Shock and Compensatory Mechanisms Clinical Considerations

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A. Summary

This essay summarises the evidence that birds experience a syndrome similar to mammalian shock, discusses the compensatory mechanisms that birds have available for dealing with shock, and fin ~ y outlines some of the implications of these mechanisms on the formulation of a rational diagnosis of and treatment for shock. A detailed explication of mammalian shock and compensatory mechanisms will not be provided due to space restrictions except where the analogous avian mechanism has not been sufficiently characterised.

B. The Nature of Shock

Shock is defined as a state in which there is insufficient tissue perfusion. Affected tissues will experience decreased oxygenation and reduced clearance of metabolic wastes. Shock can arise due to an absolute decrease in blood volume (hypovolaemic shock), an expansion of the vascular space without an increase in blood volume (effective hypovolaemic Shock) or an ineffectively pumping heart (cardiogenic shock). Hypovolaemic shock can be caused by haemorrhage, water deprivation or any other form of dehydration. Effective hypovolaemic shock can be caused by sepsis, endotoxaemia, anaphylaxis and fear. Cardiac failure can cause cardiogenic shock (Bednarski, 1989).

Regardless of the initiating cause, the consequences of shock are directly related to inadequate tissue perfusion, which affects different tissues to a greater or lesser extent, depending on the duration and severity of the shock, the level of compensation, the metabolic requirements of the tissue and the preferential status of the organ.

Inadequate perfusion of the kidneys (prerenal renal failure) will initially result in oliguria and azotaemia without renal cell injury. In the more advanced stages of shock, renal tubular cells will die and slough off, leading to irreversible organ damage unless the tubules can be repopulated. Acidosis is a feature of all forms of established shock. It arises when hypoxic tissues undergo anaerobic glycolysis, producing lactic acid in the presence of reduced lactate clearance and impaired renal acid/base regulating mechanisms (Cotran, Kumar and Robbins, 1989).

C. Compensatory Mechanisms

There is a number of compensatory mechanisms which support the cardiovascular system in the

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short to medium term during shock. In mammals they are well characterised; their primary function is to maintain tissue perfusion. This is achieved by maintenance of arterial blood pressure and/or maintenance of plasma volume.

The sympathetic nervous system is the first to respond to shock. The baroreceptor reflex, and later the central nervous system ischaemic response elicit an increased sympathetic tone, manifested both by increased sympathetic nervous outflow and catecholamine release.

This results in vasoconstriction, increased heart rate, increased cardiac contractility and, as a result, increased arterial blood pressure. Vasoconstriction is manifested to differing extents in different tissues, leading to changes in blood flow distribution. The heart and brain are preferentially supplied. Venous return and blood pressure are also maintained by blood vessel contraction in response to reduced filling pressure.

Angiotensin (AII) and vasopressin (antidiuretic hormone, ADH) promote arterial constriction and increased renal reabsorption of sodium (AII) and water (ADH). The result is vastly decreased renal water loss (with consequent oliguria) and maintenance of plasma and extracellular fluid volume. Finally, water is drawn from the interstitium and the gut to maintain plasma and total body water volume, and thirst and salt-desire are felt (Guyton, 1991).

D. Shock in Birds

In birds, the causes and consequences of shock are poorly understood. The available information covers three causes of shock: dehydration, haemorrhage and endotoxicosis. The relevance of these studies to clinical practice remains to be established, but they could conceivably model dehydration and inanition, which are common features of disease (Phillip, 1981); trauma, which commonly involves haemorrhage; and gastrointestinal disease and sepsis; which can result in endotoxaemia (Wessels et al, 1987; Miyagawa, Numata and Mkuuchi, 1991).

a. Dehydration

Lumeij (1987) documented the existence of prerenal renal failure (the manifestation of shock on the kidneys) by observing that water-deprived pigeons exhibited a 6.5 to 15-fold increase in plasma urea concentration, while creatinine and uric acid levels rose 1.2 to 1.5-fold and 1.4 to 2-fold respectively. This indicates that renal arterial blood supply is decreased during dehydration, while excretion of uric acid continues by virtue of the presence of a renal portal blood supply.

A subsequent study with pigeons, deprived of drinking water for up to 48 hours showed that packed cell volume (PCV) and serum sodium levels did not change despite 10% dehydration. Serum potassium levels also did not change, but this is most likely because avian red blood cells absorb potassium (Lumeij, 1985), and serum is therefore not an appropriate sample with which to estimate potassium status. In the same study plasma total solids and plasma osmolality rose (Martin and Kollias, 1989).

This is at variance to studies in starlings, which did show significant elevations of plasma sodium, chloride and phosphorus concentrations as well as osmolality (Roberts and Dantzler, 1989). Similarly, plasma osmolality rose in Japanese quail deprived of

water for eleven days, but not in budgerigars deprived of drinking water for the same period (Kasuya, Karakida, Okawara and Kobayashi, 1987). Kasuya et al (1987) suggested that whilst several different studies had demonstrated that chickens, white-crowned sparrows, pigeons and tree sparrows demonstrated activation of hypothalamic neurosecretion and weight loss in response to dehydration, this was not the case for such arid-country dwellers as budgerigars, zebra finches and white-throated munias. Clearly, birds' abilities to compensate for dehydration (and other insults) are variable, and extrapolation between species should be attempted with caution.

b. **Avian haemorrhagic Shock**

Wyse and Nickerson (1971) characterised the response of anaesthetised chickens to standardised haemorrhage (maintained at a rate to maintain arterial pressure at 50 mmHg). They found that a blood loss of only 22% of the initial blood volume decreased arterial pressure by 53%. Similar experiments cited by the authors in ducks and pigeons exhibited a smaller drop in blood pressure. The authors concluded that plasma volume was maintained through an influx of low-protein fluid. The volume of fluid mobilisation in this study and another (Bos, Todd, Jell, Ramsay and Fowler, 1990) in a five hour period, after a total blood loss of 71%, equalled 60% of the initial plasma volume, at a rate four times greater than the rate of fluid mobilisation in the dog. Interestingly, it was also found that acute haemorrhage did not elicit the progressive cardiovascular deterioration and haemoconcentration which characterises irreversible shock in dogs, and reinfusion of all shed blood stabilised blood pressure at a level only slightly below initial levels. This was the case even when reinfusion was delayed until after the onset of terminal cardiovascular collapse. Death was, according to the authors, mediated by respiratory collapse (Wyse and Nickerson, 1971).

c. **Avian Endotoxic Shock**

Lipopolysaccharide (LPS), or endotoxin, causes a shock-like syndrome in birds. Merrill, Rosolowski and Grover (1979) demonstrated that intravenous administration of endotoxin decreased arterial blood pressure by up to 63% within two hours without altering cardiac output in chickens. Endotoxin increased plasma corticosterone and lactic acid concentrations but did not alter blood glucose, pH or blood gas levels. A subsequent study by Merrill Russo and Halper (1981) further characterised the effect of endotoxin by studying the distribution of cardiac output in control and LPS-injected, conscious, adult chickens using radioactively labelled microspheres. Their results show that various organs are differently affected by the decline in arterial pressure. Thus, while the myocardium, adrenal glands, liver (arterial supply), testes and bone were unaffected by endotoxin challenge, the kidneys, intestines, spleen and pancreas received a significantly decreased supply, in terms of both blood flow per gram of tissue and percent of cardiac output per gram of tissue. Pectoral muscle received a significantly greater flow per gram of tissue. This study found no change the amount of shunting (Estimated by measuring radioactivity in the lungs), although a previous study by Wolfenson, Bennan, Frey and Snapir (1978) found that shunting increased to 30% during hyperthermia. Although the effects of endotoxin were found to be qualitatively consistent and the results conclusive, the dose-response relationship is considered erratic.

The effects of endotoxin on body temperature are variable. Macari Furla, Gregorut, Selato and Guerreiro (1993) reported a prostaglandin-mediated fever response in adult chickens, in which rectal temperature peaked three hours after intravenous injection of 1.5 μg/kg. This response could be mimicked by intracerebroventricular PGE_2, administration and intravenous interleucin-1, and blocked by intravenous pretreatment with indomethacin. This resembles the mammalian system, where prostaglandin E: is released in response to blood-borne interleucin-lβ, an endogenous pyrogen released in response to exogenous pyrogens. Edens, McCorkle and Simmons(1984) administered live, and killed, *Alcaligenes faecalis* bacteria intranasally to day-old turkey poults and demonstrated a decrease in colonic and foot-pad temperature, compared to control values. Colonic temperature was significantly less than control temperatures for three days after killed bacterial administration. The difference between chickens and turkeys could be the result of the immaturity of the turkeys, the use of whole bacteria or a difference in the fever response between turkeys and chickens.

It appears that birds experience a syndrome similar to mammalian shock, in which a challenge to the cardiovascular system elicits alterations in blood distribution. Such a syndrome can be initiated by dehydration, acute haemorrhage and intravenous endotoxin administration. The compensatory mechanisms which operate in birds during shock will be discussed individually.

E. Renal Compensatory Mechanisms

Dehydration challenges the cardiovascular system through reducing plasma volume. Renal compensatory mechanisms maintain plasma volume by reducing water loss. Urine concentration in birds involves a counter-current exchange mechanism and tubular reabsorption of water under the influence of arginine vasotocin (AVT), the avian antidiuretic hormone; water resorption can vary from 66% to 99% of the glomerular filtrate, based on studies of roosters and Mourning Doves *(Zenaida macroura)* (Shoemaker, 1972). Braun and Dantzler (1984) confirmed that AVT acts on the tubular membrane to enhance water conservation.

a. Avian Renal Structure and Function

Avian kidneys comprise two groups of nephrons, reptilian-type nephrons and mammalian-type nephrons, with a subgroup of nephrons which is intermediate in type between these. The reptilian type nephrons (RTNs) are the most numerous, constituting between 60% and 90% of nephrons. These nephrons are characterised by a relative lack of convolution of the proximal and distal tubules. They also lack loops of Henle (Lolls). Thus, they are incapable of producing urine that is hyperosmotic to plasma.

In contrast, the mammalian type nephrons (MTNs) possess an Loll, with both thick and thin limbs, and convoluted proximal and distal tubules. The Lolls are supplied by vasa recta, and together these are arranged within connective tissue sheaths into medullary cones in a way which permits countercurrent multiplication. Under the influence of AVT, these nephrons are capable of producing urine hyperosmotic to plasma (Dantzler, 1980).

An osmotic gradient, based on NaCl, has been demonstrated in avian medullary cones. Sorbitol and urea, which are important for the creation of the medullary osmotic

gradient in mammals, are absent in the avian medullary cones. This might explain why birds are generally unable to concentrate urine to osmolalities in excess of 2.5 times plasma osmolality, whereas mammals can establish urine:plasma (U/P) osmolality ratios in excess of 20 (Lien, Pacelli and Braun, 1993).

b. **Control of Glomerular Filtration Rate**

Another mechanism, confirmed in the sparrow *(Passer domesticus)* (Goldstein and Braun (1988), the chicken (Stallone and Braun, 1985) and the starling (Roberts and Dantzler, 1989; Dantzler, 1989) which might assist birds to conserve water is the ability to decrease whole-kidney glomerular filtration rate (GFR), mainly by selective decreases in the number of filtering RTNs. Under conditions of salt load and exogenous AVT administration (in physiological doses), up to 100% of RTNs will cease to filter while MTNs which are not functioning are recruited.

The reduction in RTN GFR is a dose-dependant effect of AVT (Braun and Dantzler, 1984), and involves both a shut-down of nephrons through constriction of the afferent glomerular arteriole (King and McLelland, 1984) and a decrease in the single nephron GFR of the remaining RTNs (Braun and Dantzler, 1974; Dantzler, 1989). The blood supply to the RTNs is shunted by aglomerular branches of the intralobular arteries to the peritubular capillary network (King and McLelland, 1984; Sturkie, 1986b). Thus, while 70% of RTNs filter in the starling under control diuresis, none filter during salt loading (Braun and Dantzler, 1984).

This shift in the filtration pattern favours nephrons which are better able to concentrate urine at the expense of the nephrons which are incapable of concentration. Also, the increase in filtration by MTNs increases the effectiveness of the medullary countercurrent concentrating mechanism, thereby further increasing the U/P osmolality ratio (Braun and Dantzler, 1984). Since all collecting ducts pass through a medullary cone, the decreased flow which results from RTN shutdown allows more time for equilibration between urine and the hypertonic medullary interstitium, thus conserving water, especially in the presence of AVT, which may increase the permeability of the collecting duct to water (Dantzler, 1989).

Recent work has, however, cast doubt on the quantitative importance of the GFR reduction mechanism to water conservation in the chicken. characterisation of the kidney's response to AVT suggests that at low to moderate plasma AVT concentrations, increased reabsorption of water and sodium from the renal tubular fluid is more important than alterations in whole-kidney glomerular filtration rate. Further, it was found that at low plasma AVT levels (less than 5 μU/ml), urine flow had decreased by 88% of the maximal response and urine osmolality and the U/P osmolar ratio had increased by 72% of the maximal response, prior to any significant reduction in GFR. At the highest plasma AVT levels, which approximated those found in dehydrated chickens, GFR decreased by 30%, the tubular responses were maximal and only a slight additional increase in water conservation was observed. Hence, a reduction in water loss is due to increased tubular reabsorption of water rather than a decreased GFR, which occurs only with severe osmotic stress. These and other findings suggest that the modulation of GFR may be primarily a mechanism to reduce cardiac output to the kidney, and only secondarily a mechanism to reduce water loss

(discussed later) (Stallone and Braun, 1985).

Starlings show a significant rise in cloacal (20% increase) and ureteral (85% increase) urine osmolality in response to dehydration, associated with significant rises in calcium, magnesium and phosphate concentrations (Roberts and Dantzler, 1989). Since these changes are mediated by AVT, it is important to determine under which conditions AVT is secreted.

c. **Control of Arginine Vasotocin**

The control of AVT secretion in chickens has been determined using radioimmunoassay (RIA), osmotic and volaemic stimuli (Stallone and Braun, 1986a). No measurable AVT was present when plasma osmolality was less than 288 mosmol/kg. At control plasma osmolalities of 308 mosmol/kg, plasma AVT concentration was 2.7 μU/ml. Above 308 mosmol/kg, AVT concentration rose by 0.77 μU/ml for each unit rise in osmolality, up to a maximum of 45 μU/ml. This response is greater than the response in water deprived chickens, where long-term adaptation mechanisms may reduce the AVT response. Since plasma AVT concentration is directly related to its rate of secretion (Arad and Skadhauge, 1984), it follows that AVT is secreted in response to rising plasma osmolality, and reduced plasma osmolality depresses AVT secretion. There was no clear direct effect in this study (Stallone and Braun, 1986a) of acute volaemic stimuli on plasma AVT concentration.

However Arad and Skadhauge (1984) demonstrated that plasma volume affects the sensitivity of AVT release to osmotic stimuli. Hence, birds with a larger plasma volume secrete relatively less AVT for a given rise in plasma osmolality, a conclusion supported by other workers (Braun and Dantzler, 1984; Skadhauge, 1981). Koike (1989) noted that blood volume does alter plasma AVT levels in ducks, where a non-hypotensive haemorrhage of 10% causes a 30% increase in plasma AVT. This rise, and the consequent antidiuresis, was reversed by blood reinfusion.

Blood volume changes may influence AVT secretion indirectly through the renin-angiotensin system as hypovolaemia causes renin release. This elevates plasma angiotensin II (AII) levels, and AII has been shown to increase AVT release and to reduce the osmotic threshold for AVT secretion (Koike, 1989).

Arad and Skadhauge (1984) found that plasma AVT concentrations are directly related to the rate of AVT secretion. It follows that the rate of plasma clearance of AVT is constant under dehydration and normal hydration. They also found that although AVT is not secreted in response to heat exposure in the absence of dehydration, the level of secretion is enhanced when heat exposure accompanies dehydration. This is not surprising, since the increase in plasma osmolality, sodium and chloride concentrations, and the decrease in potassium and calcium concentrations seen in dehydration alone are enhanced when heat exposure accompanies dehydration. Wang and Bottje (1989) found that AVT is secreted during acute heat stress (less than 150 minutes) without significant changes in plasma osmolality.

d. **Nitrogen Excretion During Shock**

The blood of renal portal system origin which perfuses the kidneys does not participate in glomerular filtration, but joins the efferent glomerular arteriolar blood to supply the peritubular network which participates in tubular secretion and reabsorption (West, Langille and Jones, 1981) but does not flow into the vasa recta. Approximately 50% of the blood flow in the peritubular capillaries derives from renal portal blood (Skadhauge, 1981).

Since 90% of uric acid is excreted by tubular secretion and since renal portal blood maintains perfusion of the peritubular capillaries in the absence of glomerular filtration, plasma uric acid levels do not rise during shock unless renal disease exists. In contrast, urea is excreted solely by glomerular filtration, but is subject to reabsorption by the peritubular capillaries. The proportion of filtered urea that is reabsorbed is inversely proportional to the rate of flow of filtrate through the tubule. Hence, when glomerular filtration decreases, urea is reabsorbed, and plasma levels rise (Skadhauge, 1981). This accounts for the findings by Lumeij (1987) that dehydrated pigeons exhibit an increased plasma urea:uric acid ratio.

However, when using blood nitrogenous waste levels to assess dehydration and prerenal renal failure, the effects of prandition need to be considered. Studies in the chicken (Hazelwood, 1972) and the Peregrine falcon (Lumeij and Remple, 1991) show that plasma uric acid levels can increase to 10-40 times their initial levels during a period of three to ten days of starvation in the chicken, and 4-fold in the falcon following a meal. Furthermore, the levels of uric acid and ammonia in the plasma are dependant on the amount of protein in the diet (Hazelwood, 1972).

e. **The Renal Portal System**

The renal portal system (RPS) is a ring of veins which receives blood from the pelvic limb, and can receive blood from the caudal oviduct, the caudal body wall and the large intestine. It can direct blood in four directions; towards the caudal vena cava, through the caudal mesenteric vein to the hepatic portal system, towards the internal vertebral venous sinus and/or to the kidney itself.

The RPS's role as a compensatory system is based on its ability to redirect blood. The common iliac veins each contain a valve, the renal portal valve (RPV), which is situated such that when the valve is open, blood from the RPS can flow directly into the caudal vena cava, bypassing the kidney parenchyma. When the valve is closed, blood flows into the kidney or into the hepatic portal system, or into the internal vertebral venous sinus.

Histochemical techniques have established the presence of adrenergic and cholinergic nervous supply to the smooth muscle of the RPV. Adrenalin relaxes the smooth muscle (opening the valve) while acetylcholine and histamine cause contraction. This is consistent with the theory that the valve has a role in diverting blood to the vena cava during times of sympathetic outflow (King and McLelland, 1984). Despite the fact that the innervation of the valve is known and that several hormones are known to affect the degree of closure of the valve, the function of the renal portal valve remains unclear. It

is possible that opening the valve increases venous return to the heart, and this could occur with haemorrhage or shock, or during exercise. It has also been suggested that the valve may open in order to improve venous drainage from the leg when, as during exercise, venous return from the leg exceeds the blood flow requirements of the kidney (Skadhauge, 1981).

Several studies have attempted to investigate this area. Sturkie (1986a) cites studies which found that blood flow in the caudal mesenteric vein was generally in the direction of the liver (established by cineradiography), and that the renal portal valve was generally open. In another study, microspheres injected into the femoral vein were distributed not only to the kidneys (44%), but also to the liver (47%) and to the posterior vena cava (8%). However, since the former study was performed in supine, anaesthetised chickens, while the blood distribution study was performed in upright, conscious but restrained chickens, these results may not reflect normal function.

In any case, the renal portal valve may not be the main regulator of renal portal blood flow to the kidney, nor does it appear usually to function in the completely open or completely closed position. Rather, the concept of three in parallel channels, as suggested by Jones and Johansen (1982) may be more useful. According to this concept, the three main outflows of the RPS (i.e. the kidney, the liver and the caudal vena cava) can be considered to function as three in parallel channels, with the proportion of blood flow in each being reciprocally related to the resistances in them. The resistance to flow to the caudal vena cava is a function of the degree of closure of the RPV, and the resistances to flow to the liver and kidneys are functions of the vascular resistance in those organs. Whether the valve is controlled by hormonal or nervous signals, the conditions under which such control is exercised and the importance of the system remain to be fully elucidated.

F Acid/Base Regulation

a Avian Respiratory Acid/Base Regulation

It is generally agreed that the avian lung, despite its very different structure, has an almost identical role to its mammalian counterpart in acid/base regulation. Skadhauge (1983) pointed out that the lung excretes at least 99% of daily acid production. Hyperventilation can occur in response to heat stress or stress generally. This may induce hypocapnia, which tends to increase pH (Teeter, Smith, Owens, Arp, Sabgiah and Breazile, 1985). Some controversy existed as to whether birds can pant to reduce body temperature without altering blood gasses, and how birds deal with combined dehydration and heat exposure. Tazawa (1986), in his review, claimed that heat exposure led to respiratory alkalosis, with a compensatory, hypocapnic, lactic acidosis. Birds with poor control of body temperature do not, according to Tazawa, undergo significant changes in blood CO_2 or pH with heat stress.

Arad (1983) and Marder and Arad (1989) demonstrated that birds are efficient at regulating body temperature during heat exposure up to 45°C with only slight respiratory alkalosis, despite a respiratory frequency 17 times the control rate. Moreover, when heat exposure (up to 44°C) is concomitant with dehydration, chickens are still able to thermoregulate effectively. This is achieved by allowing body

temperature to increase slightly, without approaching lethal brain temperature (46-47°C). Hyperthermia was mediated by a respiratory rate lower than that of hydrated, heat-exposed birds, and a consequent reduction in evaporative water loss. Regardless of the state of hydration, heat exposure resulted in a decreased blood CO_2 content (suggesting hyperventilation), but arterial pH was almost entirely compensated by lower bicarbonate levels. Dehydrated birds experience a greater decrease in blood CO_2, but the response was correlated to body temperature. That is, hyperventilation increases with increasing body temperature. In the light of other studies, Arad postulated that the adaptive responses were mediated by intrapulmonary CO_2-sensitive receptors. In summary, chickens are able effectively to regulate water balance and body temperature in the face of both dehydration which requires water sparing and heat exposure which requires evaporative cooling.

The avian lung contains CO_2-sensitive receptors in the paleopulmonic parabronchi. They respond sufficiently rapidly to adjust respiratory activity within a respiratory cycle. Thus they are equipped for a role in optimising ventilation/perfusion ratios. Sensitivity to both static and dynamic changes in inspired carbon dioxide concentrations has been demonstrated (McLelland and Molony, 1983).

Arterial chemoreceptors also exist in birds (McLelland and Molony, 1983). They are located in the carotid body, and contribute around 30% of the respiratory drive at normoxic conditions, but around 50-60% in hypoxic environments. Clearly, avian lungs play a similar role in acid/base regulation to mammalian lungs.

b. Avian Renal Acid/Base Retaliation

Regarding the role of the avian kidney in acid/base regulation, Laverty (1989) states that the avian kidney performs bicarbonate resorption, ammonium production and excretion and hydrogen ion excretion. Resorption of filtered bicarbonate is almost complete when acid urine is being produced. Acid excretion is achieved mainly in association with buffers (uric acid, phosphate and ammonium), free hydrogen ion excretion being insignificant by comparison.

During chronic metabolic acidosis, uric acid excretion decreases, while ammonium excretion increases (Laverty, 1989). Skadhauge (1983) noted that during eggshell formation, when metabolic acidosis prevails, urinary phosphate excretion drops. With a decreasing urinary pH, there is a proportional decrease in urinary bicarbonate, but an inversely proportional increase in urinary ammonium concentration.

Urate/hydroxyl and urate/bicarbonate counter transporters have been documented in the renal tubules (Laverty, 1989). Thus, it appears that despite uricotelism, the kidney plays a comparable role in avian acid/base regulation as in the mammal.

G. Cardiovascular Compensatory Mechanisms

The avian cardiovascular system is in many ways similar to the mammalian system. It comprises a four-chambered heart which pumps blood around two vascular systems; the pulmonary system and the systemic circulation. Compensation for decreased function is effected through control over cardiac output and its distribution.

a. **Control of Avian Cardiac Output**

Avian cardiac performance can be increased dramatically. West et al (1981) cite work by Berger et al (1970) which established that birds can increase their heart rate by 100% to 300% (smaller birds can generally do this less effectively than larger birds). Tucker (1968, cited in West et al, 1981) found that a house sparrow exposed to simulated high altitude (6100m) conditions remained active, and could not only fly but also gain height. Mice exposed to similar conditions died. With flight causing an oxygen requirement eight times the basal level, but with atmospheric oxygen tensions being such that arterial blood was only 24% saturated, Tucker calculated that effective ventilation would be 11.6 litres/minute, whilst cardiac output would be 2.78 litres/minute, from which a ventilation:perfusion ratio of 4:1 is evident. From this it is apparent that birds exhibit considerable resistance to anoxia.

However, the cardiovascular compensatory mechanisms of birds are not well characterised. A functional baroreceptor reflex has not been conclusively demonstrated in Aves, although several reports indicate the existence of stretch receptors in the aorta. A carotid body with vagal nerve supply exists in birds, but attempts to demonstrate its function have been unsuccessful (Hodges, 1981; Sturkie, 1986a). Almost all avian arteries and all veins are innervated both by adrenergic (sympathetic) and cholinergic (parasympathetic) nerve fibres. The femoral artery receives only adrenergic fibres (Sturkie, 1986a). According to Sturkie (1986a) fright increases blood pressure and heart rate, while exercise only increases blood pressure. West et al (1981) found that heart rate increased during flight, but did not state how flight was induced.

b. **Blood Flow Redistribution in Birds**

Evidence for blood redistribution during shock has been reviewed earlier in this essay. Evidence for a possible additional mechanism for blood redistribution, possibly mediated by mesotocin, comes from work by Bottje, Holmes, Nelson and Koike(1989) and Stallone and Braun (1985). The reduction in GFR observed during dehydration does not appear to be primarily important in reducing water loss (Stallone and Braun, 1985). Renal plasma flow decreases during haemorrhage and the reduction in renal plasma flow correlates positively with plasma mesotocin concentration, but not with lowered arterial blood pressure (Bottje et al, 1989). It might follow that the GFR reduction mechanism functions primarily to reduce blood flow to the kidneys, rather than to spare water. This mechanism may operate during haemorrhage as well as during dehydration, as mesotocin is released during dehydration (Koike, 1989).

Whether the reduced renal plasma flow was due solely to reduced GFR (arterial plasma) was not investigated.

Bottje and Holmes (1989) demonstrated that hepatic perfusion is reduced by 56% when more than 50% of blood volume is removed acutely (100 to 150 minutes). This effect was closely correlated with reduced arterial blood pressure.

According to West et al (1981), even during rest 75% of the cardiac output is distributed in the duck by the brachiocephalic artery. The brachiocephalic artery has two branches; the pectoralis artery, which supplies the wing and the flight muscles, and

the common carotid artery, which supplies the neck and head. However, since the common carotid carries only a small proportion of the brachiocephalic artery's supply, the flight apparatus is very highly perfused. This is at variance to the data, based on the chicken, presented by Jones and Johansen (1972), which suggests a distribution of only 1% of the cardiac output to the pectoral muscles, and 15% to the kidney.

During rest, the metabolic rate of the flight apparatus is not sufficiently high to warrant this level of perfusion, so that there exists a large venous oxygen reserve. During flight the level of oxygen demand increases 10- to 14-fold (West et al, 1981). This, in the pigeon at least, seems mainly to be accounted for by an increased heart rate (but not stroke volume) and doubling of the arteriovenous oxygen difference. Thus, the high resting pectoral blood supply acts to reduce the workload of the heart during times of increased oxygen demand.

c. Maintenance of Circulating Blood Volume

Arad et al (1989) found that during extreme dehydration, plasma volume is maintained at the expense of extracellular fluid volume, and water loss is minimised through complete renal shut-down. Likewise, acute haemorrhage in chickens (Wyse and Nickerson, 1971) and pigeons (Bos et al, 1990) is compensated for by replacement of plasma with low-protein fluid, evidenced by a drop in packed cell volume and plasma protein concentration. Based on measurement of plasma volume, Wyse and Nickerson (1971) found that the volume of fluid mobilisation in a five hour period prior to death, after a total blood loss of 70%, equalled 60% of the initial plasma volume, at a rate four times greater than the rate of fluid mobilisation in the dog. As expected, fluid mobilisation in both chickens and pigeons was associated with a drop in PCV (53%) and plasma protein (up to 65%)(Wyse and Nickerson, 1971; Bos et al, 1990). No fatalities were recorded. However, chickens do not maintain their blood pressure during haemorrhage as well as dogs. The authors noted that chickens are not representative of birds in the magnitude of their response to haemorrhage. Similar experiments cited by the authors in ducks and pigeons exhibited a relatively smaller drop in blood pressure, but a similar compensatory flow of low-protein fluid. This suggests that, in the birds studied, tissue perfusion is maintained by maintaining plasma volume rather than supporting arterial blood pressure.

H. The Avian Renin/Angiotensin System

The avian kidney contains all the elements of a complete renin/angiotensin system: granulated juxtaglomerular cells, with mesangium and extramesangial cells; plasma renin and angiotensinogen; and converting enzyme activity which can be specifically blocked (Wilson, 1989). Maculae densae have been documented in at least 125 avian species, and sodium depletion has been shown to increase the number of juxtaglomerular granules (Siller, 1983). The avian kidney produces renin, and angiotensin I and AII have been identified (Skadhauge, 1983). Renin is released in response to haemorrhage in the chicken, quail and pigeon (Wilson, 1989) and blood AII levels are elevated in quail after dehydration and haemorrhage (Kobayashi et al, 1980). There is evidence that a complete renin-angiotensin system may be present in the avian brain (Wilson, 1989).

A wide range of effects has been demonstrated for increased plasma AII levels. Many studies

document that AII is dipsogenic (Wilson, 1989; Kobayashi et al 1980; Koike, 1989). Angiotensin II causes increased circulating levels of the hormones AVT (leading to water conservation) and aldosterone (leading to salt conservation), although species differences are evident (Kobayashi et al, 1980). This evidence suggests that AII is important in the short-term regulation of blood pressure through blood volume maintenance. Contradictory evidence may exist, however, as infusions of AII has a diuretic effect in both chickens and ducks, effected at the level of the renal tubules. *In vivo*, this effect may be ameliorated or overridden by concurrent elevations of plasma AVT (Wilson, 1989).

Further studies cited by Wilson (1989) indicate a role for AII in regulating cardiac output (through heart rate and contractility) and blood pressure. Angiotensin II-mediated tachycardia is not dependent on the sympathetic nervous system. Rather, AII may diminish the bradycardic effect of the baroreceptor reflex. In addition to this, AII stimulates cardiac contractility, possibly through enhanced calcium influx into the cells. Beta-adrenergic stimulation induced by AII maintains pulse pressure and cardiac output despite the increased afterload which results from the rise in arterial pressure. The result is an increased blood pressure through increased cardiac output.

The response of peripheral resistance to AII is biphasic. Initially there is observed a depressor response caused by vasodilatation. This is not mediated by catecholamines or AVT, but appears to be a direct effect of AII on the vascular endothelium. The subsequent pressor response is due to vasoconstriction, mediated by the sympathetic nervous system, through both increased sympathetic nervous tone and increased adrenal catecholamine release. The vasoconstriction is alpha-adrenergic.

I. DISCUSSION (Clinical Considerations)

The compensatory mechanisms listed above can all be expected to be operating in a bird presented with clinical illness, especially if the bird is not normally closely observed and so is presented late in the development of disease. Philip (1981) observed that these mechanisms are so effective that they completely disguise the presence of disease, and the onset of the first noticeable signs of disease occurs only when the bird is severely compromised. Such a bird can, by inference from the compensatory mechanisms, be expected to reveal the following;

- Dehydration secondary to inanition, leading to
- Release of AVT, AII and sympathetic mediators, causing
- Shutdown of reptilian-type nephrons, reduced blood flow to the kidneys, liver and other tissues, resulting in
- Build-up of metabolic wastes, reduced nutrient supply to tissues and consequent tissue devitalisation.

The diagnosis of shock, and the evaluation of a shocked bird, need not be made on clinical signs alone. The following methods are documented in the literature as methods of diagnosing and evaluating shock:

- Clinical signs anecdotally associated with shock include depression, reduced skin

turgor and delayed ulnar vein refill time. Feather fluffing is held to be indicative of hypothermia (Philip, 1981).

- Accumulation of metabolic wastes, especially urea, in blood. Thus, increased urea:uric acid and/or urea:creatinine ratios are indicative of prerenal renal failure (Lumeij, 1987).

- Prandition and diet affect blood urea and uric acid concentrations. Research is currently unavailable to do this reliably, but serial blood samples should, where possible, eliminate this problem.

- Osmolality rises in direct proportion to the level of dehydration; 10% dehydration increases osmolality 10% (Lumeij, 1987).

- Future research may reveal that blood calcium, magnesium and phosphate concentrations may assist in evaluating the degree of dehydration present in a bird.

However, as in all biological systems, variation between individuals and species needs to be borne in mind. Verkest (1994) demonstrated that clinical signs and blood biochemistry analysis do not necessarily produce coherent results. Similarly, hypothermia is not necessarily present in patients exhibiting feather fluffing. It follows that as much information as can be gathered, without unduly stressing the patient, is needed to evaluate a patient with confidence.

Until further research into avian disease processes is available to guide the rational treatment of ill birds, treatment should be aimed at ameliorating the above effects. Anecdotal evidence, inference and extrapolation has suggested that the key to successful management of ill birds requires that the bird be placed in a warm, quiet, semi-dark environment, and that fluids be administered routinely based on an assumed 10% dehydration. In the process, the following points should be considered:

- the presence of reduced peripheral circulation during shock will impair absorption of fluids not administered into a vascular space,

- any drugs administered which are normally excreted by glomerular filtration or hepatic metabolism will probably experience reduced clearance in the shocked bird,

- the health of the kidneys should be preserved by instituting fluid therapy and taking care that drugs administered intramuscularly which could be toxic to the kidneys should not be injected into the pelvic limb, nor into the caudal third of the body,

- given the tolerance of birds to acute blood loss, the demonstrated short life of transfused erythrocytes (Hoefer, 1992), and the difficulty of providing homologous blood, blood transfusion may not be justified as a treatment,

- tolerance by the bird of insults and stressors will be severely curtailed by virtue of the level of compensation present to deal with shock;

- Pulmonary oedema in response to rapid intravenous fluid administration has been demonstrated in chickens in response to acute administration saline calculated to be 3%

of blood volume (Weidner, Selna, McClure and DeFouw, 1993). Although the results suggested that gas exchange surfaces were spared, care should be taken when administering fluids serially to small birds, or to birds with suspected lung disease or poor blood oxygenation. Concurrent oxygen administration may be indicated.

- In birds where pyrexia is demonstrated, indomethacin may be of assistance in reducing core temperature. This, however, is not demonstrated conclusively by research.

J. Conclusions

Although much work needs to be done to elucidate the mechanisms, effects and treatments of shock in birds, it appears that there does exist in birds a process which resembles the mammalian shock response. This is evidenced by the demonstration of altered blood flow distribution and accumulation of metabolic wastes in response to situations which impair the function of the cardiovascular system. However, characterisation of the avian shock response is not complete, and given that the class Aves comprises some 9000 species in 27 orders, inference and extrapolation are likely to continue into the foreseeable future.

Many compensatory mechanisms exist in birds which are similar to those known in mammals. In addition, there are some such as the renal portal system which are novel and whose function remains unclear.

References

Arad Z (1983). Thermoregulation and Acid-Base Status in the Panting Dehydrated Fowl, *Journal of Applied Physiology: Respiratory Environmental and Exercise Physiology* 54:234-243.

Arad Z, SS Arnason, A Chadwick and E Skadhauge (1985). Osmotic and Hormonal Responses to Heat and Dehydration in the Fowl, *Journal of Comparative Physiology B* 155:227-234.

Arad Z, M Horowitz, U Eylath and J Marder (1989). Osmoregulation and Body Fluid Compartmentalisation in Dehydrated, Heat-Exposed Pigeons, *American Journal of Physiology 257 (Regulatory integrative comparative physiology)*:R377-R382.

Arad Z and E Skadhauge (1984). Plasma Hormones (Arginine Vasotocin, Prolactin, Aldosterone and Corticosterone) in Relation to Hydration State, NaCl Intake, and Egg Laying in Fowls, *Journal of Experimental Zoology* 232:707-7 14.

Bednarski RM, R Skarda, C Swanson, D Mason and PW Hellyer (1989). *Handbook of Veterinary Anesthesia*, CV Mosby Company, St Louis, Missouri.

Bos JH, B Todd, LA Tell, EC Ramsay and ME Fowler (1990). Treatment of Anemic Birds with Iron Dextran Therapy: Homologous and Heterologous Blood Transfusions, *Proceedings of the Association of Avian Veterinarians*, 221-225.

Bottje, WG, KR Holmes, HL Neldon and TK Koike (1989). Relationship Between Renal Hemodynamics and Plasma Levels of Arginine Vasotocin and Mesotocin during Hemorrhage in the Domestic Fowl *(Gallus domesticus), Comparative Biochemistry nd Physiology 92A*(3):423-427.

Braun EJ and WH Dantzler (1974). Effects of ADH on Single-Nephron Glomerular Filtration Rates in the Avian Kidney, *American Journal of Physiology* 226:1-8

Braun EJ and WH Dantzler (1984). Endocrine Regulation of Avian Renal Function, *Journal of Experimental Zoology* 232:715-723.

Cotran RS, V Kumar and SL Robbins (1989). Robbins' Pathological basis of disease, fourth ed, WB Saunders Company, Philadelphia.

Dantzler WH (1979). Renal Mechanisms for Osmoregulation in Reptiles and Birds, in Animals and Environmental Fitness, Volume 1 Invited Lectures (R Gilles, ed), Pergamon Press, Oxford, 91-110.

Dantzler WH (1989). Glomerular Filtration Rate and Effective Renal Plasma Flow in Birds, in Progress in Avian Osmoregulation (MR Hughes and A Chadwick, eds), Leeds Philosophical and Literary Society, Leeds, 207-224.

Edens FW, FM McCorkle and DG Simmons (1984). Body Temperature Response of Turkey Poults Infected with *Alcaligenes faecalis, Avian Pathology* 13:787-795.

Goldstein DL and EJ Braun (1988). Contribution of the Kidneys and Intestines to Water Conservation and Plasma Levels of Antidiuretic Hormone During Dehydration in House Sparrows *(Passer domesticus), Journal of Comparative Physiology B* 158:353-361.

Guyton, AC (1991). Textbook of Medical Physiology, Saunders, Philadelphia.

Harvey S, TR Hall, A Chadwick and DM Ensor (1989). Osmoregulation and the Physiology of Prolactin, in Progress in Avian Osmoregulation (MR Hughes and A Chadwick, eds), Leeds Philosophical and Literary Society, Leeds, 81-109.

Hoefer, HL (1992). Transfusions in Exotic Species, Problems in Veterinary Medicine, 4(4):625-635.

Hodges RD (198 1). Endocrine Glands, in Form and Function in Birds (AS King and J McLelland, eds), Academic Press, London.

Jones DR and Johansen K (1982). The Blood Vascular System of Birds, in Avian Biology (DS Farmer and JR King, eds), Academic Press, New York, 157-285.

Kasuya Y, T Karakida, Y Okawara and H Kobayashi (1987). Comparative Studies of food and Water Balance following Water Deprivation in the Budgerigar *(Melopsittacus undulatus)* and Japanese Quail *(Coturnix coturnix japonica), Journal of the Yamashina Institute of Ornithology* 19:89-102.

King AS and J McLelland (1984) Birds, their structure and function, Bailliere and Tindall, London.

Kobayashi H, H Uemura and Y Takei (1980). Physiological Role of the Renin-Angiotensin System during Dehydration, in Avian Endocrinology (Epple A and MH Stetson, eds), Academic Press New York.

Koike TI (1989). Release of Avian Neurohypophyseal Peptides, in Progress in Avian Osmoregulation (MR Hughes and A Chadwick, eds), Leeds Philosophical and Literary Society, Leeds, 41-60.

Lamberski N, and G Daniel (1992). Fluid Dynamics of Intraosseous Fluid Administration in Birds, *Journal of Zoo and Wildlife Medicine* 23(1):47-54.

Laverty G (1989). Renal Tubular Transport in the Avian Kidney, in Progress in Avian Osmoregulation (MR Hughes and A Chadwick, eds), Leeds Philosophical and Literary Society, Leeds, 243-261.

Lien Y-HH, MM Pacelli and EJ Braun (1993). Characterisation of Organic Osmolytes in Avian Renal Medulla, a Non-Urea Osmotic Gradient System, *American Journal of Physiology 264 (Regulatory Integrative Comparative Physiology*):R1045-R 1049.

Lumeij JT (1985). The Influence of Blood Sample Treatment on Plasma Potassium Concentration in Avian Blood, *Avian Pathology* 14:257-260.

Lumeij JT (1987). Plasma Urea, Creatinine and Uric Acid Concentrations In Response to Dehydration in Racing Pigeons *(Columba livia domestica), Avian Pathology* 16:377-382.

Lumeij JT and JD Remple (1991), Plasma urea creatinine and uric acid in relation to feeding in peregrine falcons *(Falco peregrinus), Avian Pathology* 20:79-83.

Macari M, RL Furlan, FP Gregorut, ER Secato and JR Guerreiro (1993). Effects of Endotoxin, Interleukin-lB and Prostaglandin Injections on Fever Response in Broilers, *British Poultry Science* 34:1035-1042.

McLelland J and V Molony (1983). Respiration, in Physiology and Biochemistry of the Domestic Fowl (BM Freeman, ed), Academic Press, London.

Marder, J and Z Arad (1989). Panting and Acid Base Regulation in Heat Stressed Birds, *Comparative Biochemistry and Physiology, 94A*(3):395-400.

Martin HD and GV Kollias (1989). Evaluation of Water Deprivation and Fluid Therapy in Pigeons, *Journal of Zoo and Wildlife Medicine* 20(2):173-177.

Merrill GF, M Rosolowsky and GJ Grover (1979). Seasonal Variability in the Responses of Domestic Fowl, *Gallus domesticus,* to Endotoxaemia, *Journal of Comparative Physiology B* 134:287-292.

Merrill GF, RE Russo and JM Halper (198 1). Cardiac output distribution before and after endotoxin challenge in the rooster, *American Journal of Physiology 241 (Regulatory Integrative Comparative Physiology*):R67-R71.

Miyagawa S, M Numata and M Mkuuchi (1991). Portal Endotoxaemia - some recent advances, *Medical Science Research*, 19:363-364.

Philip CJ (1981). Emergencies, Shock and Post-Surgical Care, Aviary and Caged Birds, Proceedings 55, Postgraduate Committee in Veterinary Science, University of Sydney, 256-296.

Roberts JR and WH Dantzler (1989). Glomerular Filtration Rate in Conscious Unrestrained Starlings Under Dehydration, *American Journal of Physiology 256 (Regulatory Integrative Comparative Physiology)*: R836-R839.

Shoemaker, VH (1972). Osmoregulation and Excretion in Birds, in Avian Biology (DS Farmer and JR King, eds), Academic Press, New York.

Siller WG (1983). Structure of the Kidney, in Physiology and Biochemistry of the Domestic Fowl (BM Freeman, ed), Academic Press, London.

Skadhauge E (1981). Osmoregulation in Birds, Berlin, Springer-Verlag.

Skadhauge E (1983). Formation and Composition of Urine, in Physiology and Biochemistry of the Domestic Fowl (BM Freeman, ed), Academic Press, London.

Stallone E and EJ Braun (1985). Contributions of Glomerular and Tubular Mechanisms to Antidiuresis in Conscious Domestic Fowl. *American Journal of Physiology 249 (Renal Fluid Electrolyte Physiology* 18):f842-f850.

Stallone E and EJ Braun (1986). Osmotic and Volemic Regulation of Plasma Arginine Vasotocin in Conscious Domestic Fowl, *American Journal of Physiology 250 (Regulatory Integrative Comparative Physiology* 19):r644-r657.

Sturkie PD (1986a). Heart and Circulation: Anatomy, Hemodynamics, Blood Pressure, Blood Flow, in *Avian Physiology* (PD Sturkie, ed), Springer-Verlag, New York.

Sturkie PD (1986b). Kidneys, Extrarenal Salt Excretion, and Urine, in *Avian Physiology* (PD Sturkie, ed), Springer-Verlag, New York.

Tazawa H (1986). Add-Base Equilibrium in Birds and Eggs, in Add-Base Regulation in Animals (N Heisler, ed), Elsevier Science Publishers, Amsterdam.

Teeter RG, MO Smith, FN Owens, SCArp, S Sabgiah and JE Breazile (1985). Chronic Heat Stress and Respiratory Alkalosis: Occurrence and Treatment in Broiler Chicks, *Poultry Science* 64:1060-1064.

Verkest, KR (1994). Shock and Compensatory Mechanisms in Birds, Bachelor of Veterinary Biology thesis, University of Queensland.

Wang, S and WG Bottje (1989). Effect of Heat Stress on Plasma Levels of Arginine Vasotocin and Mesotocin in Domestic Fowl *(Gallus domesticus)*, *Comparative Biochemistry and Physiology* 93A(4):721-724.

Weidner, WJ, LA Selna, DE McClure and DO DeFouw (1993). Effect of extracellular fluid volume expansion on avian lung fluid balance, *Respiration Physiology*, 91: 125-136.

Wessels BC, SL Gaffin and MT Welles (1987). Circulating Plasma Endotoxin (Lipopolysaccharide) Concentrations in Healthy and Haemorrhagic Enteric Dogs: Antiendotoxin Immunotherapy in Haemorrhagic Enteric Endotoxaemia, *Journal of the American Animal Hospital Association* 23:291-295.

West NH, B Lowell Langille and DR Jones (1981). Cardiovascular System, in Form and Function in Birds (AS King and J McLelland, eds), Academic Press, London.

Wilson JX (1989). The Renin-Angiotensin System in Birds, in Progress in Avian Osmoregulation (MR Hughes and A Chadwick, eds), Leeds Philosophical and Literary Society, Leeds.

Wolfenson D, A Berman, F Frey and N Snapir (1978). Measurement of Blood Flow Distribution by Radioactive Microspheres in the Laying Hen *(Gallus domesticus)*. *Comparative Biochemistry and Physiology* 61:549-554.

Wyse DG and M Nickerson (1971). Studies on Haemorrhagic Hypotension in Domestic Fowl, *Canadian Journal of Physiology and Pharmacology* 49:919-926.