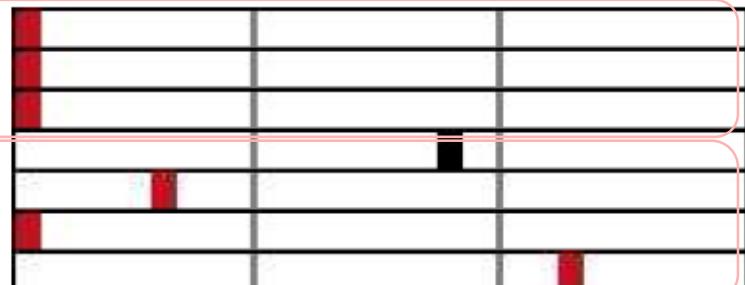
- 台灣犬
- 8歲
- 雄性已絕育
- 消瘦
- 精神沉鬱、昏睡、黏膜蒼白。
- 體表有大量跳蚤。

Case 小黑

ProCyte Dx (2014年4月15日 下午1:36)

RBC 質量

RBC	* 0.97 M/ μ L	5.85 - 8.87	低
HCT	* 8.9 %	37.3 - 81.7	低
HGB	1.8 g/dL	13.1 - 20.5	低



RBC 品質

MCV	* 71.1 fL	61.6 - 73.5	
MCH	* 18.8 pg	21.2 - 25.9	低
MCHC	* 26.1 g/dL	32.0 - 37.9	低
RDW	* 24.7 %	13.6 - 21.7	高

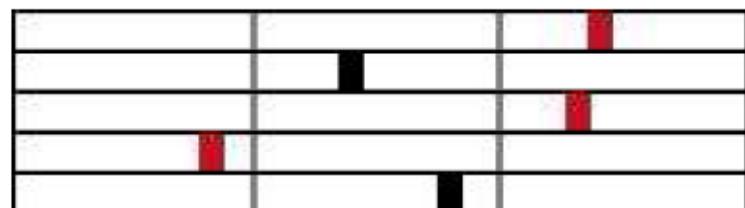
骨髓反應

%RETIC	13.1 %		
RETIC	* 127.3 K/ μ L	10.0 - 110.0	高
WBC	* 26.05 K/ μ L	5.05 - 16.76	高
%NEU	* 82.1 %		
%LYM	* 10.3 %		
%MONO	* 7.1 %		
%EOS	* 0.2 %		
%BASO	* 0.3 %		
NEU	* 21.38 K/ μ L	2.85 - 11.64	高
LYM	* 2.68 K/ μ L	1.05 - 5.10	
MONO	* 1.86 K/ μ L	0.18 - 1.12	高
EOS	* 0.05 K/ μ L	0.08 - 1.23	低
BASO	* 0.08 K/ μ L	0.00 - 0.10	



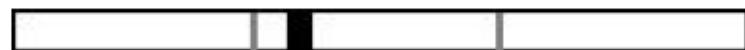
有核紅血球
(nRBC)

PLT	* 209 K/ μ L	148 - 484	
MPV	-.-- fL	8.7 - 13.2	
PDW	-.-- fL	9.1 - 19.4	
PCT	-.-- %	0.14 - 0.46	



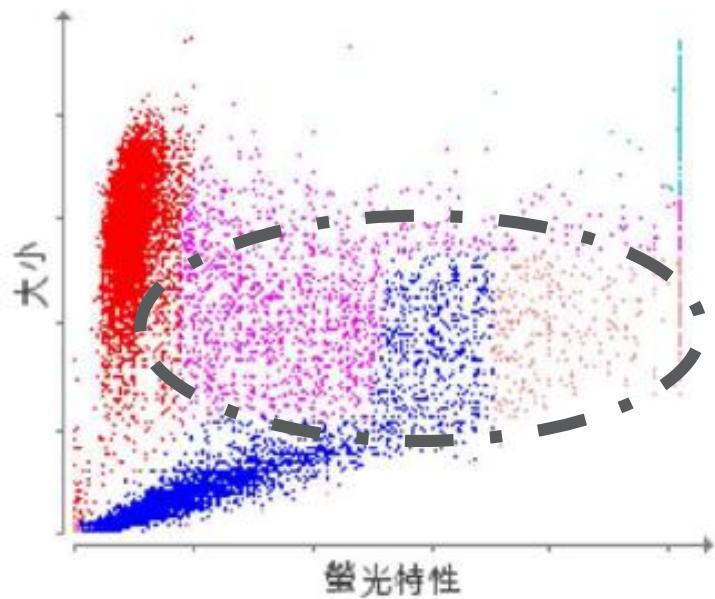
紅血球異常分布

疑似有有核紅血球(nRBC)



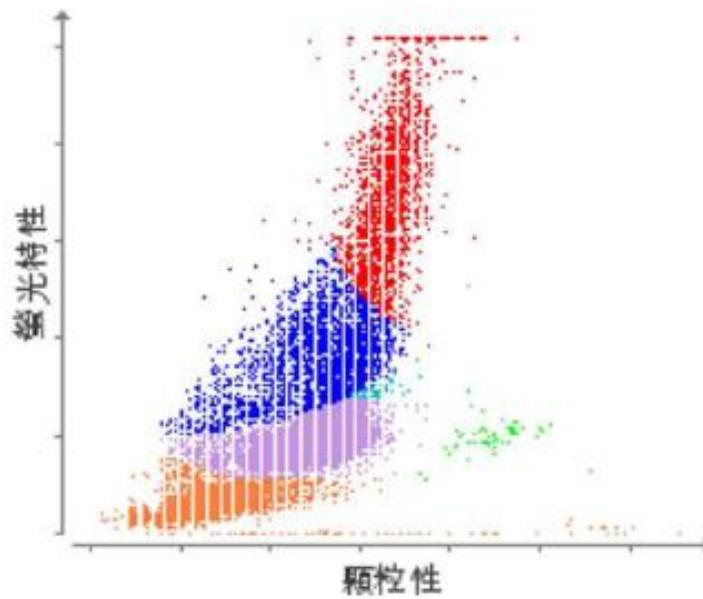
Case 小黑

紅血球測試

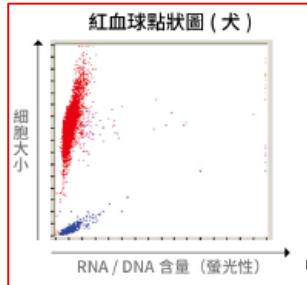


■ RBC ■ 網狀紅血球 ■ PLT ■ 紅血球碎片
■ WBC

白血球測試



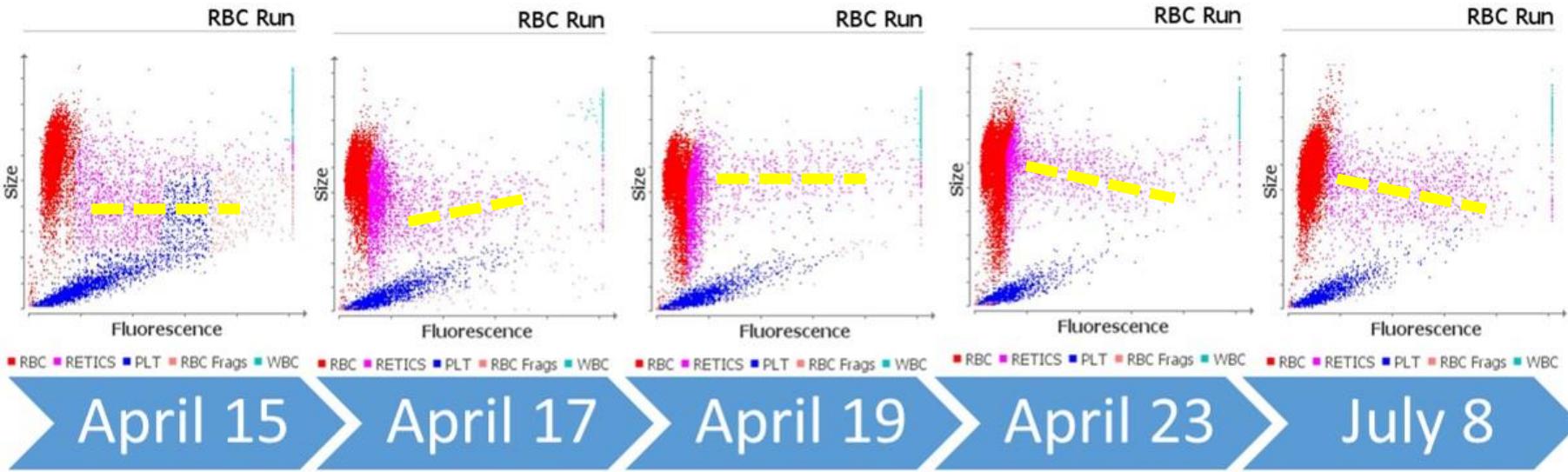
■ NEU ■ LYM ■ MONO ■ EOS ■ BASO
■ URBC



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IDEXX

Case 小黑

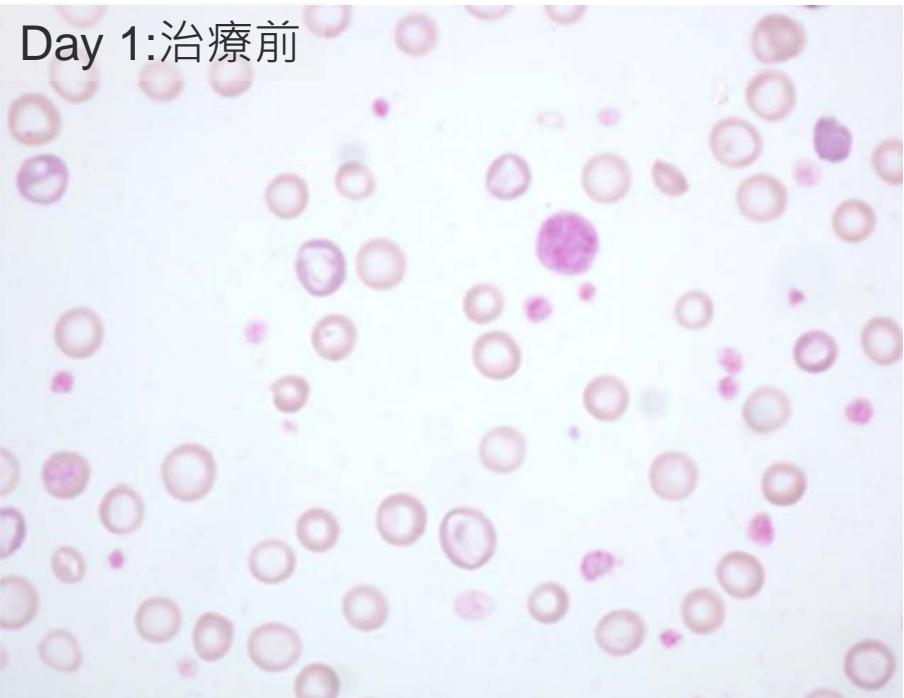


- 大貧血
- 跳蚤 +++
- HW+
- EC+
- AP+
- 血巴東+
- 輸血
- 補鐵
- 驅蟲
- 出院
- 補鐵
- 驅蟲
- 回診
- 回診

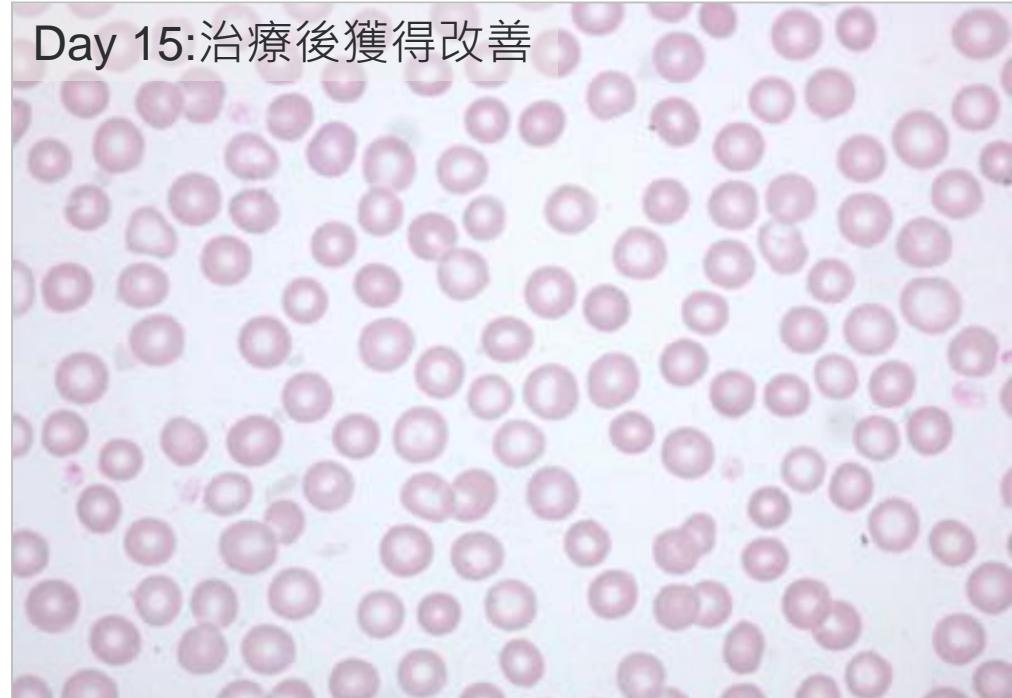
Case 小黑

治療後 紅血球質量和品質 有顯著的改善。

Day 1:治療前

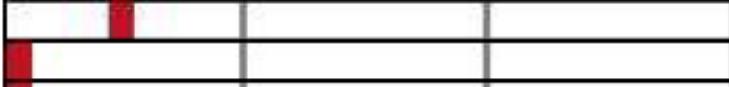
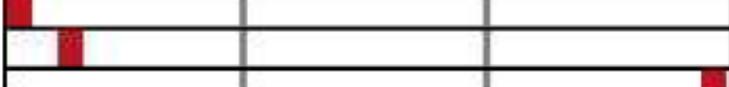
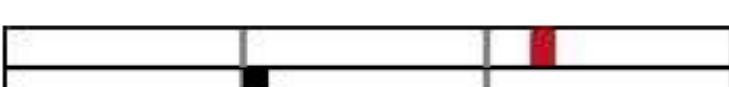
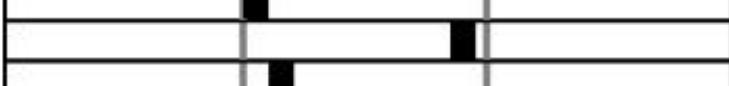
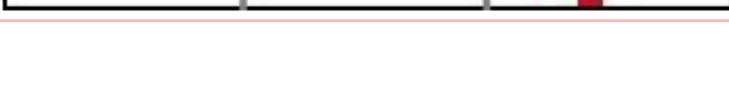
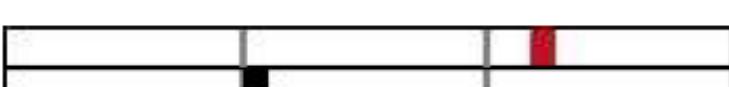
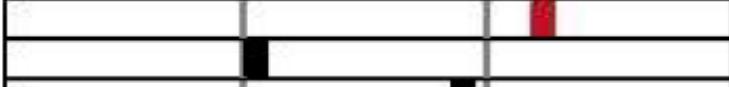
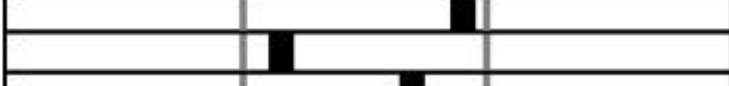
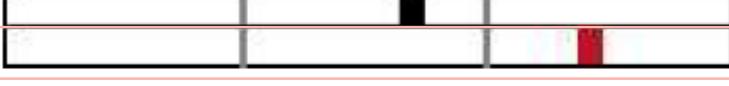
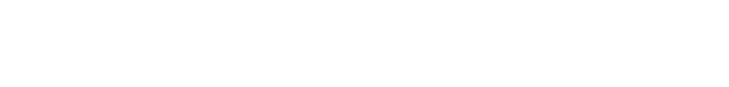
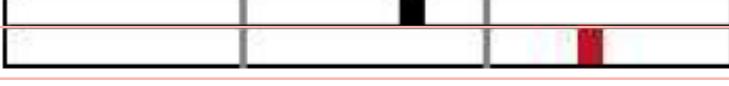


Day 15:治療後獲得改善

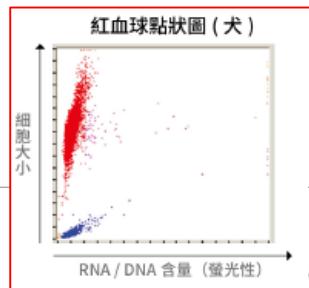


Case 麥斯

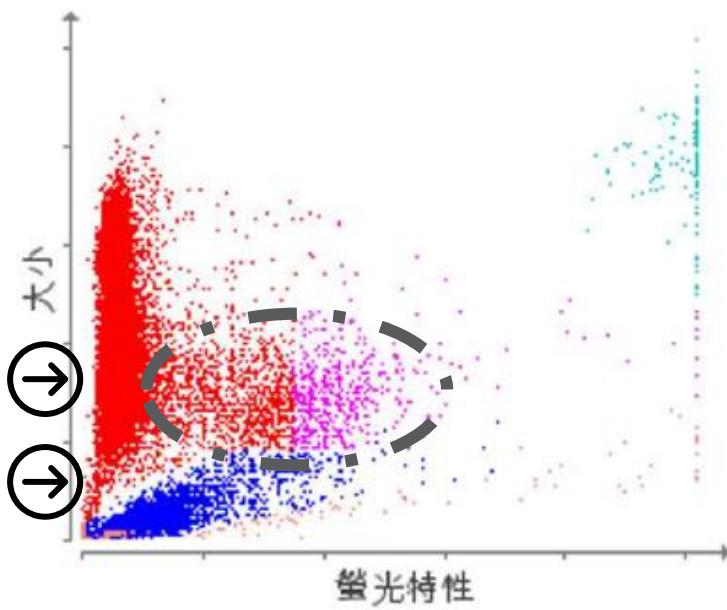
- 犬
- 10月齡
- 雄性
- 長期服用消炎止痛藥
- 後腿有化膿性創傷
- 精神沉鬱、昏睡、黏膜蒼白。
- 黑糞。

Test	Results	Reference Interval	LOW	NORMAL	HIGH
ProCyte Dx (2014年2月25日 下午2:46)					
RBC	* 3.85 M/ μ L	5.65 - 8.87	低		
HCT	* 16.9 %	37.3 - 61.7	低		
HGB	4.7 g/dL	13.1 - 20.5	低		
MCV	* 43.9 fL	61.6 - 73.5	低		
MCH	* 12.2 pg	21.2 - 25.9	低		
MCHC	* 27.8 g/dL	32.0 - 37.9	低		
RDW	* 34.1 %	13.6 - 21.7	高		
%RETIC	2.1 %				
RETIC	* 82.0 K/ μ L	10.0 - 110.0			
WBC	19.08 K/ μ L	5.05 - 16.76	高		
%NEU	86.4 %				
%LYM	6.6 %				
%MONO	5.3 %				
%EOS	1.3 %				
%BASO	0.4 %				
NEU	16.50 K/ μ L	2.95 - 11.64	高		
LYM	1.25 K/ μ L	1.05 - 5.10			
MONO	1.02 K/ μ L	0.16 - 1.12			
EOS	0.24 K/ μ L	0.06 - 1.23			
BASO	0.07 K/ μ L	0.00 - 0.10			
PLT	* 672 K/ μ L	148 - 484	高		
MPV	-- -- fL	8.7 - 13.2			
PDW	-- -- fL	9.1 - 19.4			
PCT	-- -- %	0.14 - 0.46			
紅血球異常分布					

缺鐵性貧血的重要特徵

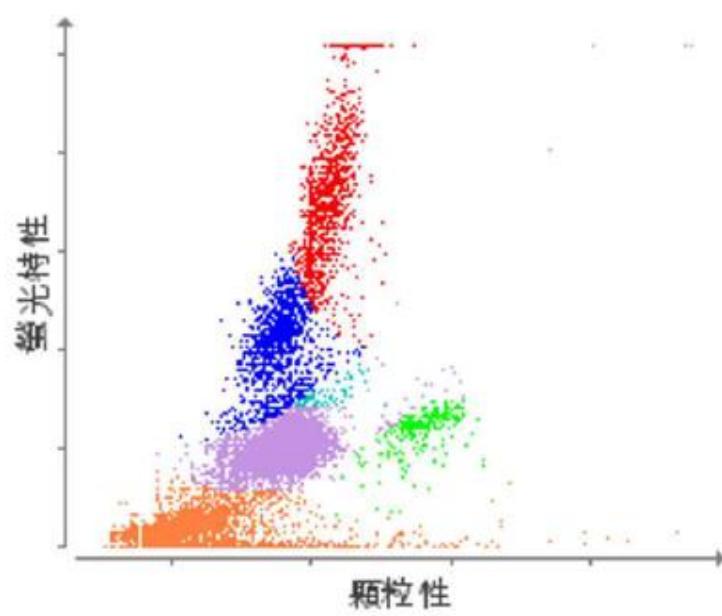


紅血球測試



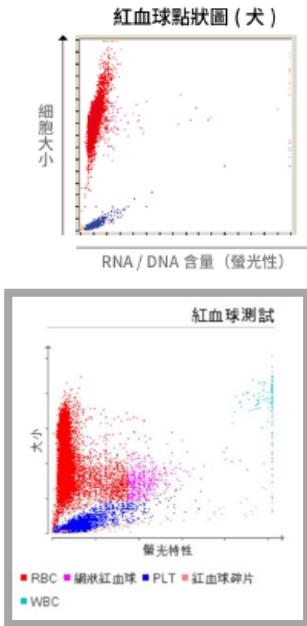
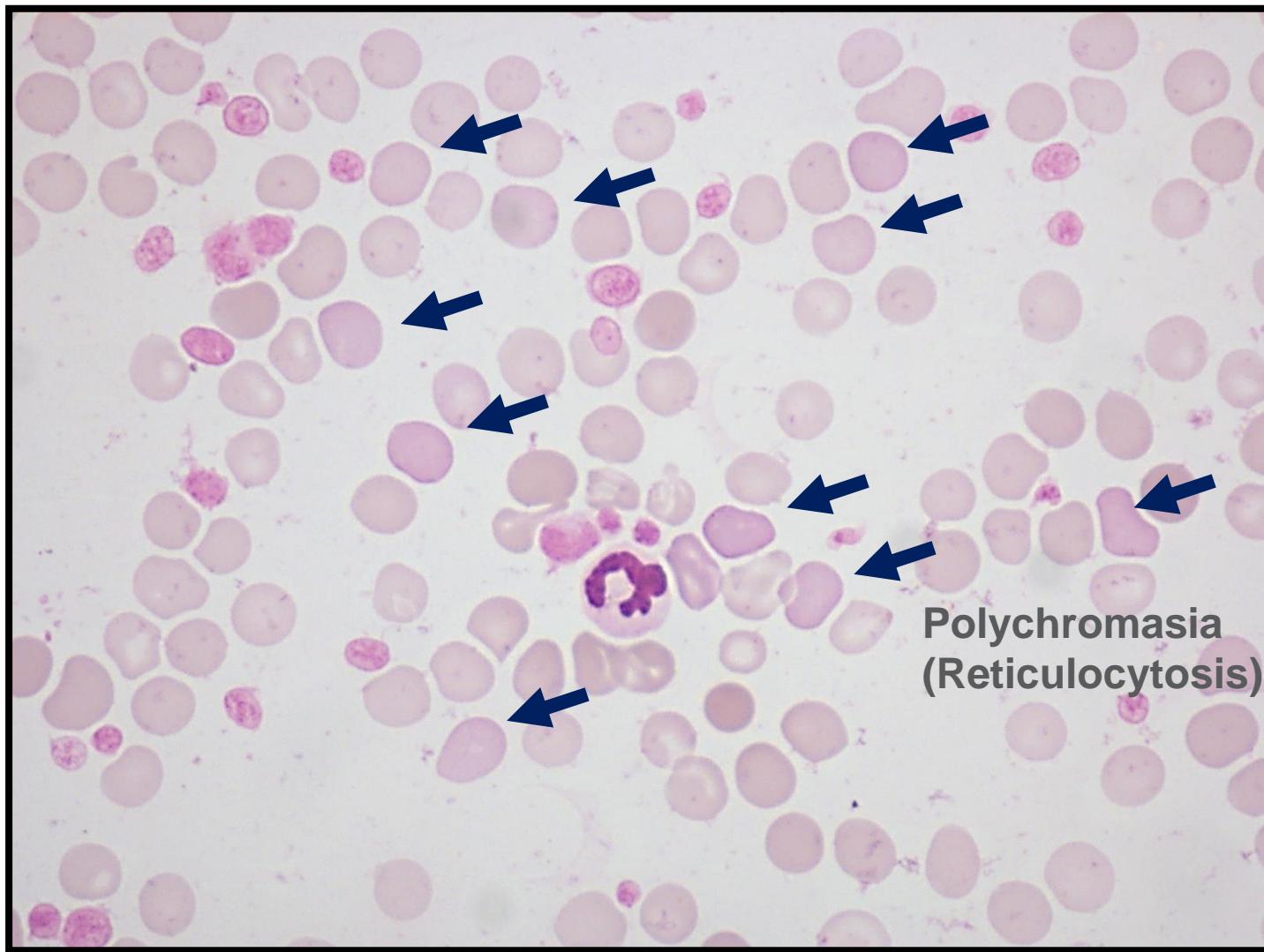
- RBC ■ 網狀紅血球 ■ PLT ■ 紅血球碎片
- WBC

白血球測試



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

顯著的網織球變小，整體RBC也比較小



IDEXX

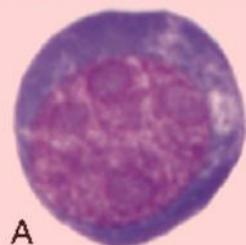
網織球血紅素 RETIC-HGB

ProCyte可以分析網織球(RETIC)的血紅素(HGB)含量

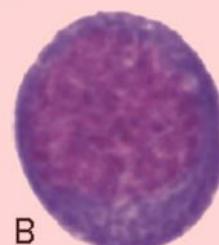
我們可以快速地在幾天內就偵測出身體缺鐵的跡象...

當缺鐵性貧血產生時，
網織球所含有的鐵質(血紅素)變少
新生紅血球(網織球)的品質產生了變化..

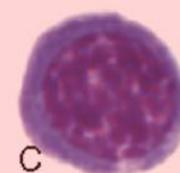
Bone marrow



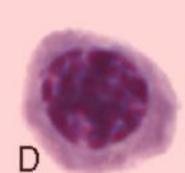
A



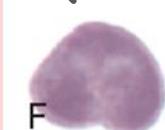
C



D



E



F

In circulation



過去要比較久的時間才能發現缺鐵性貧血

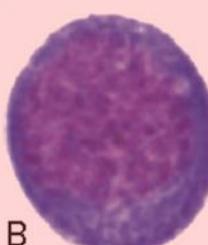
- Mean cell volume (MCV) ↓ 細胞容積變小 microcytic (小球)
- Mean cell hemoglobin (MCH) ↓ 細胞的HGB含量減少
- Mean cell hemoglobin concentration (MCHC) ↓ Hypochromic (低染)
細胞的HGB染色性減少

因為RBC可以存活3個月之久(以狗而言...)...
每日骨髓僅替換生成 1~5 % (或多或少) 的RBC...
所以要形成明顯的小球 low MCV, 低染low MCHC 要很久的時間。

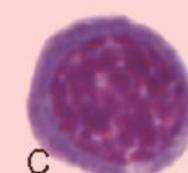
Bone marrow



A



C



D



E



F

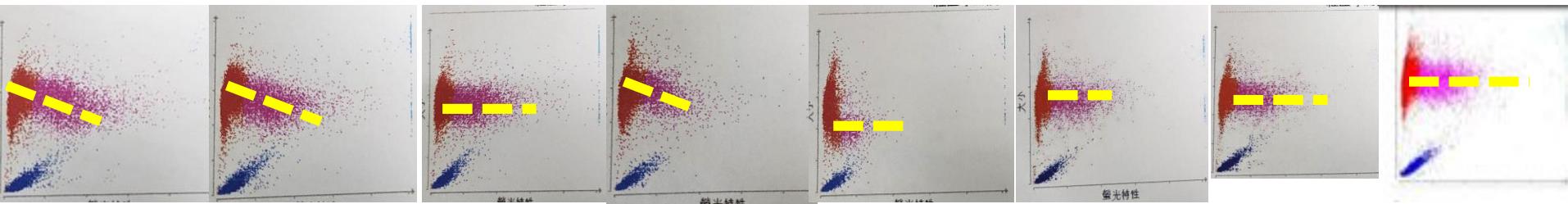
In circulation



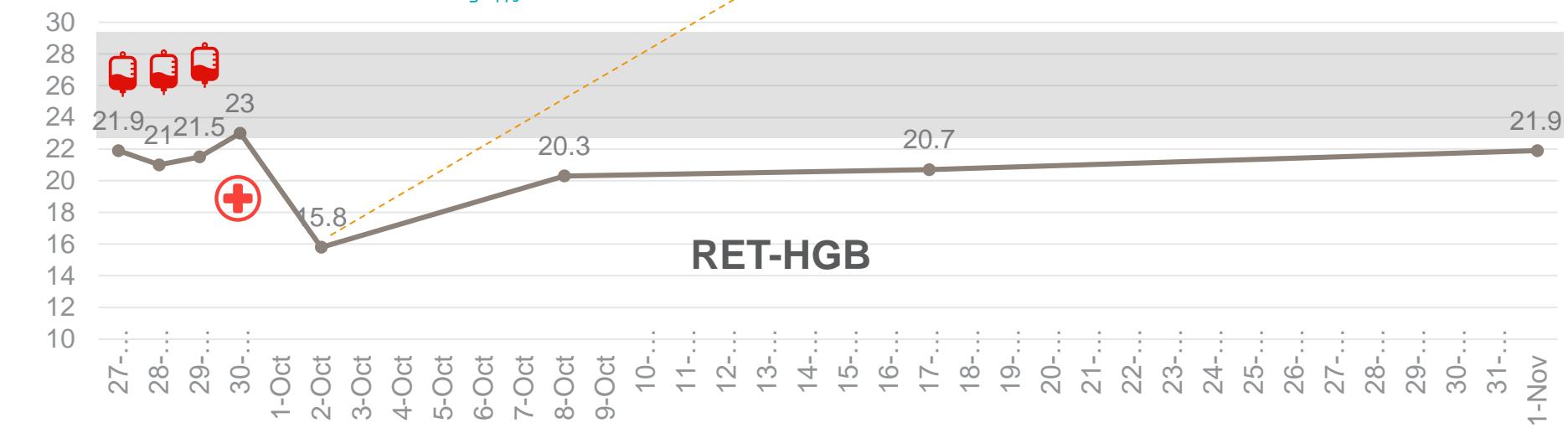
豆豆的血液學追蹤變化



Sep 27 Sep 28 Sep 29 Sep 30 Oct 2 Oct 8 Oct 17 Nov 1

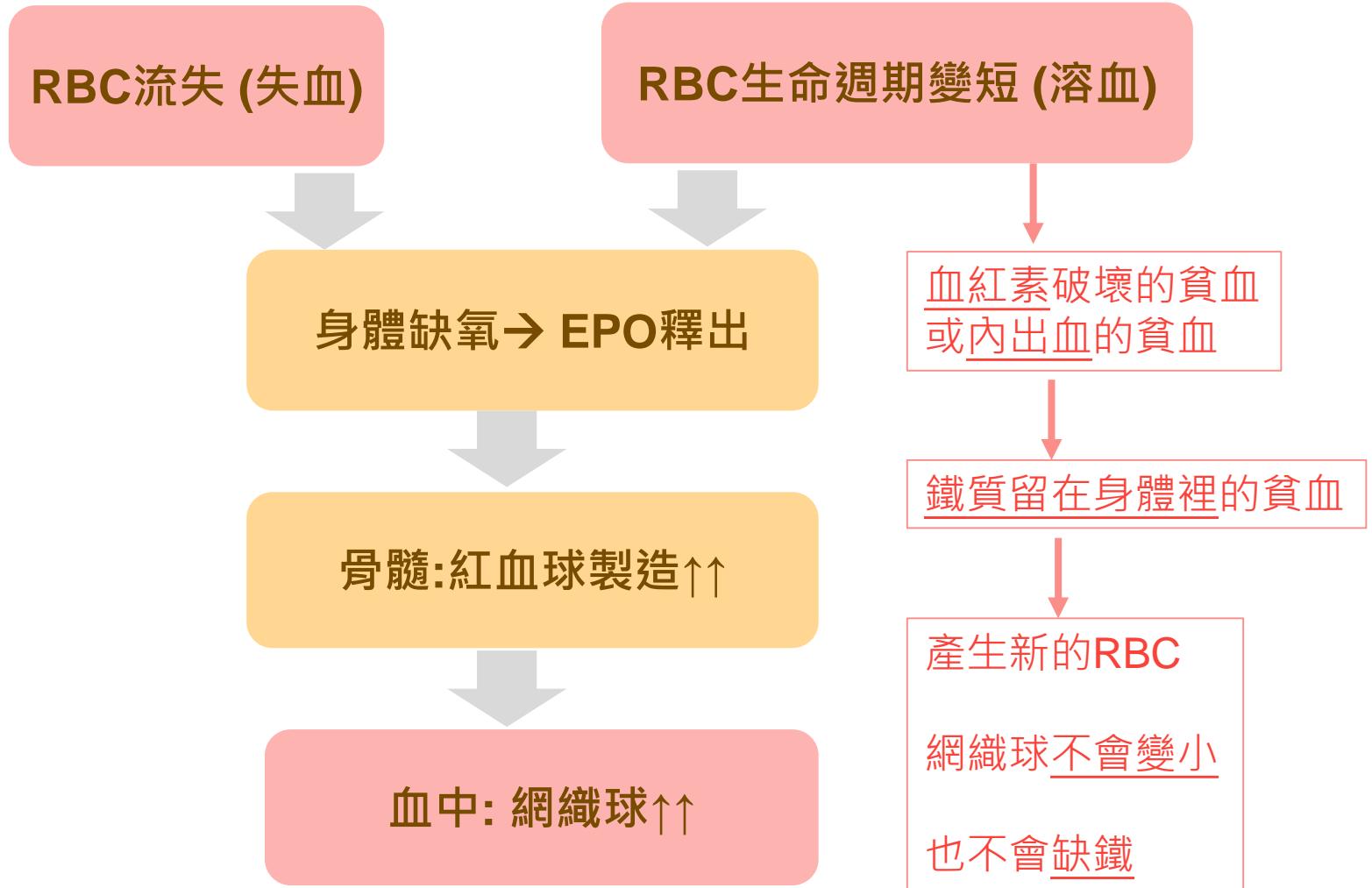


- 輸血
- 補血能
- 輸血
- 補血能
- 輸血 (pRBC)
- 術後
- 出院
- 糞便潛血 (+/-)
- 補血能
- B12
- 血液糞便PCR
- 补血能
- 大便有血腥味
- 手術



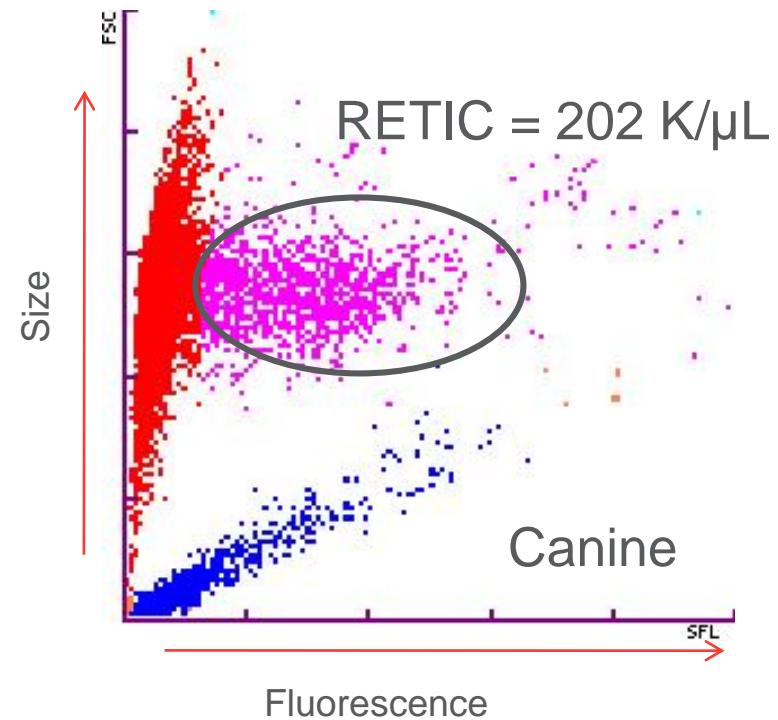
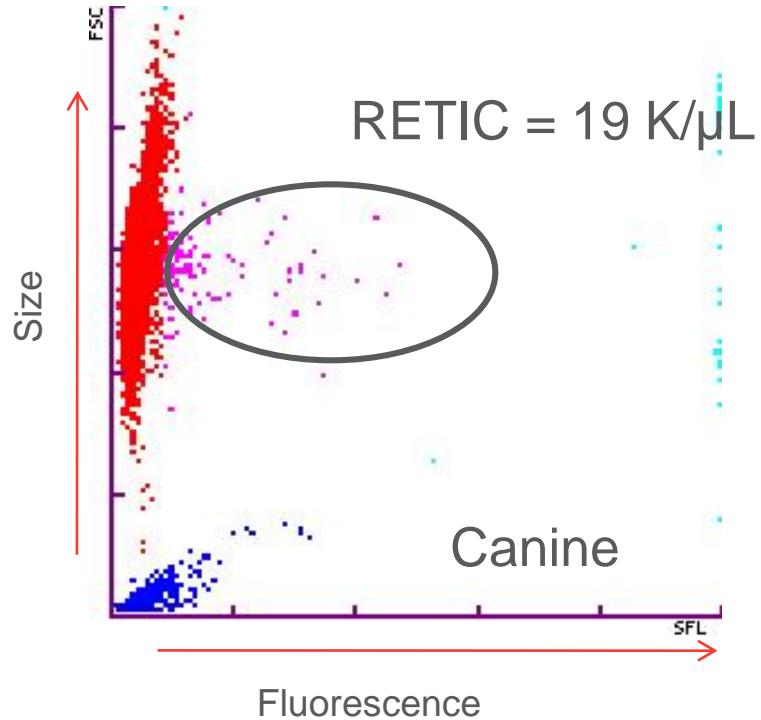
不缺鐵的再生性貧血

不缺鐵的貧血 (RBC不變小的再生性貧血)



哪一個檢體有網織球增多的情形？

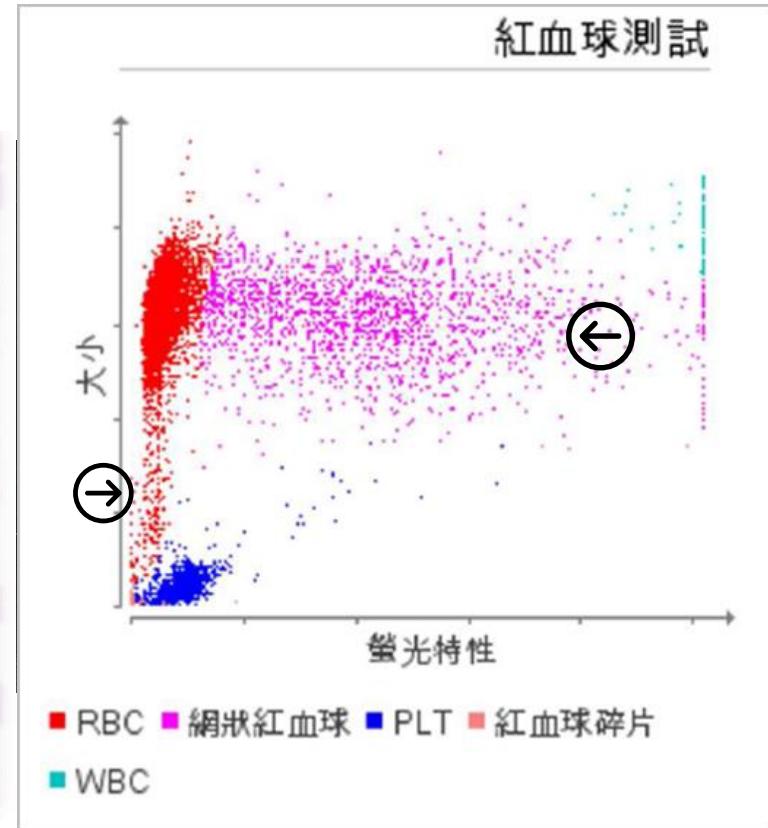
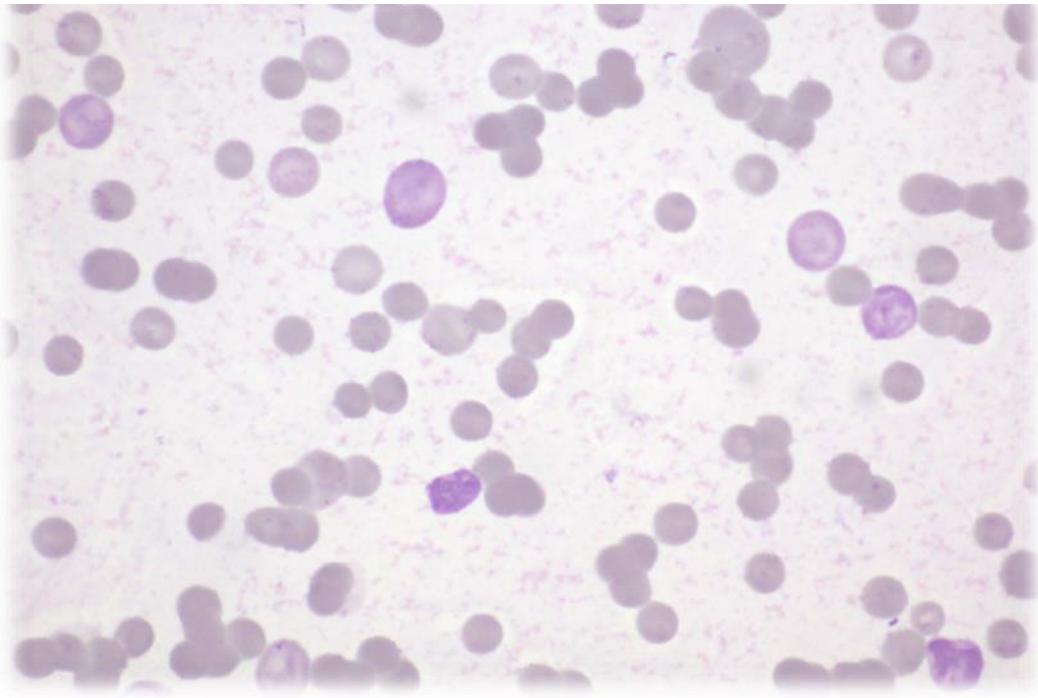
網織球增多症
Sign of regeneration!!



Case 布丁

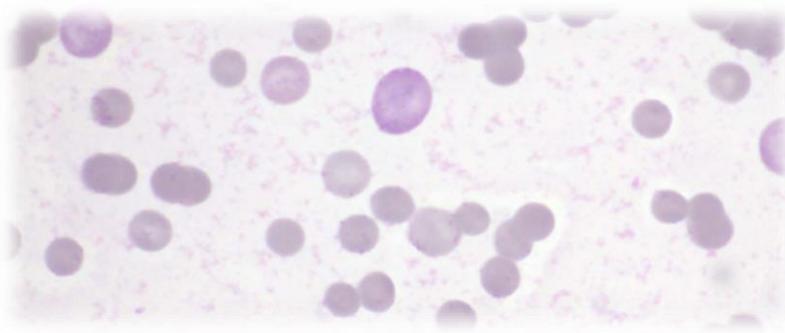
免疫媒介溶血性貧血(IMHA)

球型紅血球 (spherocytosis)

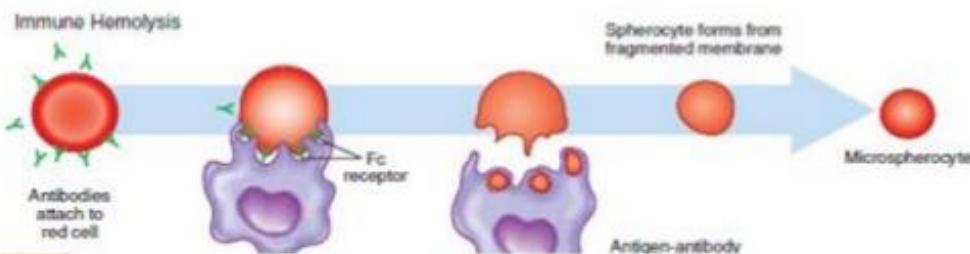


自體免疫作用: 脾臟巨噬細胞破壞..

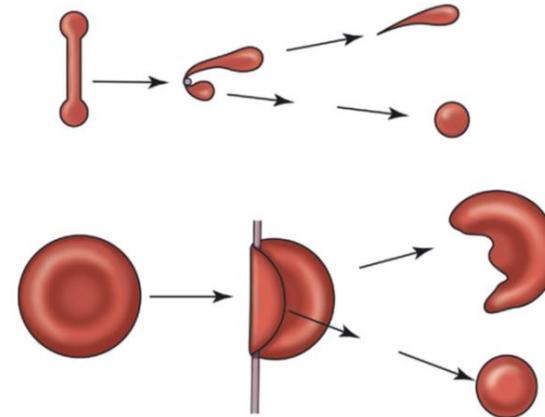
球形紅血球成因



1. 免疫系統破壞: 抗RBC抗體、自體免疫、脾臟macrophage活化。

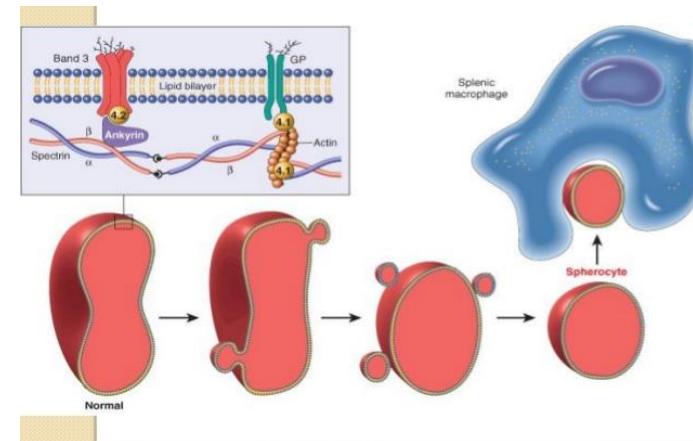


2. 物理性破壞: 血管內栓子(纖維素阻斷)、擾流...



JW Harvey. Veterinary Hematology: A Diagnostic Guide and Color Atlas

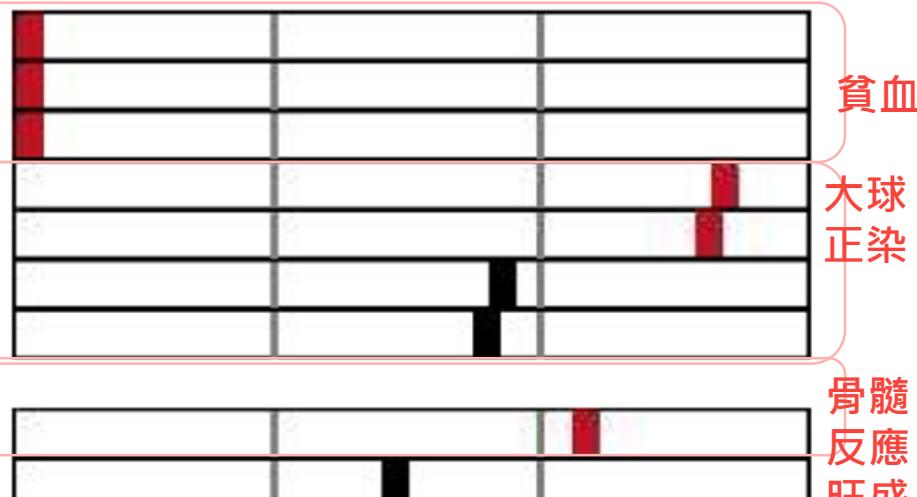
3. 細胞膜異常: (人類)遺傳缺陷



Case 布丁 (IMHA)

ProCyte Dx (2014年3月12日 上午10:47)

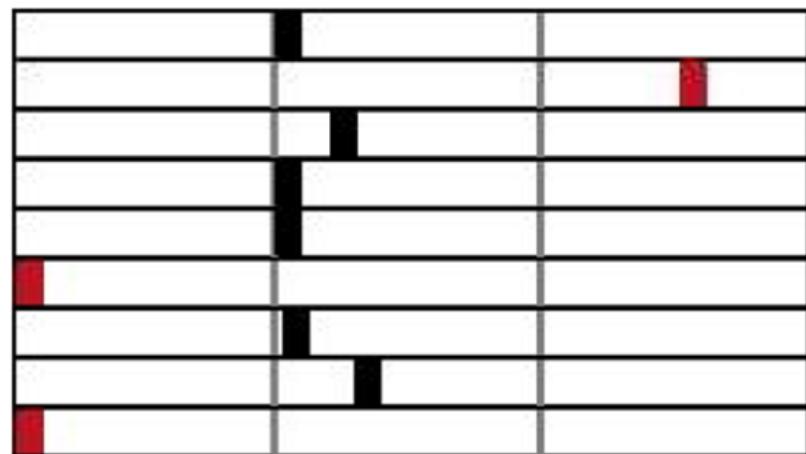
RBC	1.06 M/ μ L	5.65 - 8.87	低
HCT	8.9 %	37.3 - 61.7	低
HGB	3.3 g/dL	13.1 - 20.5	低
MCV	84.0 fL	61.6 - 73.5	高
MCH	31.1 pg	21.2 - 25.9	高
MCHC	37.1 g/dL	32.0 - 37.9	
RDW	20.1 %	13.6 - 21.7	
%RETIC	13.3 %		
RETIC	140.7 K/μL	10.0 - 110.0	高
WBC	10.46 K/ μ L	5.05 - 16.76	
%NEU	32.2 %		
%LYM	63.2 %		
%MONO	3.9 %		
%EOS	0.7 %		
%BASO	0.0 %		
NEU	3.37 K/ μ L	2.95 - 11.64	
LYM	6.61 K/μL	1.05 - 5.10	高
MONO	0.41 K/ μ L	0.16 - 1.12	
EOS	0.07 K/ μ L	0.06 - 1.23	
BASO	0.00 K/ μ L	0.00 - 0.10	
PLT	4 K/μL	148 - 484	低
MPV	9.1 fL	8.7 - 13.2	
PDW	12.7 fL	9.1 - 19.4	
PCT	0.00 %	0.14 - 0.46	低



贫血

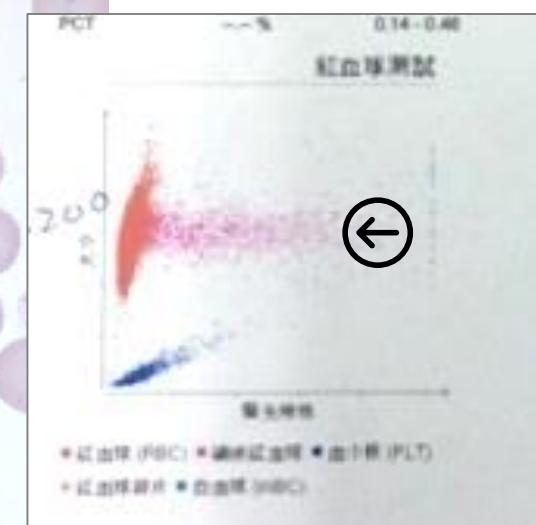
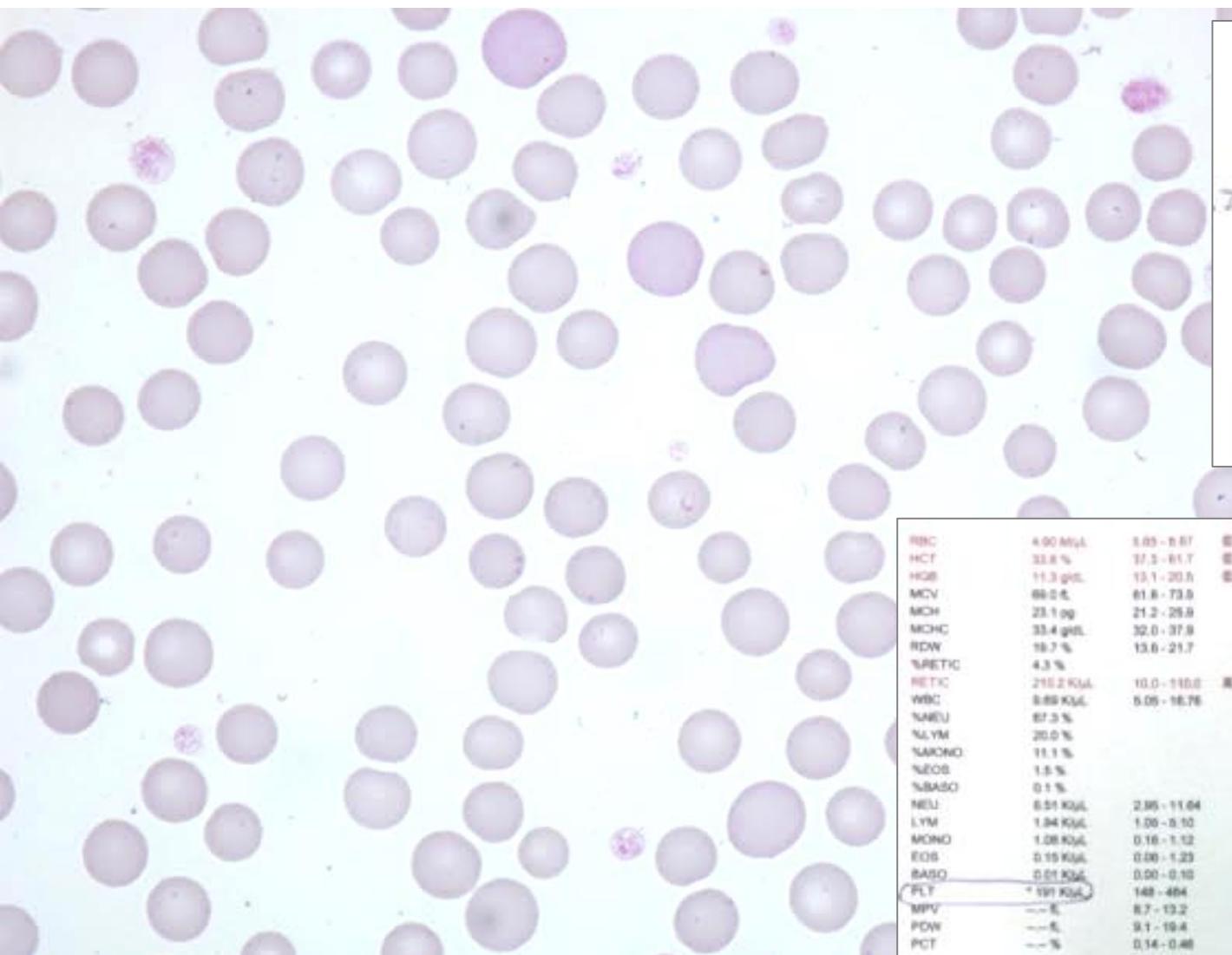
大球
正染

骨髓
反應
旺盛

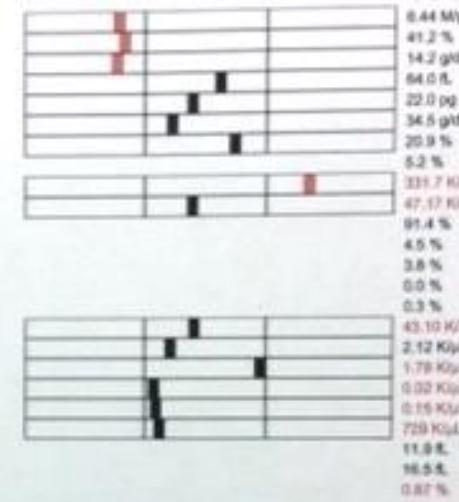


Case. 臘腸 意外的RBC再生

Babesia gibsoni 感染(小焦蟲)

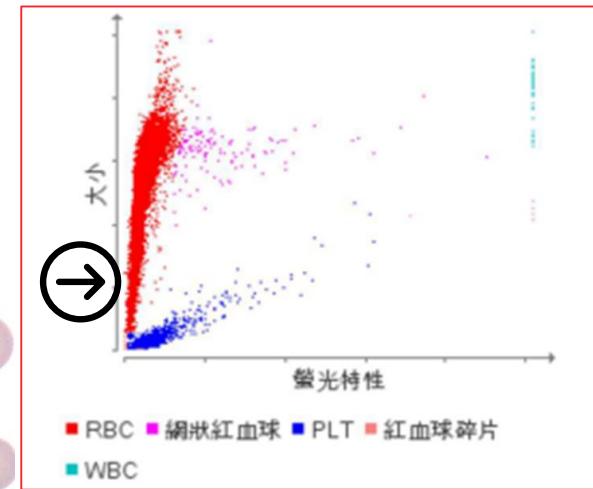
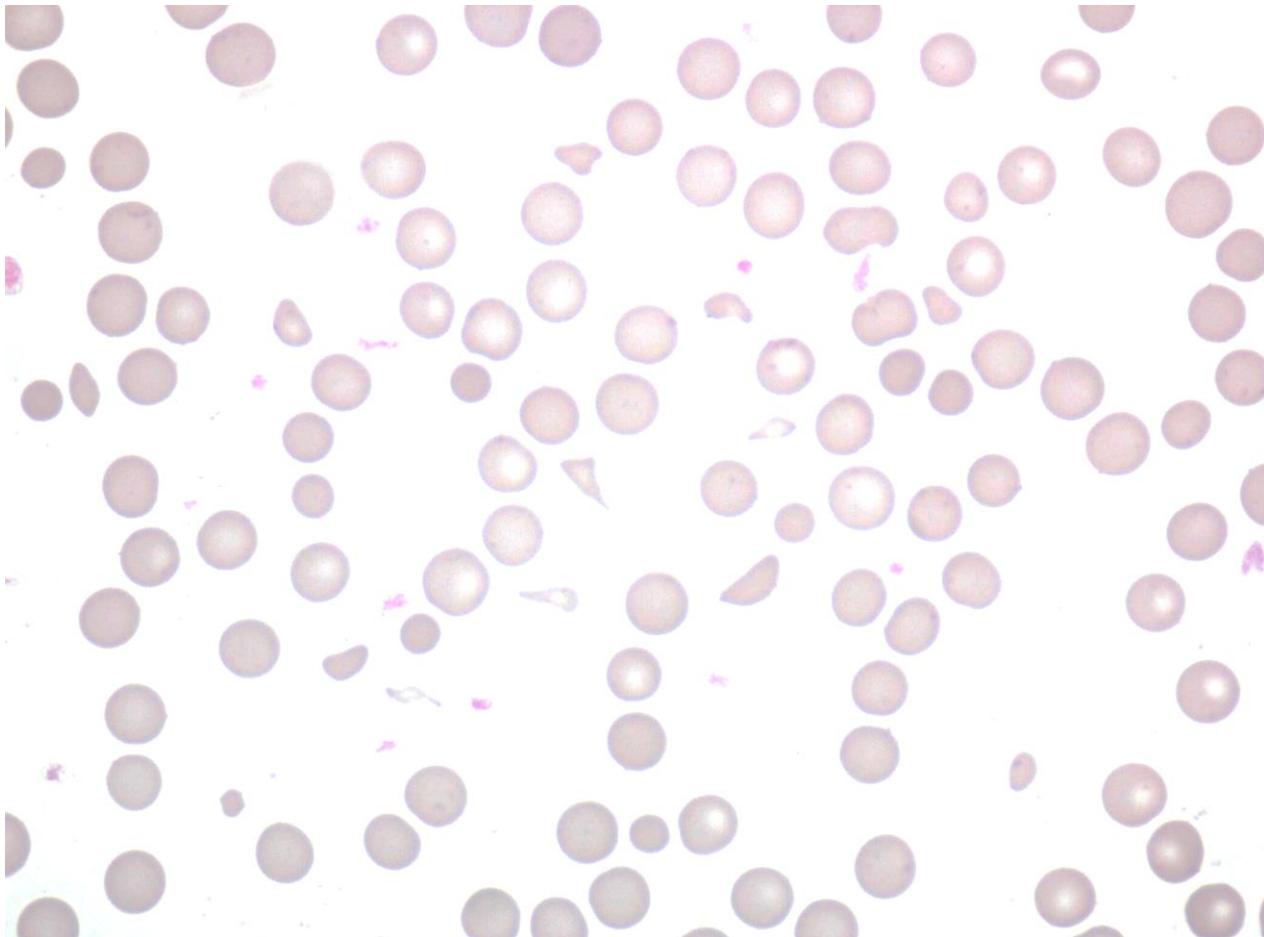


RBC	4.90 M/L	3.85 - 8.87	■
HCT	33.8 %	37.3 - 51.7	■
HGB	11.3 g/dL	13.1 - 20.5	■
MCV	88.2 fL	81.8 - 93.9	■
MCH	23.1 pg	21.2 - 28.9	■
MCHC	33.4 g/dL	32.0 - 37.9	■
RDW	18.7 %	13.6 - 21.7	■
RETIC	4.3 %		
RETIC	215.2 K/uL	10.0 - 110.0	■
WBC	8.88 K/uL	5.09 - 16.76	■
%NEU	67.3 %		
%LYM	20.0 %		
%MONO	11.1 %		
%EOS	1.5 %		
%BASO	0.1 %		
NEU	6.51 K/uL	2.86 - 11.04	■
LYM	1.84 K/uL	1.09 - 3.10	■
MONO	1.08 K/uL	0.16 - 1.12	■
EOS	0.15 K/uL	0.08 - 1.23	■
BASO	0.01 K/uL	0.00 - 0.10	■
PLT	191 K/uL	140 - 464	■
MPV	— fL	8.7 - 13.2	■
PDW	— fL	9.1 - 19.4	■
PCT	— %	0.14 - 0.46	■

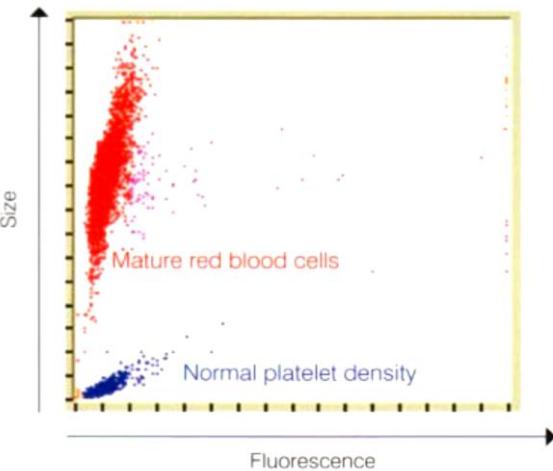


Case X

心瓣膜缺損，擾流造成RBC破壞：
紅血球碎片



Normal RBC Dot Plot (Canine)

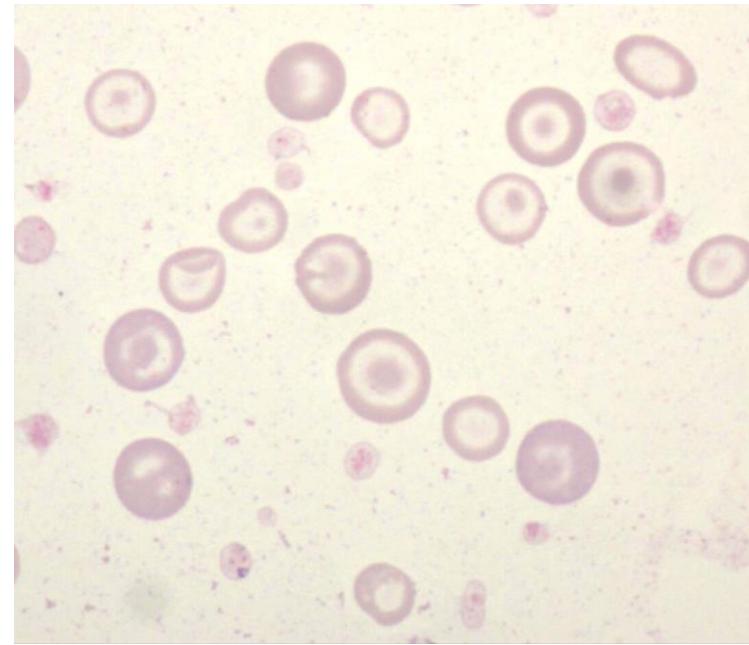


IDEXX

其他RBC壽命變短(溶血)原因

紅血球型態不良:

棘狀紅血球 (acanthocytosis)、靶狀紅血球(target cells)



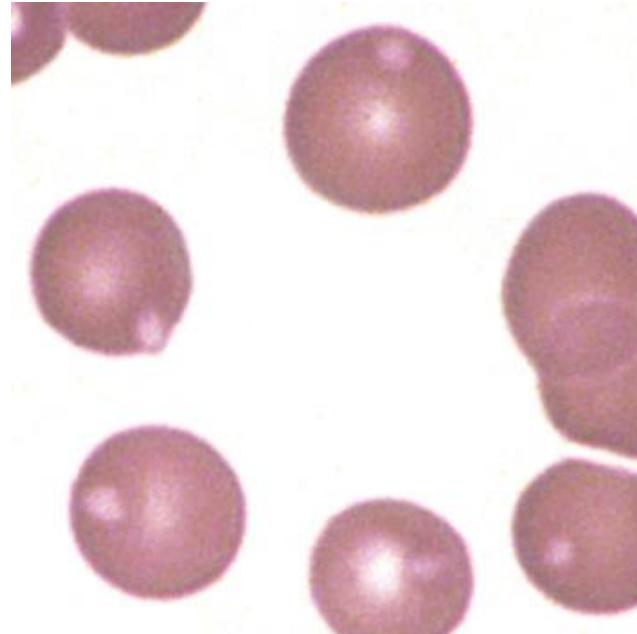
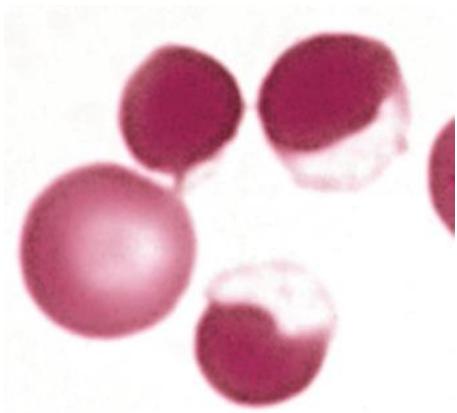
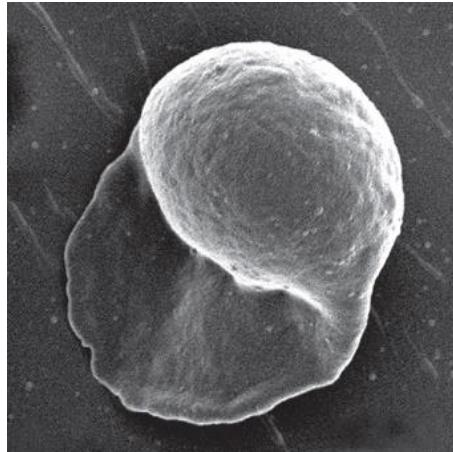
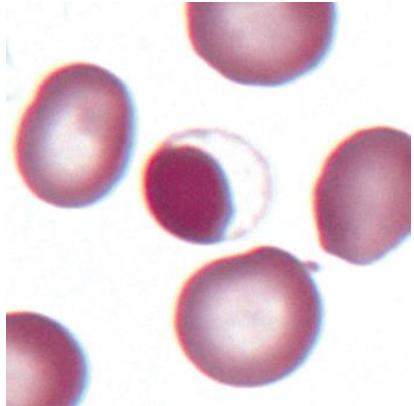
JW Harvey. Veterinary Hematology: A Diagnostic Guide and Color Atlas

細胞膜脂質代謝異常:
肝功能不良、磷酸與膽固醇失調、...

其他RBC壽命變短(溶血)原因

紅血球型態不良：

氧化性傷害→ 偏心紅血球(Eccentrocyte)、海因氏小體 (Heinz body)



JW Harvey. Veterinary Hematology: A Diagnostic Guide and Color Atlas

氧化性傷害：

藥物中毒、洋蔥中毒、酮酸血症...

IDEXX

Case.噹噹: 白掉不吃飯的貓



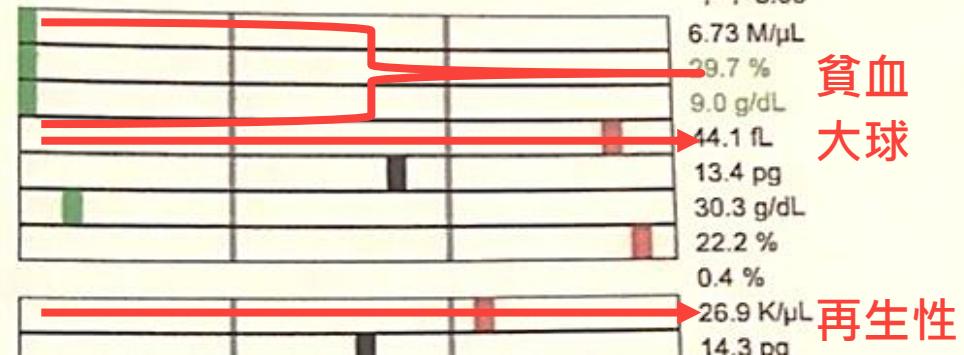
Jun 23 2019

- 5 yr , 雄性 , 短毛家貓
- 1 月時 , 有 *Mycoplasma hemofelis* 陽性 , 吃一個月 doxycycline
- 最近又怪怪的 , 白掉了 。(黏膜蒼白)
- 平常會外出的貓
- 身上有跳蚤

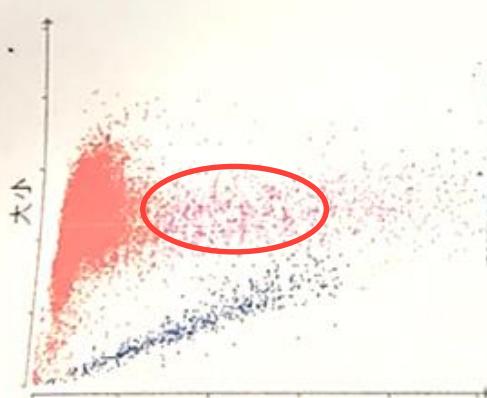
Case 噹噹：血液學檢查

檢驗項目	檢驗結果	參考區間	低	參考範圍	高
ProCyte Dx (2019年6月23日 上午 10:00)					
RBC	1.94 M/ μ L	6.54 - 12.20	低		2019/1/27
HCT	12.0 %	30.3 - 52.3	低		下午 3:06
HGB	3.1 g/dL	9.8 - 16.2	低		6.73 M/ μ L
MCV	61.9 fL	35.9 - 53.1	低		29.7 %
MCH	16.0 pg	11.8 - 17.3	高		9.0 g/dL
MCHC	25.8 g/dL	28.1 - 35.8	低		44.1 fL
RDW	33.9 %	15.0 - 27.0	高		13.4 pg
%RETIC	4.7 %		高		30.3 g/dL
RETIC	90.2 K/ μ L	3.0 - 50.0	高		22.2 %
RETIC-HGB	17.9 pg	13.2 - 20.8	高		0.4 %
...					26.9 K/ μ L
					再生性
					14.3 pg

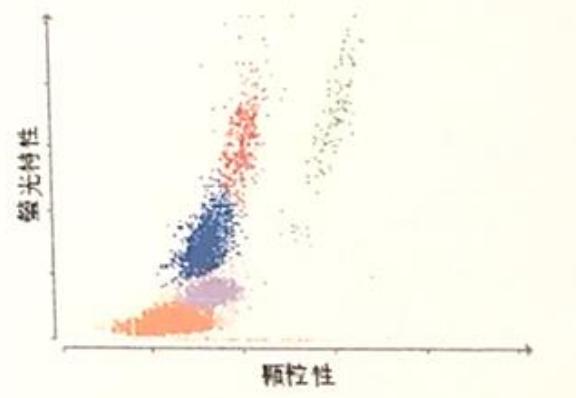
貧血
大球



紅血球測試



白血球測試

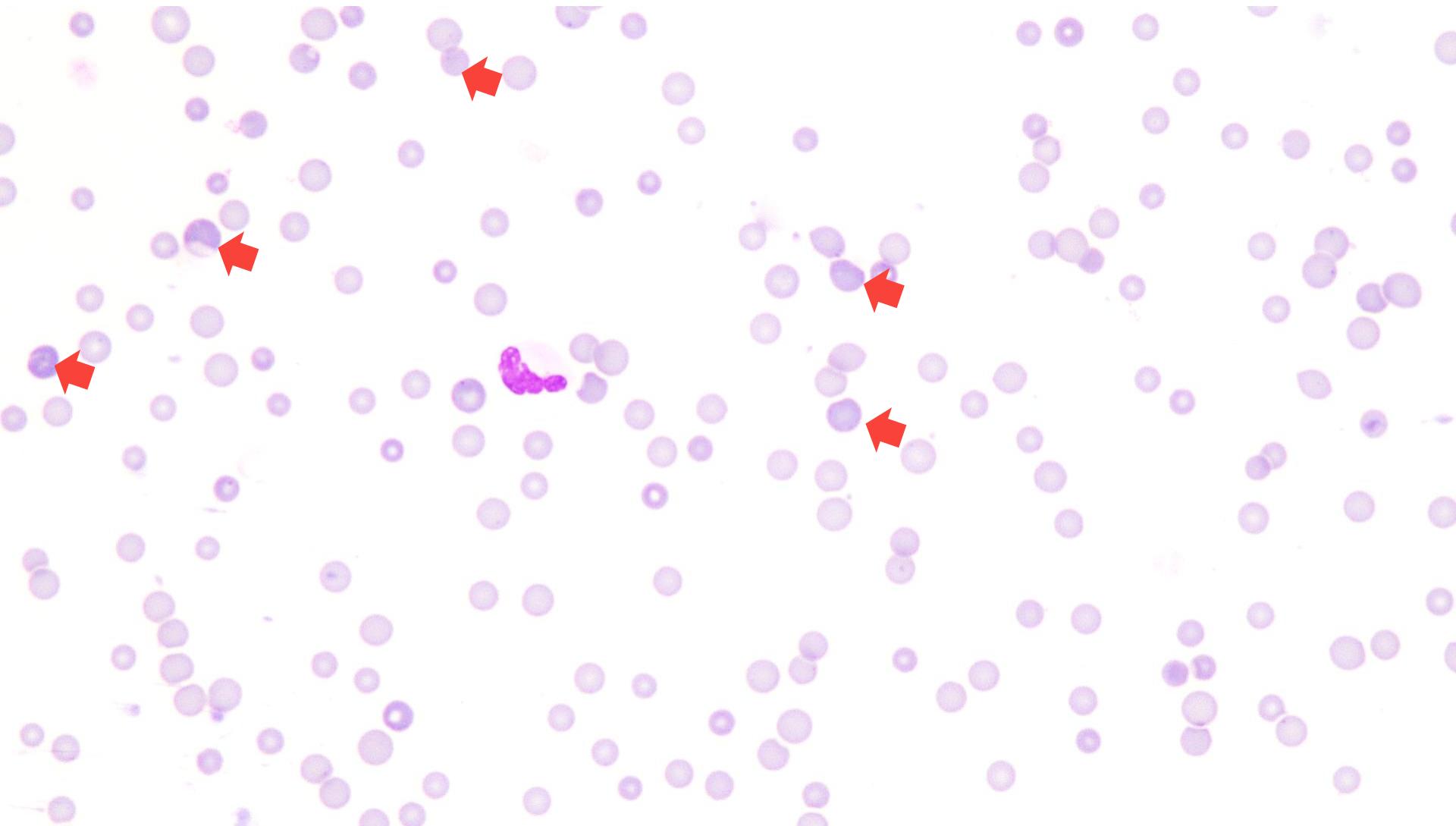


IDEXX

噹噹：血液學檢查

- WBC
- RET↑ ↙
- PLT↓

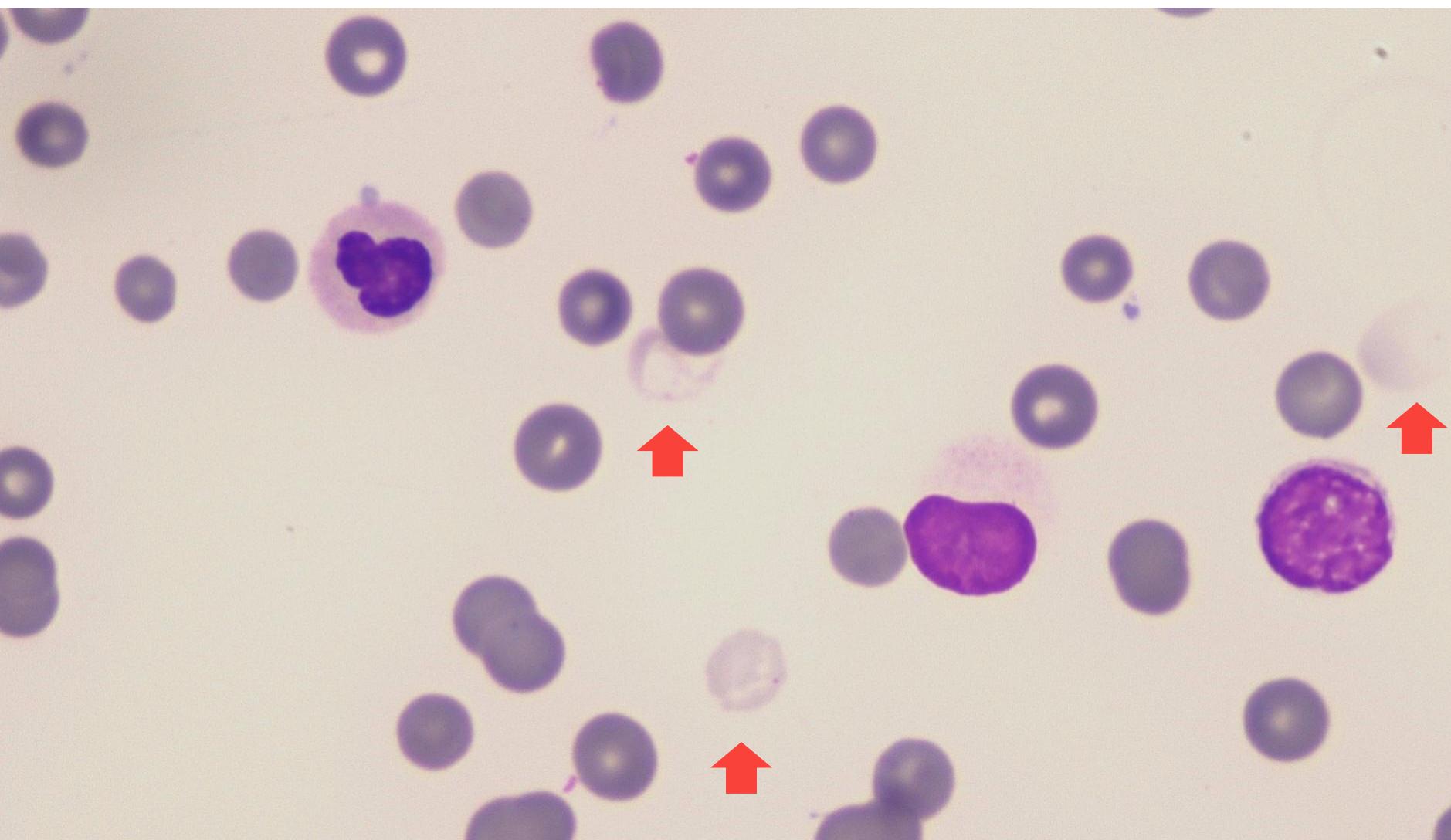
網織球(RET)數量增加，RBC大小不一。



噹噹：血液學檢查

網織球(RET)數量增加，RBC大小不一。

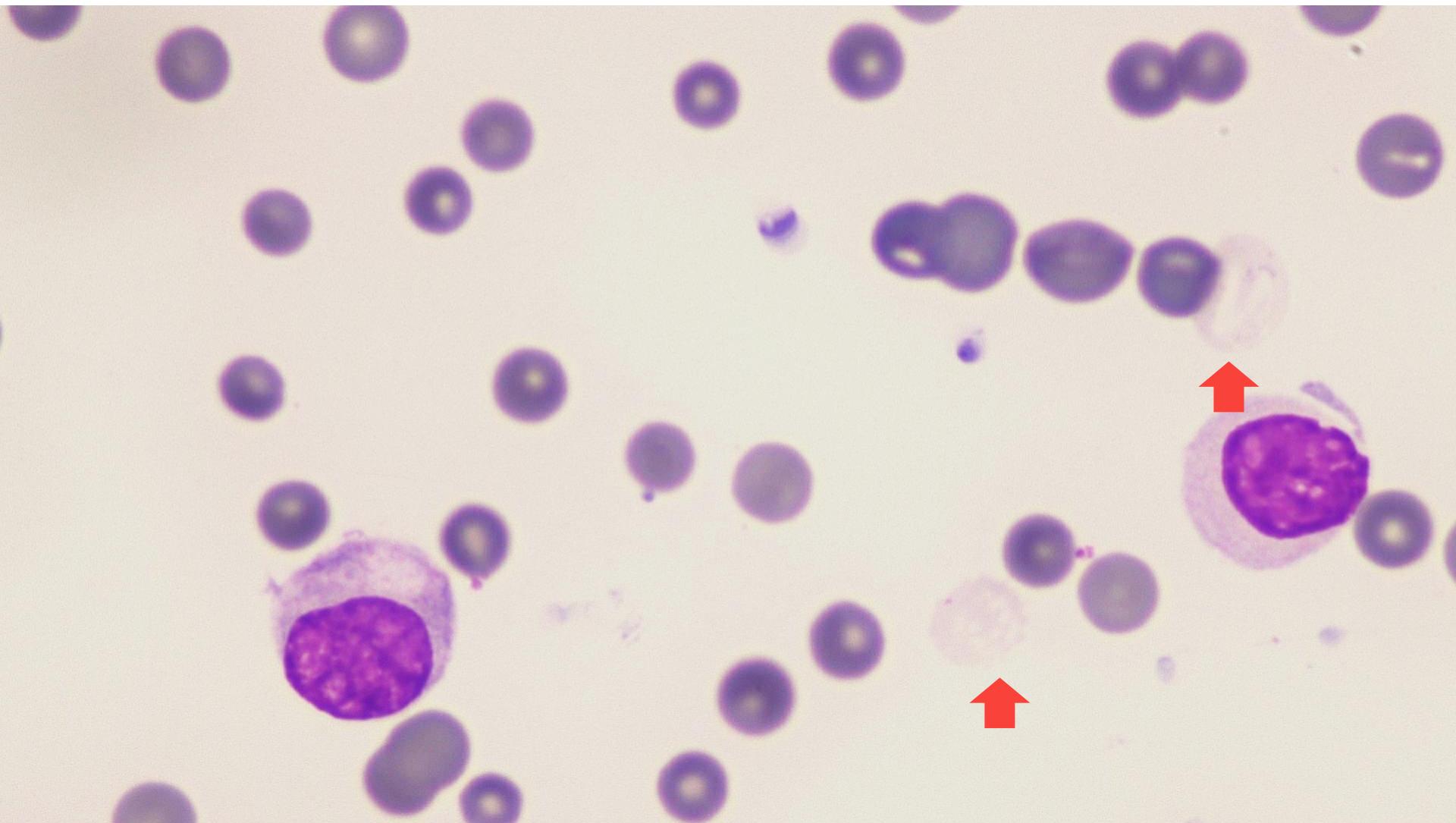
遭到破壞的RBC (ghost cell)，所以存在血管內溶血性貧血(RBC 生存時間變短)



噹噹：血液學檢查

網織球(RET)數量增加，RBC大小不一。

遭到破壞的RBC (ghost cell)，所以存在血管內溶血性貧血 (RBC 生存時間變短)





2019 Jun 27

 Graphing

Result Details ▾

6/27/19
2:35 AM

Molecular Diagnos...

Feline Calicivirus RealPCR	NEGATIVE
Cytauxzoon felis RealPCR	NEGATIVE
Bartonella spp. RealPCR	NEGATIVE
Anaplasma spp. RealPCR	NEGATIVE
Ehrlichia spp. RealPCR	NEGATIVE
Feline Coronavirus RealPCR	NEGATIVE
Mycoplasma haemofelis RealPCR	POSITIVE
Candidatus Mycoplasma haemominutum RealPCR	NEGATIVE
Candidatus Mycoplasma turicensis RealPCR	NEGATIVE
FeLV RealPCR	NEGATIVE
FIV RealPCR	NEGATIVE
Cryptococcus spp. RealPCR	NEGATIVE
Salmonella spp. RealPCR	NEGATIVE
Toxoplasma gondii RealPCR	NEGATIVE
Feline Panleukopenia Virus RealPCR	^a NEGATIVE

Fever of Unknown Origin RealPCR™ Panel-Feline
貓不明原因發燒病原偵測套組



噹噹 鄭

Feline | Scottish Fold | Male Neutered | 8y

2019 Jun 29 Jun 23 Jan 27 Jan 20

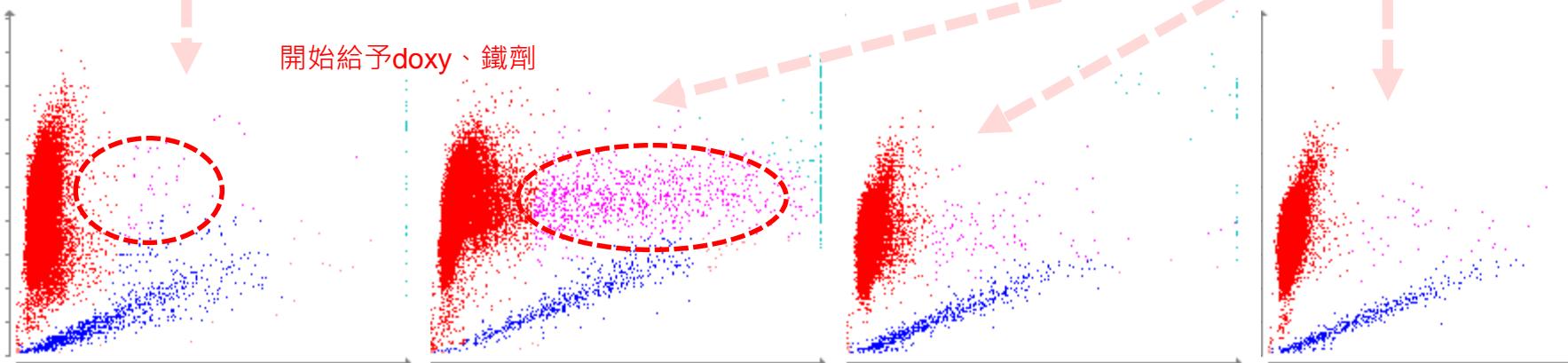
Mycoplasma Hemofelis +
吃了一個月的Doxycycline

怪怪的，貓白掉了

Graphing Result Details ▾

Hematology	6/29/19 6:00 PM		6/23/19 10:00 AM		1/27/19 3:06 PM		1/20/19 6:28 PM
> RBC	4.97	6.54 - 12.2 M/ μ L	1.94		6.73		7.44
> Hematocrit	31.8	30.3 - 52.3 %	12.0		29.7		32.0
> Hemoglobin	8.4	9.8 - 16.2 g/dL	3.1		9.0		10.0
> MCV	64.0	35.9 - 53.1 fL	61.9		44.1		43.0
> MCH	16.9	11.8 - 17.3 pg	16.0		13.4		13.4
> MCHC	26.4	28.1 - 35.7 g/dL	25.8		30.3		31.3
> RDW	36.4	15.0 - 27.0 %	33.9		22.2		22.4
> % Reticulocyte	0.2	%	4.7		0.4		0.2
> Reticulocytes	8.4	3 - 50 K/ μ L	90.2		26.9		11.9
> Reticulocyte Hemoglobin	19.5	13.2 - 20.8 pg	17.9		14.3		14.7
> Platelets	104	151 - 600 K/ μ L	24		96		76
> MPV	20.7	11.4 - 21.6 fL	25.3		20.2		20.2
> Plateletcrit	0.22	0.00 - 0.79 %	0.06		0.19		0.15

開始給予doxy、鐵劑



噹噹的治療目標

- **RBC 耗損增加**

- 創傷
- 失血
- 吸血的寄生蟲



- **RBC生存時間縮短**

- 血球生成不良
- 血球被感染 (血球受到破壞)
- 自體免疫
- 毒素



- ✓ Mycoplasma 感染，造成RBC破壞，細胞生存時間變短。
- ✓ 治療目標在於殺滅病原，減少RBC破壞。
- ✓ 控制跳蚤的感染，減少血液流失。同時，避免再度感染 Mycoplasma。
- ✓ 支持治療貧血的症狀，等待RBC生長回正常數量。

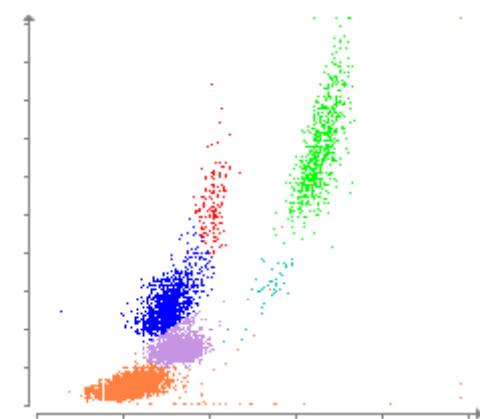
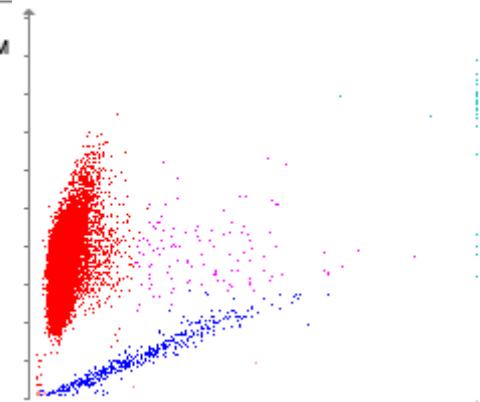
Hematology



10/5/19

4:15 PM

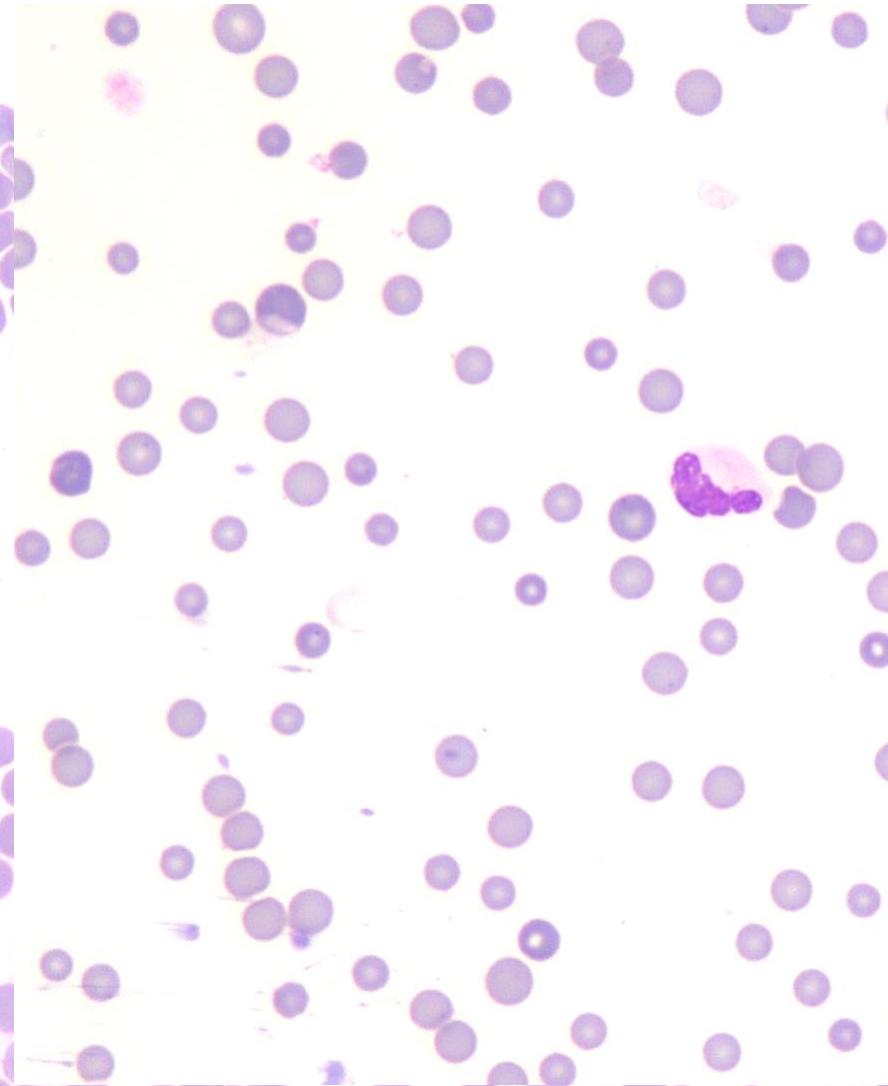
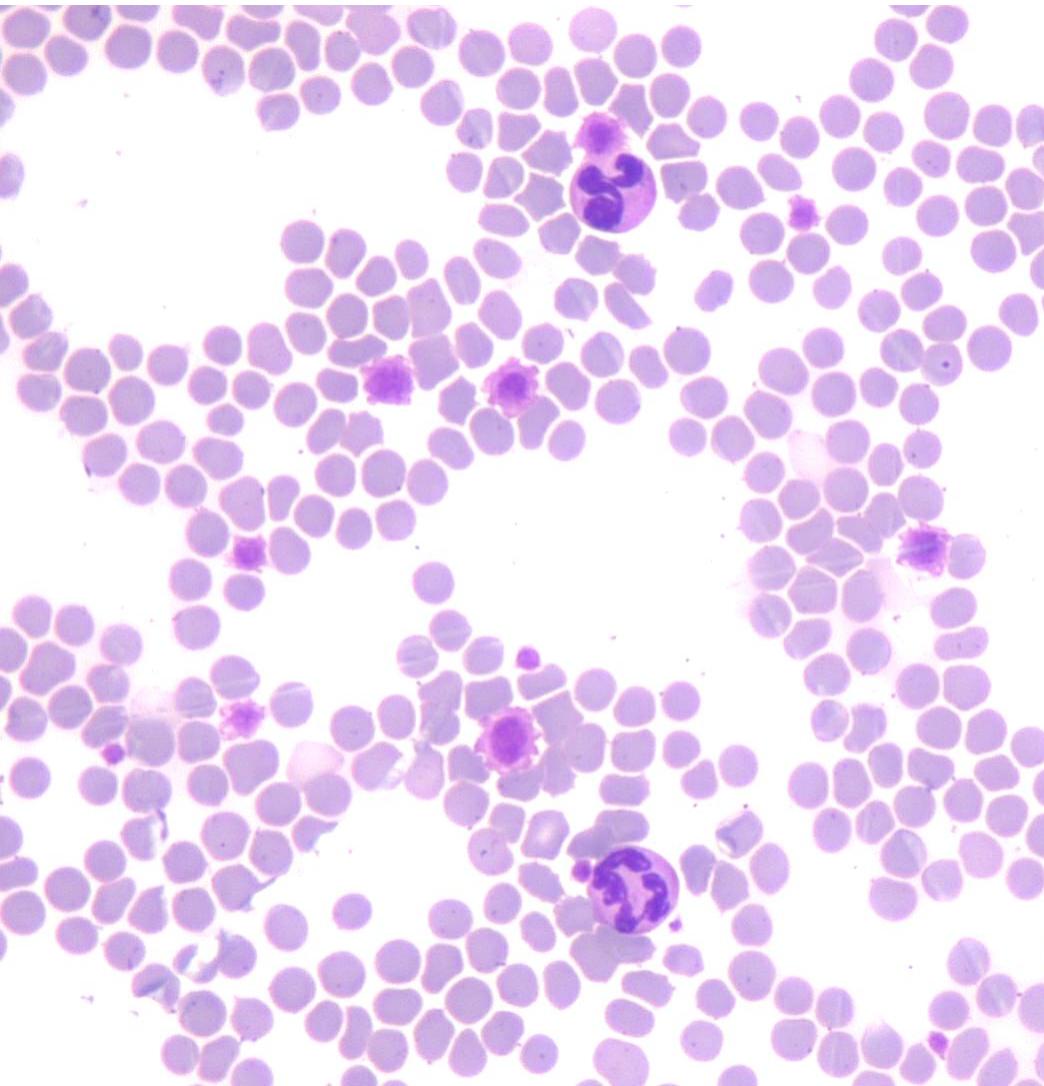
TEST	RESULT	REFERENCE VALUE			
RBC	7.78	6.54 - 12.2 M/ μ L		4.97	
Hematocrit	33.9	30.3 - 52.3 %		31.8	
Hemoglobin	10.8	9.8 - 16.2 g/dL		8.4	
MCV	43.6	35.9 - 53.1 fL		64.0	
MCH	13.9	11.8 - 17.3 pg		16.9	
MCHC	31.9	28.1 - 35.8 g/dL		26.4	
RDW	25.6	15.0 - 27.0 %		36.4	
% Reticulocyte	0.4	%		0.2	
Reticulocytes	33.5	3 - 50 K/ μ L		8.4	
Reticulocyte Hemoglobin	14.9	13.2 - 20.8 pg		19.5	
WBC	6.45	2.87 - 17.02 K/ μ L		3.74	
% Neutrophils	61.0	%		50.0	
% Lymphocytes	25.6	%		43.0	
% Monocytes	2.3	%		1.6	
% Eosinophils	10.5	%		4.3	
% Basophils	0.6	%		1.1	
Neutrophils	3.93	2.3 - 10.29 K/ μ L		1.87	
Lymphocytes	1.65	0.92 - 8.88 K/ μ L		1.61	
Monocytes	0.15	0.05 - 0.87 K/ μ L		0.06	
Eosinophils	0.68	0.17 - 1.57 K/ μ L		0.16	
Basophils	0.04	0.01 - 0.26 K/ μ L		0.04	
Platelets	87	151 - 600 K/ μ L		104	
MPV	20.9	11.4 - 21.6 fL		20.7	
Plateletcrit	0.18	0.17 - 0.86 %		0.22	

6/29/19
6:00 PM6/23/19
10:00 AM

Case 噹噹: 血液學檢查 Oct 22 2019

- WBC
- RET
- PLT

RBC型態與品質大幅改善。
血小板數量恢復正常。



不再生的貧血

如果今天是一個沒有再生的貧血.....

貧血的成因

- RBC 耗損增加
Increased blood loss.
(創傷, 失血, 吸血的寄生蟲)
- RBC 生存時間縮短
Increased blood cell destruction.
(血球生成不良, 血球被感染, 自體免疫, 毒素)

再生性的貧血

Regenerative Anemia

- RBC 生成減少
Decreased blood cell production.

OR



非再生性的貧血

Non-regenerative
Anemia

非再生性貧血的病因思考

- 骨髓的抑制

- 系統性炎症
- 艾莉希體感染
- 缺鐵
- 肝功不良

- 缺乏造血的訊號

- 慢性腎病 (EPO缺乏)

- 缺乏造血細胞

- 自體免疫 (Pure red cell aplasia)
- 骨髓壞死 (病毒感染 Ex. Parvo)
- 中毒 (藥物、Estrogen、中金屬)
- 腫瘤轉移到骨髓

- 癌化

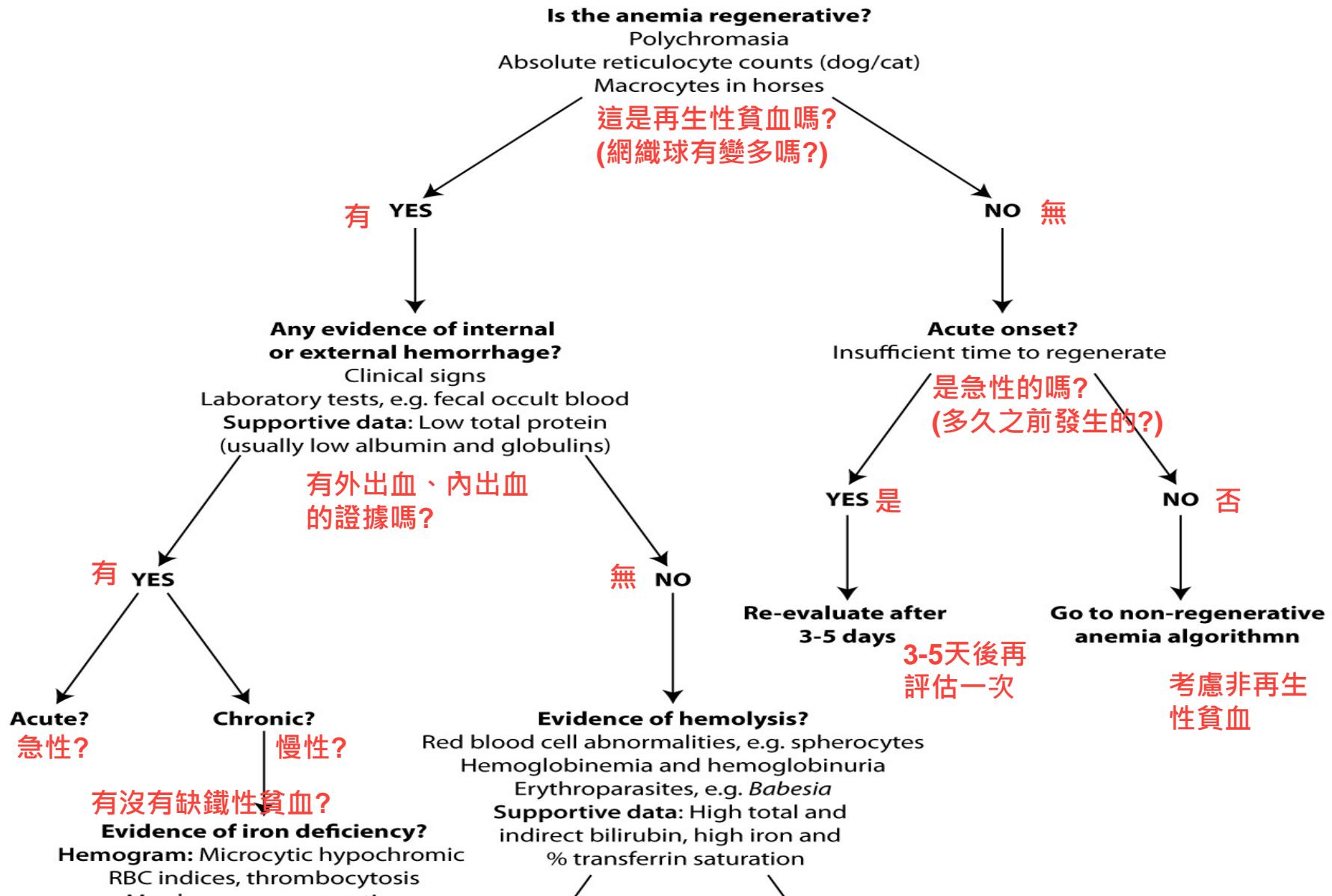
- 血球生成不良 (dysplasia)
- 血液腫瘤

✓ 許多預後不良的病因。
✓ 往往需要考慮骨髓採樣。

總結

利用網織球進行區別診斷

<https://eclinpath.com/hematology/anemia/mechanism-of-anemia/anemia-algorithmn/>



acute?

Chronic?

有再生性貧血 ·
但找不出出血的證據 ·
也沒有缺鐵...

有沒有缺鐵性貧血?

Evidence of iron deficiency?

Hemogram: Microcytic hypochromic RBC indices, thrombocytosis
May be non-regenerative
Blood smear: Hypochromasia, fragmentation
Chemistry: Low iron and % transferrin saturation
Bone marrow: Low iron

▼ Evidence of hemolysis? 有溶血的證據嗎?

Red blood cell abnormalities, e.g. spherocytes
Hemoglobinemia and hemoglobinuria
Erythroparasites, e.g. Babesia
Supportive data: High total and indirect bilirubin, high iron and % transferrin saturation

YES 有

NO 無

Hemolytic anemia

Review smear for causes

溶血性貧血
(觀察RBC型態)

Unknown mechanisms

Hemoglobinemia and hemoglobinuria?

Smear: Ghost RBC

血紅素尿、血紅素血症

Additional diagnostic tests,
as indicated, e.g. Coombs test

YES 有

NO 無

血管內溶血

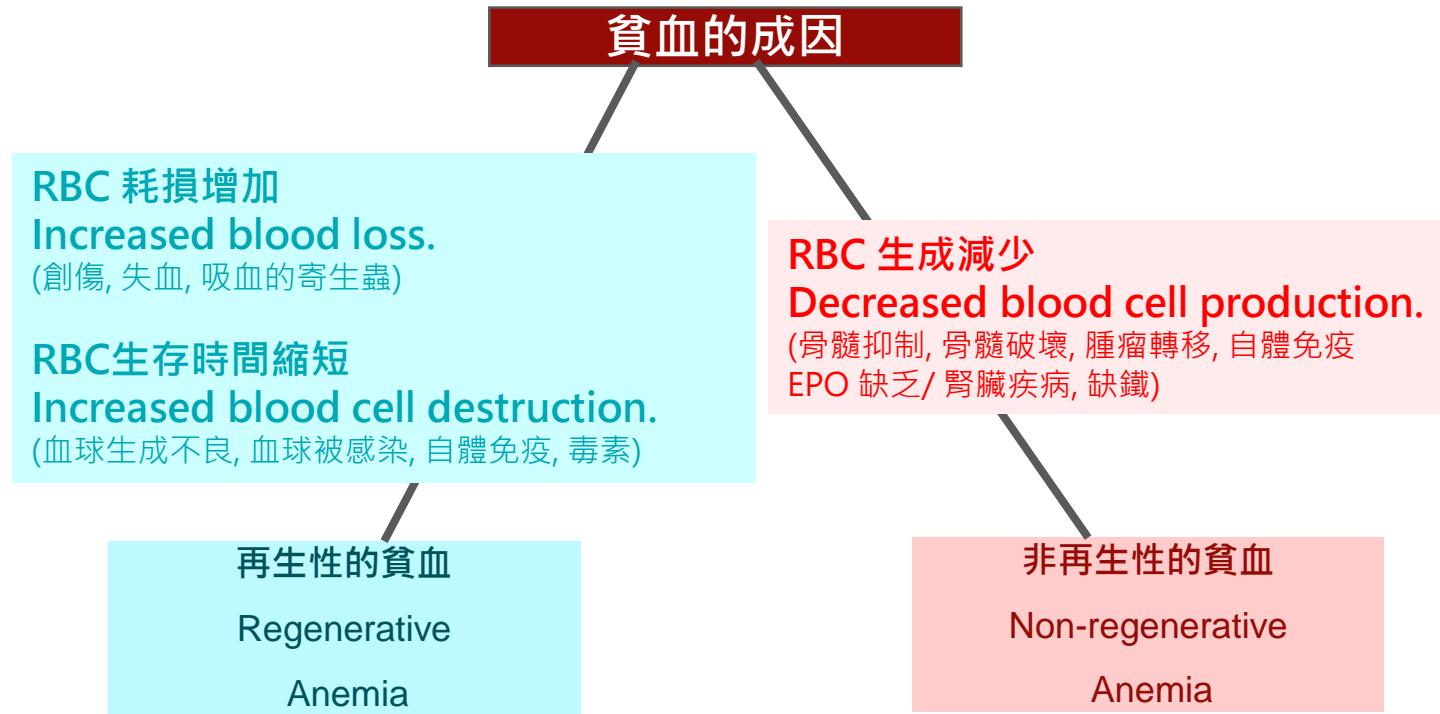
Intravascular and extravascular hemolysis

血管外溶血

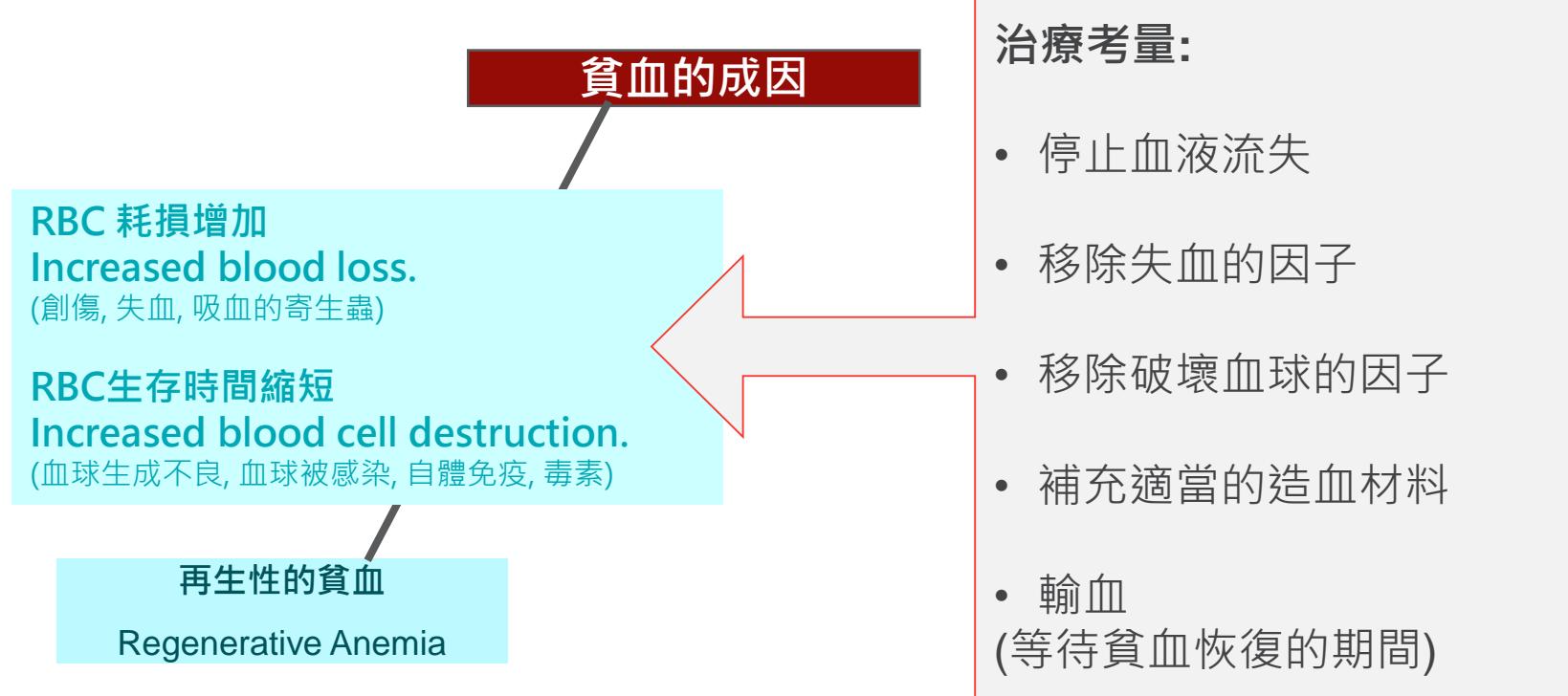
Extravascular hemolysis

IDEXX

區別貧血的種類：



治療方案的選擇



治療方案的選擇

治療考量:

- 移除抑制骨髓的因子
- 抑制腫瘤發展
- 嘗試供給造血因子
- 輸血 (延長生命)



貧血的成因

RBC 生成減少
Decreased blood cell production.
(骨髓抑制, 骨髓破壞, 腫瘤轉移, 自體免疫
EPO 缺乏/ 腎臟疾病, 缺鐵)

非再生性的貧血
Non-regenerative
Anemia

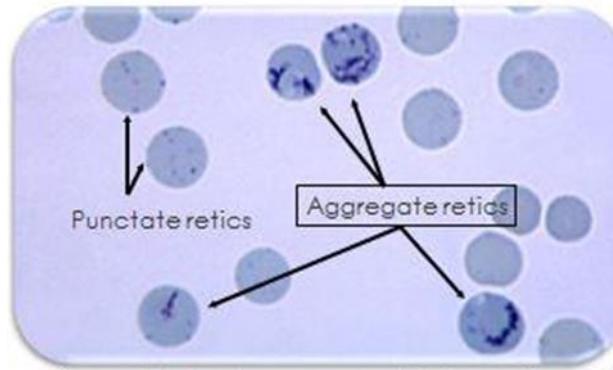
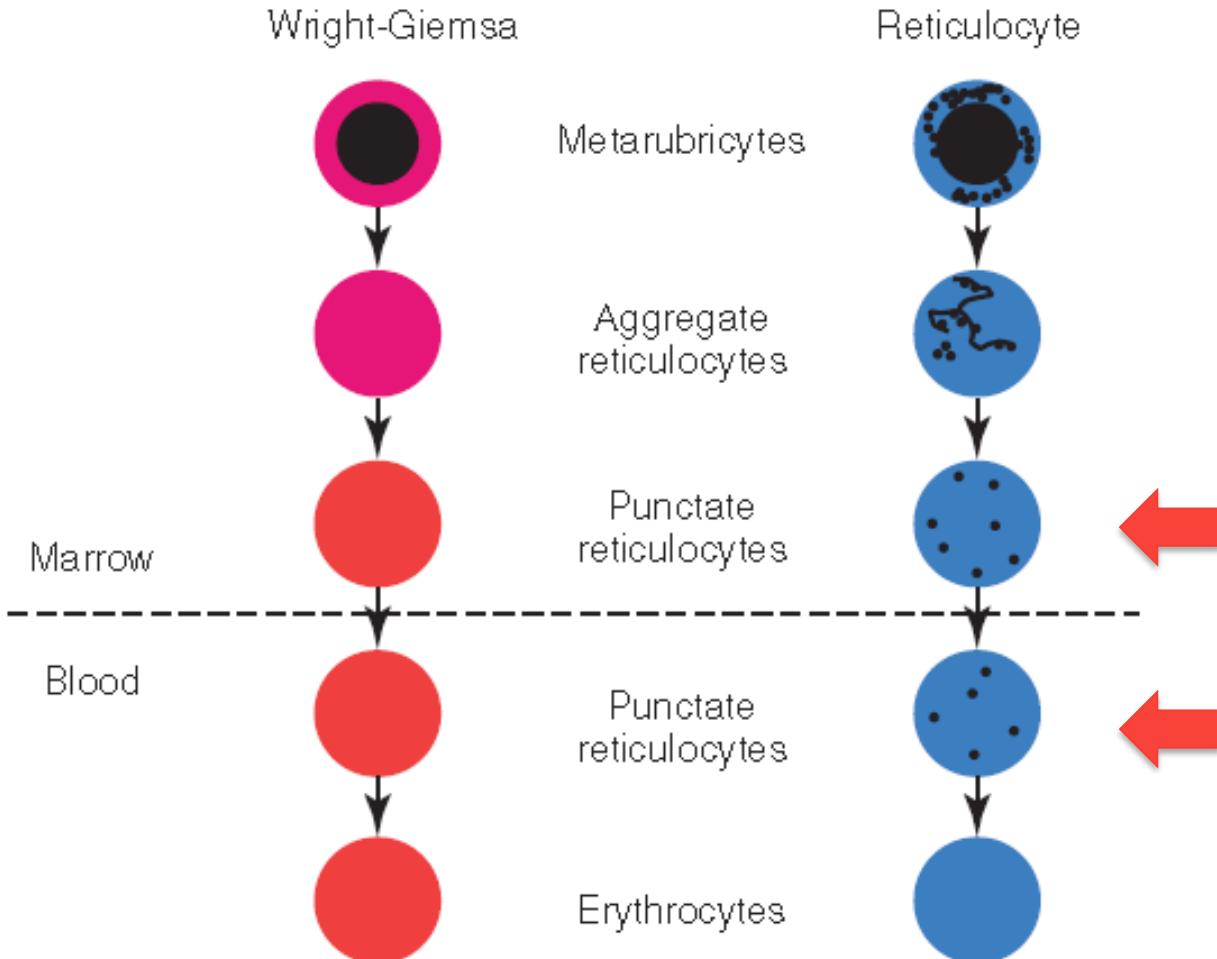
如果骨髓破壞不可逆轉
則預後極差!!

善用網織球的資訊

1. 幫助找到貧血的原因
2. 決定治療的方向
3. 評估預後

感謝大家凝聽！

貓星人的網織球



凝集型網織球

針點型網織球

為血液中主要的網織球型態