

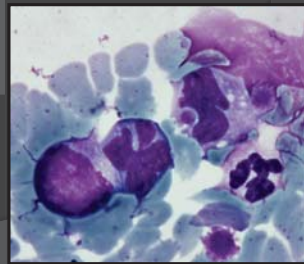
# Ehrlichiosis

## Etiology

- Tick-born disease
  - *Rhipicephalus sanguineus* – brown dog tick
- Rickettsia
- *Ehrlichia canis*
- *Ehrlichia platys* → *Anaplasma platys*

## Pathogenesis of *E. canis*

- Incubation period: 8 –20 days
- Mononuclear cells
  - Liver, spleen, lymph nodes
- Acute phase
- Subclinical phase
- Chronic phase



## Acute phase

- Physical examinations
  - Bleeding diathesis
    - Petechiation of mucous membranes or subcutaneous ecchymoses as a result of thrombocytopenia
  - Fever
  - Enlarged lymph nodes
  - Respiratory sign
  - Neurological signs

## Acute phase

- Blood examinations
  - Thrombocytopenia
  - Mild anemia
  - Leukopenia at beginning
  - Leukocytosis
  - Hyperglobulinemia 1-3 weeks after infection
  - Nonspecific : increased liver enzyme, BUN, creatinine

## Chronic phase

- Physical examinations
  - Petechiation of mucous membranes or subcutaneous ecchymoses
  - Anemia, pale mucous membranes
  - Splenomegaly, hepatomegaly
  - Uveitis, hyphema, retinal hemorrhage and detachment with blindness, corneal edema
  - Neurological signs

## Chronic phase

- ⦿ Blood examinations
  - Typically, pancytopenia (thrombocytopenia, severe anemia, leukopenia)
  - Hyperglobulinemia ( polyclonal gammopathy or monoclonal)
  - BUN, creatinine may elevate

## Definite diagnosis

- ⦿ Antibody test – commercial kit
  - Idexx –Snap®: HWD, *Ehrlichia Canis*, *Anaplasma platys*, Lyme
    - During the first 7 days post infection the titer consists IgA and IgM, and by the 20 days the majority of antibody is IgG.
- ⦿ Antigen detecting
  - PCR test from blood or spleen
- ⦿ Blood smear
  - Morula in mononuclear cell

## Treatment

- ⦿ Doxycycline 5-10mg/kg, bid
- ⦿ Tetracycline 22mg/kg, bid – tid
- ⦿ Oxytetracycline 25 mg/kg, tid, IV, IM
- ⦿ Prednisolone 0.5-1mg/kg sid- bid (depend on thrombocytopenia)
- ⦿ Androgen
  - Nandrolone 1.5mg/kg, im, qw
- ⦿ Blood transfusion (when PCV <15)
- ⦿ Vit B<sub>12</sub> (cyanocobalamine, 100-200µg/dog/day)

## CASE 1

## Signalment

- ⦿ Name: 寶寶
- ⦿ Species: Canine
- ⦿ Breed: Mixed
- ⦿ Sex: Intact female
- ⦿ Age: 4 Y/O
- ⦿ BW: 10.7 kg

## CC & Past history

- ⦿ Adopted for 5 months
- ⦿ Decreased activity and appetite for 2 weeks
- ⦿ Attended to LVH, fever (40.6 °C) and pancytopenia were noted
- ⦿ Vaccinated when adopted
- ⦿ Decrease defecate and urine volume

## Differential diagnosis

- Infectious disease
  - Bacterial infection (Ex. Leptospirosis)
  - Protozoal infection (Ex. Babesiosis)
  - Rickettsial infection (Ex. Ehrlichiosis)
  - Viral infection (Ex. CD, parvo)
- Immune-mediated hemolytic anemia
- Neoplasia

## Physical examinations

- BW: 10.7 kg, BT: 39.5 °C
- HR: 88bpm, RR: panting
- Normal hydration
- BCS: III/V
- Auscultation: unremarkable
- Pink to pale mm

## Blood exams

	8/12 (LVH)	8/13 (NTU)	Ref	
Hb	10.8	8.3	12-18	IDEXX 4in 1: A.P. Ab: (+) Ehrlichia canis Ab: (+) D. Immitis Ag: (-) Lyme borreliosis Ab: (-)
Hct	28.1	23.8	37-55	
RBC	4.3	3.71	5.5-8.5	
MCV	65.4	64	60-77	
MCHC	37.9	39	32-36	Leptospirosis MAT: (-)
WBC	3200	3400	6000-17000	
Platelets	35	29	200-900	Parvo kit: (-)
Albumin	1.5	2.2	2.3-4.0	
ALKP	160	132	20-150	
ALT	242	175	5-60	
AST	822	108	5-55	
t. bili		< 0.1	0-0.4	
BUN	18		7-27	-Normocytic, hyperchromic, non-regenerative anemia
Crea	0.8		0.5-1.8	-Leukopenia
Glucose	65	65	60-125	-Thrombocytopenia
TP	6.6	6.3	5.1-7.8	-Hypoalbuminemia
Autoagglutination		(-)		-Low A:G ratio
Parasite		(-)		
A/G	0.29	0.54		

## Tentative diagnosis & Treatment

- Acute phase Ehrlichiosis
- Doxycyclin 10mg/kg Q12H
- Sucrafate PRN

## Blood exams

	8/12 (LVH)	8/13 (NTU)	8/20	9/24	Ref
Hb	10.8	8.3	11.2	15.7	12-18
Hct	28.1	23.8	28.3	42	37-55
RBC	4.3	3.71	4.67	6.57	5.5-8.5
MCV	65.4	64	64.1	63.9	60-77
MCHC	37.9	39	37.5	37.3	32-36
WBC	3200	3400	9200	7900	6000-17000
Platelets	35	29	275	234	200-900
Albumin	1.5	2.2	2.8	3.4	2.3-4.0
ALKP	160	132	88	88	20-150
ALT	242	175	67		5-60
AST	822	108			5-55
t. bili		< 0.1	0.1	0.1	0-0.4
BUN	18				7-27
Crea	0.8				0.5-1.8
Glucose	65	65	82	90	60-125
TP	6.6	6.3	6.9	5.9	5.1-7.8
Autoagglutination		(-)	(-)	(-)	
Parasite		(-)	(-)	(-)	
A/G	0.29	0.54	0.69	1.36	
BT	40.6	39.5	38.5	38.5	

CASE 2

## Signalment

- Name: 匠匠
- Species: Canine
- Breed: Dachshund
- Sex: Castrated male
- Age: 6 Y/O
- BW: 6.8 kg

## CC & Past history

- For anemia and ecchymosis consultation
- Ehrlichiosis was diagnosed by IDEXX kit and treated at LVH about 2 months ago without improvement (Doxycyclin and steroids)
- Blood transfusion twice in 1 and 2 months ago respectively
- Normal activity and appetite
- Hematochezia noted yesterday

## Differential diagnosis

- Ehrlichiosis
- Babesiosis
- Immune-mediated hemolytic anemia
- Neoplasia
- Coagulopathy
- Viral infection
- Bone marrow insufficiency

## Blood exams

	8/16 (LVH)	8/23 (LVH)	8/27 (LVH)	9/21 (NTU)	Ref
Hb		4.1		0.5	12-18
Hct		10.3		10	37-55
RBC	3.74	1.54	4.62	3.5	5.5-8.5
MCV		67.1		64	60-77
MCHC		39.5		40.8	32-36
WBC	800	800	700	400	6000-17000
Platelets	28		17	18	200-900
Albumin				2.7	2.3-4.0
ALKP				61	20-150
ALT				6	5-60
AST				17	5-55
t. bili				0.3	0-0.4
BUN				10	7-27
Crea				0.6	0.5-1.8
Glucose				107	60-125
TP				6.5	5.1-7.8
Autoagglutination				(-)	
Parasite				(-)	
A/G				0.71	

IDEXX 4in 1:  
 A.P. Ab: (+)  
 Ehrlichia canis Ab: (+)  
 D. Immitis Ag: (-)  
 Lyme borreliosis Ab: (-)

Parvo kit: (-)

APTT: 14.9 / PT: 7.7

-Normocytic, hyperchromic, non-regenerative anemia  
 -Leukopenia  
 -Thrombocytopenia

## Tentative diagnosis

- Ehrlichiosis (Chronic phase)
- Babesiosis
- Immune-mediated hemolytic anemia
- Neoplasia
- Coagulopathy
- Viral infection
- Bone marrow insufficiency

## Treatment

- Blood transfusion (150ml = 21ml/kg)
  - Diphenhydramine 2 mg/kg IV

	9/21 Before	9/21 After	Ref
Hb	6.5	8.6	12-18
Hct	16	22.3	37-55
RBC	2.5	3.63	5.5-8.5
MCV	64	61.9	60-77
MCHC	40.8	38.3	32-36
WBC	400	2000	6000-17000
Platelets	18	36	200-900

- Expected PCV:  $21/20 \times 8 + 16 = 24.4\%$ 
  - Ongoing losing might be considered
- Doxycyclin 10 mg/kg Q12H
- Sucralfate, Gelfos

## Follow up

	9/21 (NTU)	9/21 (After)	9/26	11/2	11/30	12/21	2/1	5/1	8/30	1/10	3/21	7/11	Ref
Hb	15.5	8.6	11.1	8.1	10.3	10.6	12.2	13.6	13.6	15.6	16.8	16.7	12-18
Hct	16	22.5	28.2	31.3	30	31.6	35.2	38.4	39.6	43.8	46.8	47.6	37-55
RBC	2.5	3.05	4.7	3.46	4.82	5.06	6.1	5.94	6.5	7.33	7.89	7.80	5.5-8.5
MCV	64	61.9	62.1	61.6	62.3	61.7	57.7	64.6	60.9	59.8	59.3	61	60-77
MCHC	40.8	38.3	37.9	38.3	34.4	34.2	34.7	35.4	34.3	35.6	35.9	35.1	32-36
WBC	460	2000	500	1400	1300	1400	2800	1700	2500	2700	3100	5300	6000-17000
Platelets	16	46	30	38	60	100	33	36	93	43	132	116	200-900
Albumin	2.7		2.9	2.8	3.3		3.9	3.2	3.0	3.4	3.4	3.4	2.3-4.0
ALKP	61						57			52		95	20-150
ALT	6						34			30		32	5-60
AST	17						24			36		27	5-55
t. bili	0.3												0-0.4
Glucose	107		97	98	95		99	86	90	78	77	83	60-125
TP	6.5		7.1	6.9	7.4		7.2	6.3	6.4	6.4	6.6	6.8	5.1-7.8
Autoagglutination	(-)	(-)						(-)	(-)	(-)	(-)	(-)	
Parasite	(-)	(-)	(-)	(-)			(-)	(-)	(-)	(-)	(-)	(-)	
A/G	0.71		0.69	0.68	0.8		1.2	1.1	0.88	1.1	1.1	1.0	

Large  
Pit

## CASE 3

## Signalment

- Name: Jill
- Species: Canine
- Breed: Shi-tzu
- Sex: Intact male
- Age: 8 Y/O
- BW: 8.05 kg

## CC & past history

- Presenting at NTUVH for dental treatment and tooth extraction
- Regular HWD prevention and vaccination
- Ticks were ever noted before

## Physical Examinations

- BW: 8.05kg, BT: 38.8
- Normal hydration
- Hepatomegaly
- Splenomegaly

## Blood exams

	NTU	Ref
Hb	13.9	12-18
Hct	39.4	37-55
RBC	6.33	5.5-8.5
MCV	62.2	60-77
MCHC	35.5	32-36
WBC	1600	6000-17000
Platelets	219	200-900
Albumin	3.4	2.3-4.0
ALKP	123	20-150
ALT	29	5-60
BUN	17	7-27
Glucose	101	60-125
TP	9.6	5.1-7.8
Parasite	(-)	
A/G	0.55	

IDEXX 4in 1:  
Ehrlichia canis Ab: (+)

D. Immitis Ag: (-)  
Lyme borreliosis Ab: (-)

-Leukopenia

## Tentative diagnosis & Treatment

- Subclinical phase of Ehrlichiosis
- Doxycycline 10 mg/kg Q12H for 7 days

## Babesiosis

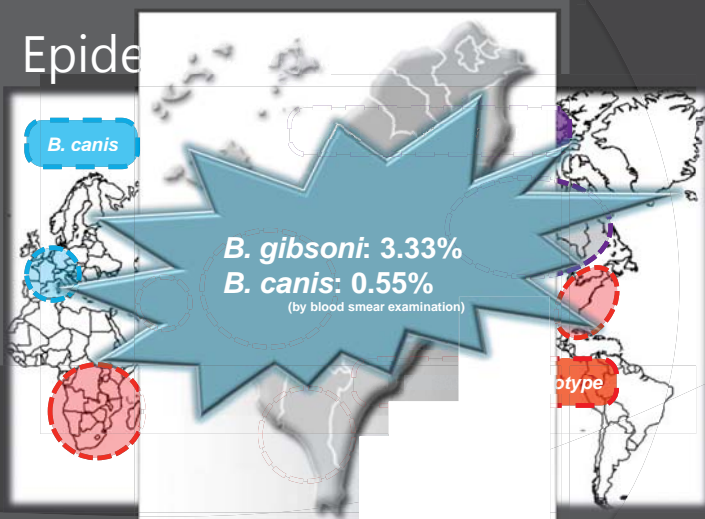
## Canine babesiosis

- Tick-borne disease
- Hemoprotzoan parasites
  - Genus *Babesia*
    - *Babesia canis* (*B. canis*)
    - *Babesia gibsoni* (*B. gibsoni*)
      - *B. gibsoni* Asian genotype
      - *B. gibsoni* North American genotype

## Transmission

- Ticks
  - *Haemaphysalis bispinosa* (*H. bispinosa*)
  - *Rhipicephalus sanguineus* (*R. sanguineus*)  
(Leisewitz *et al.*, 1996)
- Dog-to-dog transmission
  - Bitten wounds
    - American Pit Bull Terrier (APBT) in the USA  
(Birkenheuer *et al.*, 2005)
    - Tosa dog in Japan  
(Miyama *et al.*, 2005)
  - Blood transfusion  
(Jefferies *et al.*, 2007)
  - Transplacental transfusion  
(Fukumoto *et al.*, 2005)

## Epidemiology



## *B. gibsoni* Asian genotype

- Clinical findings
- Clinical laboratory findings
- Blood smear examinations
- Nucleic acid detection

## *B. gibsoni* Asian genotype

- **Clinical findings**
  - Anorexia
  - Lethargy
  - Fever
  - Weakness
  - Weight loss
- Clinical laboratory findings
- Blood smear examinations
- Nucleic acid detection

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## *B. gibsoni* Asian genotype

- Clinical findings
- Clinical laboratory findings
- Blood smear examinations
- Nucleic acid detection

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## *B. gibsoni* Asian genotype

- Clinical findings
- **Clinical laboratory findings**
  - Regenerative anemia
  - Thrombocytopenia
- Blood smear examinations
- Nucleic acid detection

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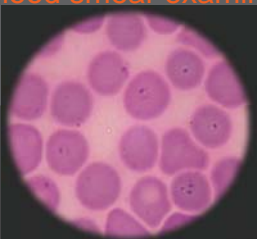
## *B. gibsoni* Asian genotype

- Clinical findings
- Clinical laboratory findings
- Blood smear examinations
- Nucleic acid detection

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## *B. gibsoni* Asian genotype

- Clinical findings
- Clinical laboratory findings
- **Blood smear examinations**



- Nucleic acid detection

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## *B. gibsoni* Asian genotype

- Clinical findings
- Clinical laboratory findings
- Blood smear examinations
- Nucleic acid detection

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# Treatment of babesiosis

- ◉ Diminazene aceturate
- ◉ Imidocarb dipropionate
- ◉ Clindamycin
- ◉ Atovaquone
- ◉ Phenamidine isethionate
- ◉ Doxycycline
- ◉ Metronidazole



Reduce parasitemia  
Eliminate pathogen completely

(Matsuu et al., 2004, Taboada, 2006)

# Combinations of drugs

- ◉ Atovaquone + Azithromycin (Birkenheuer et al., 2004)
- ◉ Clindamycin + Doxycycline + Metronidazole (Suzuki et al., 2007)
- ◉ Diminazine + Doxycycline (Birkenheuer et al., 1999)

# Combinations of drugs

- ◉ **Atovaquone + Azithromycin** (Birkenheuer et al., 2004)
  - Advantages
    - Elimination of infection
    - Suppression of parasitemia
      - Below the limit of detection
  - Disadvantages
    - Drug-resistant
    - More expensive
    - Not officially available



Diminazine + Imidocarb + Clindamycin (2012)

# Results

Total (30)

AA group (17)

CDI group (13)

Recovery  
52.9% (9/17)

Relapse  
41.2% (7/17)

Non-remission  
5.9% (1/17)

Recovery  
84.6% (11/13)

Relapse  
15.4% (2/13)

Questions! ?

