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LEPTOSPIROSIS : PATHOGENESIS AND RED CELL DESTRUCTION

A thesis presented in partial fulfilment of  
the requirements for the  
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## ABSTRACT

A study was made of the morphological changes in red blood cells (RBC's) from hamsters and calves during the development of haemoglobinaemia following infection with *Leptospira interrogans* serovars *ballum* and *pomona* respectively.

The major changes seen by scanning electron microscopy of RBC's from the haemoglobinaemic animals were spherocytosis and surface pitting. The major change seen by transmission electron microscopy was vacuolation of abnormally shaped RBC's with some vacuoles containing a small amount of a fine granular material. Few RBC's showed evidence of haemoglobin loss even though the animals from which the RBC's came were severely haemoglobinaemic. Those RBC's which did show haemoglobin loss contained membrane-bound dense granular inclusions in addition to the vacuoles observed in the fully haemoglobinated RBC's. The spherocytes from the haemoglobinaemic animals probably arose from echinocytes which were seen in prehaemoglobinaemic hamsters. Echinocytes seen in calves injected with 'toxin' can probably be considered as equivalent to echinocytes seen in the prehaemoglobinaemic hamsters. These echinocytes had membrane-bound portions of cytoplasm segregated from the remainder of the cytoplasm. It is thought that these portions of cytoplasm are defective and subsequently become digested in autophagocytic vacuoles with complete digestion resulting in the empty vacuoles or those containing a small amount of fine granular material as seen in the fully haemoglobinated RBC's. Inability of the cell to either fully digest or expel material within autophagocytic vacuoles may explain dense granular inclusions seen within partially haemoglobinated RBC's which are considered the most severely affected RBC's.

Present studies support other work that a 'toxin' elaborated by the organisms rather than mechanical damage is responsible for the

lesions observed. The original lesion is thought to be biochemical although biochemical studies were beyond the scope of the present work. This biochemical lesion is likely to be similar in all affected tissues. Sufficient biochemical and physiological differences exist between adults and neonates and between individuals of similar age of the same species, and between different animal species to explain the differences in susceptibility of RBC's to leptospiral 'toxins'.

RBC's from cattle, hamsters and humans suspended in non-immune plasma and incubated with *ballum* and *pomona* were never haemolysed while those suspended in saline were always haemolysed. Normal plasma thus has a protective effect. The protective action of plasma demonstrated *in vitro* required reconciliation with some conflicting findings of parallel studies *in vivo* in which RBC's were destroyed resulting in haemoglobinaemia. It therefore appears that another mechanism may be responsible for RBC destruction *in vivo*. Because RBC sequestration resulting in lowering of the PCV and haemoglobin occurred in the prehaemoglobinaemic animals, involvement of the reticulomacrophage system appeared likely. Other workers have suggested that RBC's which already have an abnormality may be further damaged or lysed within the splenic circulation. Thus in leptospiral infections, leptospiral 'toxins' may induce changes in RBC's leading to their sequestration within the spleen resulting in further damage and ultimately lysis and haemoglobinaemia.

The ground is now set for further studies to identify the putative biochemical lesions which would pave the way for development of new therapeutic regimes to prevent the more severe clinical features of the disease.

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## CONTENTS

	Page
ABSTRACT	(ii)
ACKNOWLEDGEMENTS	(iv)
CONTENTS	(vi)
LIST OF TABLES	(viii)
LIST OF FIGURES	(x)
LIST OF APPENDICES	(xviii)
INTRODUCTION	1
CHAPTER 1 LITERATURE REVIEW	2
CHAPTER 2 MATERIALS AND METHODS	35
CHAPTER 3 CLINICAL SIGNS AND CLINICAL PATHOLOGY OF <i>POMONA</i> INFECTED CALVES AND <i>BALLUM</i> INFECTED HAMSTERS	46
Experiment I : <i>ballum</i> infected hamsters	
Experiment V : <i>pomona</i> infected calves	
CHAPTER 4 MORPHOLOGICAL CHANGES IN RED BLOOD CELLS IN LEPTOSPIROSIS	80
Experiment I : <i>ballum</i> infected hamsters	
Experiment II : <i>ballum</i> infected hamsters	
Experiment III : <i>pomona</i> infected hamsters	
Experiment IV : bled hamsters (reticulocyte production)	
Experiment V : <i>pomona</i> infected calves	
Experiment VI : <i>balcanica</i> infected cattle	
Experiment VII : <i>ballum</i> infected human	

	Page
CHAPTER 5 PATHOLOGY OF HAEMOLYTIC LEPTOSPIRAL INFECTIONS OF CALVES AND HAMSTERS	95
Experiment I : <i>ballum</i> infected hamsters	
Experiment IV : bled hamsters (reticulocyte production)	
Experiment V : <i>pomona</i> infected calves	
CHAPTER 6 PATHOLOGY OF NON-HAEMOLYTIC LEPTOSPIRAL INFECTIONS OF HAMSTERS AND CATTLE	132
Experiment II : <i>ballum</i> infected hamsters	
Experiment III : <i>pomona</i> infected hamsters	
Experiment VI : <i>balcanica</i> infected cattle	
CHAPTER 7 <i>IN VITRO</i> HAEMOLYTIC STUDIES	160
Experiment A	
Experiment B	
Experiment C	
Experiment D	
CHAPTER 8 INTRAVASCULAR HAEMOLYSIS IN GAMMA IRRADIATED, <i>BALLUM</i> INFECTED HAMSTERS	183
Experiment VIII : <i>ballum</i> infected hamsters	
CHAPTER 9 GENERAL DISCUSSION	214
APPENDICES	
BIBLIOGRAPHY	

## LIST OF TABLES

		Page
Table 1-1	Summary of the major references pertaining to the pathology and pathogenesis of experimental and natural leptospiral infections of man and domestic animals	4-6
Table 1-2	Alterations in blood clotting factors during leptospirosis	18
Table 1-3	Circulating leucocytes	21
Table 1-4	Biochemical changes in the blood during leptospirosis	25
Table 1-5	Urinary changes during leptospirosis	28
Table 1-6	Cellular pathology of the kidney during leptospirosis	29-31
Table 2-1	Strains of leptospire, their field source and method of typing	37
Table 2-2	Dates of death of control and <i>ballum</i> infected hamsters from Experiment I, part 1.	40
Table 2-3	Treatment of calves in Experiment V, an experimental <i>pomona</i> infection	43
Table 3-1	Normal haematological values for ten hamsters aged 19-42 days used in Experiment I, part 1	50
Table 3-2	Normal haematological values for 12 calves 10-21 days of age	51

	Page	
Table 3-3	Data from selected hamsters demonstrating the decrease in PCV and haemoglobin levels, the increase in the MCHC and the alterations in icterus index, total protein and white blood cells	60
Table 5-1	Summary of clinical pathological results from <i>ballum</i> infected hamsters in Experiment I, part 2	105
Table 6-1	Clinical pathological data from euthanased hamsters infected with <i>pomona</i> in Experiment III	140
Table 6-2	Summary of clinical data from the hamsters infected with <i>pomona</i> : Experiment III, A comparison of three strains	141
Table 6-3	Summary of clinical pathological data from the hamsters infected with <i>ballum</i> : Experiment II, A comparison of five strains	142
Table 7-1	Results of Experiment B : Percentage of washed and unwashed hamster, cattle and human RBC's haemolysed by two strains of <i>pomona</i> and two strains of <i>ballum</i>	173
Table 7-2	Results of Experiment C : Percentage of washed and unwashed RBC's haemolysed by two strains of <i>pomona</i> up to 14 days post infection	175

## LIST OF FIGURES

## CHAPTER 3

Figures following page 58

- Fig. 3-1(i) Graph showing the changes in the PCV's of ten experimental calves, five of which were infected with *pomona* and two of which were injected with a *pomona* -derived 'toxin'.
- Fig. 3-1(ii) Graph showing the changes in the haemoglobin levels of ten experimental calves, five of which were infected with *pomona* and two of which were injected with a *pomona* -derived 'toxin'.

Figure following page 61

- Fig. 3-2 Microhaematocrit tubes of blood from hamsters with varying degrees of jaundice and haemoglobinaemia following infection with *ballum*.

Figures following page 65

- Fig. 3-3 Blood smear from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 3-4 Bone marrow smear from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 3-5 Bone marrow smear from a haemoglobinaemic calf infected with *pomona*.

Figures following page 67

- Fig. 3-6(i) Graph of the alteration of GGT levels in ten experimental calves, five of which were infected with *pomona* and two of which were injected with a *pomona*-derived 'toxin'.

- Fig. 3-6(ii) Graph of the alteration of AAT levels in ten experimental calves, five of which were infected with *pomona* and two of which were injected with a *pomona*-derived 'toxin'.

#### CHAPTER 4

Figures following page 89

Scanning electron microscope (SEM) preparations

- Fig. 4-1 RBC's from a control hamster.
- Fig. 4-2 Echinocytes from a non-haemoglobinaemic hamster infected with *ballum*.
- Fig. 4-3 Early development of spherocytes from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 4-4 Spherocytes from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 4-6 RBC's from a control calf.
- Fig. 4-7 Spherocytes and other abnormally shaped RBC's from a haemoglobinaemic calf infected with *pomona*.
- Fig. 4-8 Echinocytes from a calf injected with a *pomona*-derived 'toxin'.
- Fig. 4-9 RBC's from a leptospiraemic and non-haemoglobinaemic calf following infection with *pomona*.
- Fig. 4-10 RBC's and reticulocytes from a 'bled' hamster.
- Fig. 4-11 RBC's from a 'bled' hamster.
- Fig. 4-12 RBC's from a normal human.
- Fig. 4-13 RBC's and knizocytes from a leptospiraemic human infected with *ballum*.

Transmission electron microscope (TEM) preparations

- Fig. 4-14 Normal RBC's.

- Fig. 4-15 RBC showing changes typical of those seen in non-haemoglobinaemic hamsters following infection with *ballum* and calves following injection with a *pomona*-derived 'toxin'.
- Fig. 4-16 RBC's showing changes typical of those seen in non-haemoglobinaemic hamsters following infection with *ballum* and calves following injection with a *pomona*-derived 'toxin'.
- Fig. 4-17 Spherocytes from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 4-18 Spherocytes from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 4-19 Spherocytes and an abnormally shaped RBC from a haemoglobinaemic calf infected with *pomona*.
- Fig. 4-20 Low power view of abnormal RBC's from a haemoglobinaemic calf infected with *pomona*.
- Fig. 4-21 High power view of abnormal RBC's from a haemoglobinaemic calf infected with *pomona*.
- Fig. 4-22 Apparent discontinuity in the membrane of a RBC from a haemoglobinaemic calf.
- Fig. 4-23 Artefactual lines in hamster spherocyte.
- Fig. 4-24 Typical reticulocyte.

## CHAPTER 5

Figure following page 102

- Fig. 5-1 Post mortem appearance of calf 17 demonstrating lesions resulting from leptospiral induced haemoglobinaemia and haemoglobinuria.

Figures following page 117

### Histological Preparations

- Fig. 5-2 Normal appearance of the liver of control hamsters.

- Fig. 5-3            Liver from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-4            Kidney from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-5            Leptospire within the liver of a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-6            Leptospire within the kidney of a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-7            Normal appearance of a neonatal calf lens.

#### Electron Microscope Preparations

- Fig. 5-8            Normal hamster hepatocyte.
- Fig. 5-9            Hepatocyte from the 'bled' calf.
- Fig. 5-10           Hepatocyte from a non-haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-11           Hepatic macrophage containing phagocytosed RBC's in a haemoglobinaemic hamster following *ballum* infection.
- Fig. 5-12           Hepatic macrophage containing phagocytosed RBC's in a haemoglobinaemic calf following *pomona* infection.
- Fig. 5-13           Hepatic macrophage containing a phagocytosed leptospire in a hamster infected with *ballum*.
- Fig. 5-14           Hepatocytes from a calf injected with a *pomona*-derived 'toxin'.
- Fig. 5-15           Hepatocytes from a leptospiraemic non-haemoglobinaemic calf following infection with *pomona*.
- Fig. 5-16           Hepatocytes and the space of Disse in a leptospiraemic, non-haemoglobinaemic calf infected with *pomona*.
- Fig. 5-17           Erythrophagocytosis in a normal hamster spleen.

- Fig. 5-18            Contact between a mononuclear cell and a RBC within the spleen of a hamster infected with *ballum*.
- Fig. 5-19            Sequestration of RBC's within the spleen of a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-20            Splenic macrophage containing a leptospire in a hamster following *ballum* infection.
- Fig. 5-21            Reticular cell structures within the spleen of a hamster following infection with *ballum*.
- Fig. 5-22            Epithelial cells from the kidney of a haemoglobinaemic calf infected with *pomona*.
- Fig. 5-23            Epithelial cells and the lumen of a proximal tubule of a haemoglobinaemic hamster following a *ballum* infection.
- Fig. 5-24            Epithelial cells and the lumen of a proximal convoluted tubule of a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-25            Glomerular capillary and endothelial cells from a haemoglobinaemic hamster infected with *ballum*.
- Fig. 5-26            Glomerular capillary from a haemoglobinaemic hamster following a *ballum* infection.
- Fig. 5-27            Migrating leptospire in the kidney of a hamster infected with *ballum*.
- Fig. 5-28            Leptospires associated with abnormal microvilli in a proximal convoluted tubule of a calf infected with *pomona*.
- Fig. 5-29            Leptospires associated with normal microvilli in a proximal convoluted tubule of a calf infected with *pomona*.

## CHAPTER 6

Figures following page 151.

### Histological Preparations

- Fig. 6-1            Hepatocyte dissociation in a hamster infected with *pomona*.

Fig. 6-2            Hepatocyte vacuolation in a hamster infected with *pomona*.

Fig. 6-3            Renal lesions in a hamster following infection with *pomona*.

#### Electron Microscope Preparations

Fig. 6-4            Hepatocyte from a hamster following infection with *pomona*.

Fig. 6-5            Hepatocyte from a hamster following infection with *pomona*.

Fig. 6-6            Cytoplasmic detail of a hepatocyte from a hamster infected with *pomona*.

Fig. 6-7            Cytoplasmic detail of a hepatocyte from a hamster infected with *pomona*.

Fig. 6-8            Degenerating hepatic mitochondria from a hamster infected with *pomona*.

Fig. 6-9            Leptospire within the liver of a hamster following a *pomona* infection.

Fig. 6-10           Phagocytosed leptospores within a splenic macrophage from a hamster infected with *pomona*.

Fig. 6-11           High power view of the phagocytosed leptospores.

Fig. 6-12           Abnormally shaped mitochondria within a splenic macrophage from a hamster infected with *pomona*.

Fig. 6-13           Cytoplasmic inclusions within a splenic macrophage of a hamster infected with *pomona*.

Fig. 6-14           Intracellular leptospire within a splenic macrophage from a hamster following a *pomona* infection.

Fig. 6-15           Apex of an epithelial cell from the proximal convoluted tubule of a hamster infected with *pomona*.

Fig. 6-16           Cytoplasmic detail from an epithelial cell of a proximal convoluted tubule of a hamster infected with *pomona*.

- Fig. 6-17            Leptospire migrating between epithelial cells  
of a proximal convoluted tubule of a hamster following  
infection with *pomona*.

## CHAPTER 7

Figures following page 173

- Fig. 7-1(i)            Test tubes containing unwashed calf RBC's following  
incubation with *pomona*, *balcanica*, *hardjo*, distilled water  
and culture media.
- Fig. 7-2(ii)            Test tubes containing washed calf RBC's following  
incubation with *pomona*, *balcanica*, *hardjo*, distilled water  
and culture media.
- Fig. 7-2(i)            Test tubes containing unwashed calf RBC's following  
incubation with *pomona*, *ballum*, distilled water and  
culture media.
- Fig. 7-2(ii)            Test tubes containing washed calf RBC's following  
incubation with *pomona*, *ballum*, distilled water  
and culture media.
- Fig. 7-3                SEM appearance of washed cattle RBC's immediately  
after combination with a *pomona* culture.
- Fig. 7-4                SEM appearance of washed cattle RBC's six hours  
after incubation with a *pomona* culture.
- Fig. 7-5                SEM appearance of washed cattle RBC's 18 hours  
after incubation with a *pomona* culture
- Fig. 7-6                Graph showing the decrease in foetal haemoglobin  
in neonatal calves.

## CHAPTER 8

Following page 197

- Fig. 8-1                SEM appearance of RBC's from a control hamster.
- Fig. 8-2                SEM appearance of echinocytes from a hamster five  
days after irradiation.

Fig. 8-3 SEM appearance of spherocytes from a haemoglobinaemic hamster in six days following irradiation and infection with *ballum*.

Figures following page 203

Fig. 8-4 Histological appearance of the spleen of a hamster eleven days following irradiation.

Fig. 8-5 Histological appearance of the bone marrow of a hamster five days following irradiation.

## CHAPTER 9

page 217

Fig. 9-1 Progression of infection during leptospirosis

## LIST OF APPENDICES

- APPENDIX I Paper: Colostral transfer of gamma glutamyl transpeptidase in calves
- APPENDIX II Letter: A rapid method for the detection of leptospiraemia
- APPENDIX III Abstract: Morphological changes in red blood cells of calves and hamsters with leptospirosis
- APPENDIX IV Paper: Experimental infection of sheep and cattle with *Leptospira interrogans* serovar *balcanica*
- APPENDIX V Preparation of tissue for electron microscopic examination
- APPENDIX VI Summary of abbreviations for clinical pathological data and bone marrow differentials
- APPENDIX VII a) Clinical pathological data from control hamsters of Experiment I, part I, euthanased on day 0  
b) Bone marrow differentials of control hamsters from Experiment I, part I, euthanased on day 0
- APPENDIX VIII a) Clinical pathological data from *ballum* infected hamsters of Experiment I, part I euthanased on day 1, am  
b) Bone marrow differentials of *ballum* infected hamsters from Experiment I, part I, euthanased on day 1, am
- APPENDIX IX a) Clinical pathological data from *ballum* infected hamsters of Experiment I, part I, euthanased on day 2, am  
b) Bone marrow differentials of *ballum* infected hamsters from Experiment I, part I, euthanased on day 2, am
- APPENDIX X a) Clinical pathological data from *ballum* infected hamsters of Experiment I, part I, euthanased on day 3, am  
b) Bone marrow differentials of *ballum* infected hamsters from Experiment I, part I, euthanased on day 3, am

- APPENDIX XI a) Clinical pathological data from *ballum* infected hamsters of Experiment I, part I, euthanased or found dead on day 4, am
- b) Bone marrow differentials of *ballum* infected hamsters from Experiment I, part I, euthanased on day 4, am
- APPENDIX XII a) Clinical pathological data from *ballum* infected hamsters from Experiment I, part I, euthanased or found dead on day 4, pm
- b) Bone marrow differentials of *ballum* infected hamsters from Experiment I, part I, euthanased on day 4, pm
- APPENDIX XIII a) Clinical pathological data from *ballum* infected hamsters of experiment I, part I, euthanased on day 5, am
- b) Bone marrow differentials of *ballum* infected hamsters from Experiment I, part I, euthanased on day 5, am
- c) Organ weight/body weight ratios from *ballum* infected hamsters of Experiment I, part I, found dead on day 5, am
- APPENDIX XIV a) Clinical pathological data from control hamsters of Experiment I, part I, euthanased on day 6
- b) Bone marrow differentials of control hamsters from Experiment I, part I, euthanased on day 6
- APPENDIX XV Means, standard deviations and ranges of organ weight: body weight rations of ten untreated control hamsters from Experiment I, part I.
- APPENDIX XVI Clinical pathological data from *pomona* infected calf 11
- APPENDIX XVII Clinical pathological data from 'toxin' injected calf 12
- APPENDIX XVIII Clinical pathological data from 'toxin' injected calf 13
- APPENDIX XIX Clinical pathological data from *pomona* infected calf 14
- APPENDIX XX Clinical pathological data from *pomona* infected calf 15
- APPENDIX XXI Clinical pathological data from *pomona* infected calf 16
- APPENDIX XXII Clinical pathological data from *pomona* infected calf 17
- APPENDIX XXIII Clinical pathological data from control calf 18
- APPENDIX XXIV Clinical pathological data from control calf 19
- APPENDIX XXV Clinical pathological data from the bled calf 20

- APPENDIX XXVI Bone marrow differentials from control and *poona* infected calves
- APPENDIX XXVII Haematological and urinary results from untreated control heifers
- a) Untreated control heifer: number 19
  - b) Untreated control heifer: number 67
- APPENDIX XXVIII Haematological and urinary results from negative control heifers
- a) Heifer inoculated with noninfected media: number 44
  - b) Heifer inoculated with noninfected liver and kidney homogenate: number 61
- APPENDIX XXIX Haematological and urinary results from heifers infected using *balcanica* infected hamster livers and kidneys
- a) *balcanica* infected heifer: number 1
  - b) *balcanica* infected heifer: number 53
  - c) *balcanica* infected heifer: number 59
  - d) *balcanica* infected heifer: number 64
- APPENDIX XXX Haematological and urinary results from heifers infected using *balcanica* culture
- a) *balcanica* infected heifer: number 27
  - b) *balcanica* infected heifer: number 39
  - c) *balcanica* infected heifer: number 41
  - d) *balcanica* infected heifer: number 62
- APPENDIX XXXI Results of *in vitro* Experiment A: Tube haemolysis of washed and unwashed RBC's taken from calves soon after birth to 47 days of age
- APPENDIX XXXII Haematological and bone marrow data of control and irradiated hamsters from Experiment VIII, part I
- APPENDIX XXXIII Summary of clinical and pathological data from Experiment VIII, part II
- APPENDIX XXXIV Bone marrow differentials of hamsters from Experiment VIII, part II