

The use of soluble aspirin as a means to limit ischemic necrosis of wing membrane in entangled Flying-foxes (*Pteropus* spp.) by increasing blood perfusion to traumatised tissue.

Dave Pinson and Connie Kerr.

Abstract. Within Australia, four large species of Pteropid bat regularly become entangled on barbed wire fences and fruit netting during their nightly foraging activities. Initial primary trauma typically includes rips and tears to wing membrane, and in some cases; deep laceration, bone fracture and damage to plagiopatagiales muscle strands. Secondary trauma caused by struggling and often vain efforts to free their selves can also occur, such as facial, dental and self-mutilating injuries to fine wing bones. Tertiary effects, dependent upon time trapped, will include dehydration, starvation, myiasis and infection. These tertiary effects will ultimately cause fatality. Many of these trapped animals are reported and promptly rescued by a network of wildlife care groups and following treatment for presented injuries, the natural progression associated with membrane trauma typically assumes the path of further necrotic dieback due to disrupted vascular flow to often large areas of dermal tissue; presenting mostly as dry, although sometimes wet gangrene. Areas of membrane necrosis can typically increase by up to 50% with regard to total surface area lost before healing commences. In many cases however, the total surface area lost can render animals incapable of future sustained flight, with such animals requiring euthanasia. For many years, a solution has been sought to limit this necrotic progression, with the aim of increasing the total number of animals fully recovering to successful release back into the wild. A three-year trial using soluble aspirin as a means to reduce fatal embolism evolved into the possibility of using aspirin to increase blood perfusion to damaged tissue. This trial has yielded highly promising results and we will show that administration of aspirin is both increasing successful release rates, with the added benefit of reducing average total time spent in rehabilitation.

Keywords: Aspirin; Necrotic; Perfusion; *Pteropus*; Wing Membrane.

Recommendations

Based on current research, findings, results, observations and accepted medical and veterinary practices, we would make the following recommendations to veterinarians and wildlife carers considering aspirin administration with regard to entangled flying-foxes:

- Following initial hydration, and taking into account preclusions listed below, we recommend oral administration to all flying-foxes rescued from any form of

entanglement; whether initially presenting with inflammatory signs or not, because thrombi and deep vascular disruption cannot be detected by means of visual examination.

- For cases of inflammation or likely inflammation (preventative) from entanglement, we recommend prompt administration. Our testing shows that playing *wait and see* would be counterproductive. Once ischemic damage is done, administration may be of limited to nil value.
- We recommend such administration for the full duration of the inflammatory phase and part of the proliferative phase (until new growth is observed). Thus a course of treatment would typically last anywhere from 5 – 14 days.
- For entangled animals held for observation only (i.e. no observable inflammation or damage on intake) we recommend cessation of treatment for such entangled animals still showing no inflammatory signs after 5 days.
- When administering aspirin, we can only recommend Aspro Clear 300® as it was the only aspirin product tested. With regard to solid (non-effervescent) aspirin, we have no data on aqueous solubility^[1] or indeed efficacy, and there is potentially too much room for error with crushing, dividing and mixing solid tablets.
- Despite current lack of veterinary experience regarding oral administration of aspirin to flying-foxes, we always recommend that veterinary consultation is sought regarding possible physical factors affecting administration (such as head trauma, shock, internal bleeding etc) and any proposed or existing concurrent use with other drugs.
- Do not administer concurrently with any other NSAIDs. Combining aspirin with other NSAIDs has been shown to further increase the risk of GI bleeding (Sørensen *et al.* 2000).
- Based on current lack of pharmacological testing, we do not recommend exceeding the active dose rate of 10mg/kg (aspirin).
- We recommend the use of aspirin for most cases (under veterinary advice) of actual or potential inflammation only i.e. barbed wire and fruit netting entanglement presenting with or likely to produce (preventative) inflammatory signs. Therefore we do not recommend its use as a primary general purpose analgesic for pain associated with conditions such as burns, bacterial abscess, mouth or dental damage, or laceration, as there are far better alternatives suited to such purposes.
- Once prepared, keep the solution refrigerated and discard after 3 days: making up fresh solution as required.

- All NSAIDs can produce renal dysfunction. For this reason, do not administer until the animal is fully hydrated. If in doubt, seek veterinary advice – and possible blood work with regard to creatinine. Normal creatinine range for flying-foxes: 18 - 70 $\mu\text{mol/L}$ or 0.04 - 0.09 mmol/L . Mean: 48 $\mu\text{mol/L}$ or 0.06 mmol/L (Pinson 2009).
- All NSAIDs can (on rare occasion) produce hepatic dysfunction. For this reason, do not administer to animals suffering from, suspected of, or showing signs of clinical malnutrition. If in doubt, seek veterinary advice – and possible blood work with regard to Blood Urea Nitrogen (BUN) and Total Serum Protein (TSP). Normal BUN range: 1.2 - 4.3 mmol/L . Mean: 1.99 mmol/L (Pinson 2009). Normal TSP range: 57 - 87 g/L . Mean: 74.3 g/L (Pinson 2009). NB: Greater than normal creatinine figures may indicate dehydration, urinary tract obstruction, reduced renal blood flow, or renal failure. Greater than normal BUN figures may indicate congestive heart failure, hypovolaemic shock, reduced blood flow to the kidneys caused by dehydration, kidney damage, renal disease, or renal failure. Lesser than normal figures may indicate liver failure, low protein diet, or malnutrition. Greater than normal TSP figures may indicate chronic infection, severe dehydration. Lesser than normal figures may indicate inadequate protein in the diet - or failure to synthesise protein, malnutrition, chronic liver or kidney disease, pulmonary oedema.
- Apart from minor bleeding associated with wing capillary damage, do not use in cases of actual extended bleeding or in any cases of suspected internal bleeding.
- Do not use in any cases of actual or suspected head trauma unless advised by your veterinarian.
- Do not use in any cases of actual or suspected hypovolaemic shock. NSAIDs may facilitate further hypotension (reduction in blood pressure).
- Aspirin is generally not recommended for pregnant and lactating mothers. However we recommend seeking veterinary advice and/or proceeding with caution. Whilst it has been shown that aspirin freely crosses the placental barrier, we have experienced no increase in premature parturition or birth abnormalities [in *results: further notes* above]. As is often the case, the decision will be a balancing act: if we lose the mother we may well lose both mother and pup.
- If lactating, caution may be exercised by removing the pup temporarily. A later decision can then be made as to whether to try re-introduction or continue hand-rearing.
- We would recommend seeking veterinary advice with regard to administration on flying-fox young: bearing in mind that baby flying-foxes are rarely (if ever) entangled.
- As with any drug, do not administer if not required.

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References

- Armstrong KN, Anstee SD (2000) The ghost bat in the Pilbara: 100 years on. *Australian Mammalogy* **22**, 93–101.
- Barrett, Janine (2004) Australian Bat Lyssavirus - thesis by Janine Barrett 26th March 2004. B.V.Sc. M.V.Sc.
- Beck, M., (2004) Ku-ring-gai Bat Conservation Society Inc (KBCS). Flying-fox rescues from Backyard Fruit Tree Netting Entanglement. Surveyed results from 13 wildlife care organisations.
- Bishop, J., *pers. comm.*
- Bishop, J., *pers. obs.*
- Booth, C., Barbed Wire Action Plan (2006). Queensland Conservation.
- Bjork I, Lindahl U. (1982). "Mechanism of the anticoagulant action of heparin". *Mol. Cell. Biochem.* **48**: 161–182.
- Cesarman-Maus G, Hajjar KA (May 2005). "Molecular mechanisms of fibrinolysis". *British journal of haematology* **129** (3): 307–21.
- Chuang YJ, Swanson R. *et al.* (2001). "Heparin enhances the specificity of antithrombin for thrombin and factor Xa independent of the reactive center loop sequence. Evidence for an exosite determinant of factor Xa specificity in heparin-activated antithrombin". *J. Biol. Chem.* **276** (18): 14961–14971.
- Cox, M.; Nelson D. (2004). *Lehninger, Principles of Biochemistry*. Freeman. pp. 1100. ISBN 0-71674339-6.
- Crowley, G.V., Hall, L.S (1994). *Histological Observations on the Wing of the Grey-headed Flying Fox (Pteropus poliocephalus) (Chiroptera: Pteropodidae)*. *Aust. J. Zool.*, 1994, 42, 215 - 31.

Field, Hume E. (2005). *The Ecology of Hendra virus and Australian bat lyssavirus*. PhD Thesis, School of Veterinary Science, The University of Queensland.

Gardner A, *et al.* Radiographic evaluation of cardiac size in Flying fox species (*Pteropus rodricensis*, *P hypomelanus*, and *P. vampyrus*) *Journal of Zoo and Wildlife Medicine* 38(2):192-200. 2007

Guyton, A. C.; Hall, J. E. (2006). *Textbook of Medical Physiology*. Elsevier Saunders. pp. 464. ISBN 0-7216-0240-1.

Hall, L.S. (1987) Identification, distribution and taxonomy of Australian flying-foxes (Chiroptera: Pteropidae). *Australian Mammalogy*, 10, 75-79.

Hall, L.S. & Richards, G.C. (2000) *Flying foxes: fruit and blossom bats*. University of New South Wales Press, Sydney.

Hersh, E.; Moore, P.; Ross, G. (2000). "Over-the-counter analgesics and antipyretics: A critical assessment". *Clinical Therapeutics* **22** (5): 500.

Hirsh J, Fuster V, Ansell J, Halperin JL (2003). "American Heart Association/American College of Cardiology Foundation guide to warfarin therapy". *J. Am. Coll. Cardiol.* **41** (9): 1633–52.

Hirsh J, Raschke R (2004). "Heparin and low-molecular-weight heparin: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy". *Chest* **126** (3 Suppl): 188S–203S.

Holbrook AM, Pereira JA, Labiris R, *et al.* (2005). "Systematic overview of warfarin and its drug and food interactions". *Arch. Intern. Med.* **165** (10): 1095–106.

Horton JD, Bushwick BM (February 1999). "Warfarin therapy: evolving strategies in anticoagulation". *Am Fam Physician* **59** (3): 635–46.

Jeffreys, Diarmuid (August 11, 2005). *Aspirin: The Remarkable Story of a Wonder Drug*. Bloomsbury USA. pp. 73.

Johnson, A., Johnson, B., *pers. obs.* On the witnessed multiple entanglements of Little red flying-foxes *Pteropus scapulatus* on barbed wire fences on the Atherton Tablelands (1994).

Julian, D G; D A Chamberlain, S J Pocock (1996-09-24). "A comparison of aspirin and anticoagulation following thrombolysis for myocardial infarction (the AFTER study): a multicentre unblinded randomised clinical trial". *BMJ* (British Medical Journal) **313** (7070): 1429–1431.

Kallen, F. C. (1970). Cardiovascular system of bats. *In*: William, A. W. (ed.). *Biology of Bats*, vol. 2. Academic Press, New York, New York. Pp. 290–330.

Kerr, C., *pers. comm.*

Kerr, C., *pers. obs.*

Kingston, M.B., Turnbull, J.W., Hall, P.W., Boulton, S.C., & Storey, R.J.H. (1999). Tweed vegetation management plan. Tweed Shire Council, Murwillumbah.

Lewis, H D; J W Davis, D G Archibald, W E Steinke, T C Smitherman, J E Doherty, H W Schnaper, M M LeWinter, E Linares, J M Pouget, S C Sabharwal, E Chesler, H DeMots (1983-08-18). "Protective effects of aspirin against acute myocardial infarction and death in men with unstable angina. Results of a Veterans Administration Cooperative Study". *The New England journal of medicine* **309** (7): 396–403.

Linhardt RJ, Gunay NS. (1999). "Production and Chemical Processing of Low Molecular Weight Heparins". *Sem. Thromb. Hem.* **3**: 5–16.

Maclean, J. 2009. Tolga Bat Hospital. Statistics from surveyed reports on barbed wire entanglement for the *wildlife friendly fencing project* website www.wildlifefriendlyfencing.com

Pinson, D., *pers. comm.*

Pinson, D., *pers. obs.*

Pinson, *unpubl. data.*

Pinson, D. 2009. The Flying-fox Manual 2009, 2nd Edition. Murwillumbah, NSW: Stickeebatz Publishing. ISBN: 978-0-9805340-0-9.

Pinson, D., Kerr, C (2009) Feed and Growth Chart for Grey-headed & Black Flying-foxes.

Sørensen HT, Mellemkjaer L, Blot WJ, *et al.* (September 2000). "Risk of upper gastrointestinal bleeding associated with use of low-dose aspirin". *Am. J. Gastroenterol.* **95** (9): 2218–24.

Su M, Stork C, Ravuri S, *et al.* (2001). "Sustained-release potassium chloride overdose". *J. Toxicol. Clin. Toxicol.* **39** (6): 641–8.

Temminck, C.J. (1825) Monographies de mammalogie. G. Dufour & E. D'Ocagne, Paris.

The Merck Veterinary Manual, Ninth Edition (2005) Merck Publishing. ISBN: 0-911910-50-6

Ueber Aspirin. *Pflügers Archiv : European journal of physiology*, Volume: 84, Issue: 11-12 (March 1, 1901), pp: 527-546.

van der Ree, Rodney (1999) 'Barbed Wire Fencing as a Hazard for Wildlife', *The Victorian Naturalist* 116(6): 210-217.

Vane, J.R (1971). "Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs". *Nature - New Biology* **231** (25): 232-5.

Vane, J.R., Botting, R.M (2003). The mechanism of action of aspirin. Review Article. *Thrombosis Research*, Volume 110, Issues 5-6, 15 June 2003, Pages 255-258.
doi:10.1016/S0049-3848(03)00379-7

Warner, T.D., Mitchell, J.A (2002) "Cyclooxygenase-3 (COX-3): filling in the gaps toward a COX continuum?". *Proc Natl Acad Sci USA* **99** (21): 13371-3. 2002-10-15.

Whitlon DS, Sadowski JA, Suttie JW (1978). "Mechanism of coumarin action: significance of vitamin K epoxide reductase inhibition". *Biochemistry* **17** (8): 1371-7.