Front. Biol. 2013, 8(2): 134–159
DOI 10.1007/s11515-012-1206-2

REVIEW

Avian metabolism: its control and evolution

Colin G. SCANES (✉)[1], Eldon BRAUN[2]

[1] *Department of Biological Science, University of Wisconsin, Milwaukee, WI 53211, USA*
[2] *Department of Physiology, University of Arizona, Arizona Health Sciences Center, Tucson, AZ 85724, USA*

Abstract **This review discussed metabolism in poultry and wild birds with an emphasis on what remains to be elucidated. Circulating concentrations of glucose are much greater in both poultry and wild birds than in mammals which in turn are higher than in reptiles. The basis for this difference is unknown but does not appear to be related to the requirements of flight. Furthermore, birds exhibit a refractoriness to potential adverse effects of very high circulating concentrations of glucose. Again the basis of this is unclear. There is substantial information on the control of metabolism in poultry, although which hormones are exerting physiologic roles remains to be clarified. There is a tacit but unverified assumption that the control mechanisms are the same in wild birds and in poultry. Despite, significant research focus on metabolism in poultry and to a less extent wild birds, there is a dearth of studies determining metabolism in a quantitative manner.**

Keywords metabolism, bird, circulating glucose, glucagon, insulin

Introduction

The circulating concentrations of glucose are very high in both wild and domestic birds compared to mammals when animals of similar body mass are compared (Braun and Sweazea, 2008) (Table 1 and Fig. 1). Allometric analysis of a large database (n = 97 for wild birds and n = 162 for mammals) shows parallel lines with identical slopes when plasma glucose concentrations are plotted against the log of body mass:

In birds, circulating concentration of glucose (mM) = 15.3 – 0.44 log body mass (kg).

In mammals, circulating concentration of glucose = 7.6 – 0.44 log body mass (kg).

The y intercept of the two lines is 15.3 mM (or 275 mg/dL) in wild birds and 7.6 mM (137 mg/dL) in mammals (Braun and Sweazea, 2008); differing by a factor of two. Thus, non-domestic birds have plasma glucose concentrations twice as high as that of mammals. When individual speciesare compared, it is apparent that some birds have plasma glucose levels that are 6 fold higher that mammals of similar body mass. It has been suggested that as birds are less long-lived than mammals, the relatively high plasma glucose concentrations are of little consequence to the pathologies of these animals. A simple empirical observation of a 20 gm body mass mouse and a 20 gm parakeet belies this suggestion; the mouse is senescent at 18 – 24 months and the parakeet will live 20 to 20 five years.

Glucose excretion by birds

Under normal glucose homeostasis, little or no glucose appears in the uretheral urine of birds. Although it should be noted that when the excreta of birds are collected, small quantities of glucose will be present as result of bacterial fermentation in the lower gastrointestinal tract. It is of interest that no glucose escapes in the uretheral urine of birds considering the high plasma concentration and the glomerular filtration rates (GFRs) that, on an allometric basis, do not differ significantly from those of mammals (Yokota et al., 1985). Plasma concentration of glucose multiplied by the GFR yields a parameter called the filtered load (FL) of glucose. This is a much higher value for birds given the high plasma glucose levels. Yet no glucose appears in the urine. It has been determined and quite well characterized for mammal

Received December 31, 2011; accepted February 27, 2012
Correspondence: Colin G. SCANES
E-mail: scanes@uwm.edu

Table 1 Comparisons of circulating concentrations of glucose (mg/dL) in mammals, birds and reptiles in selected examples

	Fed	Fasted	References
Class Mammalia			
Human	131[1]	~80[2]	Edwards et al., 2001
Horse	115	84	Christensen et al., 1997; Nadal et al., 1997
Rat	137	88	Simon et al., 2011
Class: Aves (Birds)			
Chicken	241	215	Simon et al., 2011
Ducks	178	175	Applegate et al., 1999; Farhat and Chavez, 2001
Hummingbird	756	306	Beuchat and Chong, 1998
King penguin		180	Bernard et al., 2003
Ostrich	218		Verstappen et al., 2002
Class Reptilia			
Turtle *Melanochelys trijuga*		70–114	Chandavar and Naik, 2008
Mediterranean pond Turtles (*Mauremys leprosa*)	74		Hidalgo-Vila et al., 2007
Loggerhead sea turtle (*Caretta caretta*)	18		Lutz and Dunbar-Cooper, 1987
Morelet's crocodiles (*Crocodylus moreletii*)	7.0		Padilla et al., 2011
Alligators (*Alligator mississippiensis*)	134 (43–264)	139 (83–218)	Lance et al., 1993
Snake (*Psammophis Sibilans*)	127	117	Algauhari, 1967
Boa constrictor	17–26		Silva et al., 2011

[1]: 7.3 mmol/L; [2]: 4.6 mmol/L

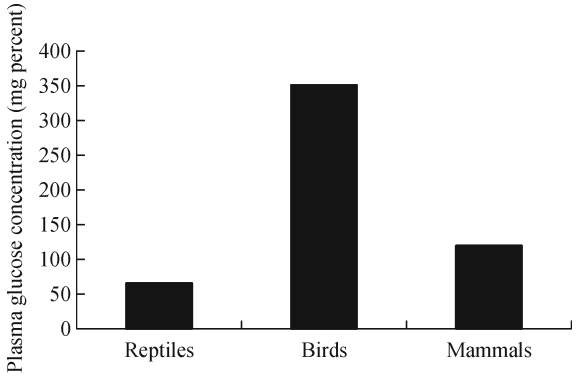

Figure 1 Mean plasma glucose concentrations in 55 species of reptiles, in birds (97 species of wild birds) and in 162 species of mammals. The striking feature is the very high plasma level of plasma glucose in birds compared to the levels in either reptiles or mammals.

kidneys that there are two glucose transport proteins (sodium/glucose co-transport proteins, SGLTs) present in the proximal renal tubule that, under normal glucose homeostasis, reabsorb all the glucose that is filtered at the glomerulus (Turk and Wright, 1997). For birds, all that is known at this time is that no glucose appears in the urine. Therefore, some isoform of the SGLTs must be present within the avian kidney. SGLT1 appears in the chicken genome, but it is the protein that is present in the lower gastrointestinal tract. To date, little or no work has been conducted on the glucose transport capacity of the avian kidney. This is an area that warrants attention.

Control of carbohydrate metabolism in birds

There is a marked tendency for researchers to consider birds either as wild birds or one of the domesticated species or poultry. There might to be changes in the physiological control mechanisms due to domestication and/or to intensive selective breeding either for laying or for rapid growth. Chickens were developed from the ancestral Red Jungle Fowl (West and Zhou, 1988). Comparative genomics of chickens with the ancestral Red Jungle Fowl has identified deletions (Rubin et al., 2010). The available evidence (discussed below) supports close consistency in the control of metabolism in wild and domesticated birds.

Pancreatic hormones and metabolism

Glucagon

Glucagon is generally considered as the major hormone controlling metabolism in birds. There have been extensive studies on the effects of glucagon, particularly in domesticated birds. Its role is thought to be well established:

• Stimulating lipolysis (chickens: Langslow and Hales, 1969; turkeys: Kurima et al., 1994; king penguins: Bernard et al., 2003).

• Suppressing hepatic lipogenesis (chickens: Goodridge, 1973; ducks: Bedu et al., 2002).

• Elevating circulating concentrations of glucose (chickens: early research reviewed Hazelwood, 1986; turkeys: Kurima et al., 1994).

• Stimulating glycogenolysis in chick embryo hepatocytes (Picardo and Dickson, 1982).

• Stimulating gluconeogenesis (discussed below).

In chickens and presumably other birds, the liver is the major organ converting lactate to glucose (Watford, 1985). Glucagon stimulates hepatic gluconeogenesis (Watford, 1985). On the other hand, the kidneys are the major gluconeogenic organ that uses either pyruvate or amino-acids as the substrate (Watford, 1985). Renal cytosolic phosphoenol pyruvate carboxykinase activity is increased by cAMP (Watford, 1989). What is not known is whether glucagon or other metabolic hormones act at physiological concentrations to influence renal gluconeogenesis. For instance, does administration of glucagon antagonists suppress the elevated gluconeogenesis observed in the kidneys of fasted birds. Moreover, effects of glucagon antagonists on liver gluconeogenesis have not been reported.

Although glucagon can markedly elevate circulating concentrations of glucose in birds that does not *per se* demonstrate that glucagon is physiologically controlling circulating concentrations of glucose. Glucagon does not appear to be playing a role in the tonic control of circulating concentrations of glucose at least in the fed state. Circulating concentrations of glucose were unaffected by administration of a glucagon antagonist in fed chickens (Simon et al., 2000; Dupont et al., 2008); this being when concentrations of glucagon are low (Christensen et al., 2012a). What is not clear is whether blocking glucagon's effect with an antagonist influences glycemia in the fasted state. Fasting markedly increases circulating concentrations of glucagon in chickens (Christensen et al., 2012a). Moreover, it might be questioned whether glucagon when administered is mimicking other glucagon like peptides. There is further evidence that argue against glucagon being the only or even the principal hormone responsible for restoring homeostasis in the fasted state. The circulating concentrations of glucagon peak within six hours of fasting and decline as fasting is extended despite the increasingly severe relative hypoglycemia (Table 2). It is noted that the effects of glucagon on chicken adipose tissue are attenuated over prolonged exposure to glucagon (Campbell and Scanes, 1987; Oscar, 1992) due to downregulation of the glucagon receptors (Oscar, 1996a).

The available but limited evidence of the role of glucagon in wild birds is consistent with its role in poultry. For instance, glucagon increases circulating concentrations of non-esterified fatty acids in red-winged blackbirds indicating stimulation of lipolysis (Hintz, 2000). There is clearly a strong case for fundamental studies on the role of glucagon and other hormones in wild species of birds. It is argued that metabolism in poultry is markedly different from the ancestral wild state due to intensive selection.

The effects of glucagon on lipolysis are influenced by other hormones with pancreatic polypeptide and triiodothyronine (T_3) being stimulatory while somatostatin (SRIF) and growth hormone (GH) are inhibitory (this is discussed in more detail under each hormone below).

The factors controlling secretion of glucagon in domesticated birds are summarized in Table 3. It is presumed that similar control mechanisms exist in wild species. For instance, glucose is reported to depress circulating

Table 2 Examples of hormonal and metabolic perturbations on the circulating concentrations of glucose, insulin and glucagon in chickens

Treatment	Glucose mg/dL	Insulin ng/mL	Glucagon pg/mL	References
Fasting				
Fed	243	1.54	152	Christensen et al., 2012a
Fasted 6 hours	219	0.85	451	Christensen et al., 2012a
Fed control	243	1.51	142	Christensen et al., 2012a
Fasted 24 hours	194	0.73	406	Christensen et al., 2012a
Blocking insulin				
Fed + 1 hour	264	–	120	Dupont et al., 2008
Fed + anti-insulin + 1 hour	434	–	390	Dupont et al., 2008
Fed + 5 hour	232	–	50	Dupont et al., 2008
Fed + anti-insulin + 5 hour	747	–	1080	Dupont et al., 2008
Glucose loading[1]				
Basal	194	0.37		Zhao et al., 2009b
Glucose load (+ 30 minutes)	284	1.16		Zhao et al., 2009b
Glucose load + arginine (+ 30 minutes)	264	1.54		Zhao et al., 2009b
Corticosterone plus glucose load (+ 30 minutes)	261	2.67		Zhao et al., 2009b
Corticosterone (+ 2 hours)	238	1.20		Zhao et al., 2009b

[1]: Data calculated from Zhao et al., 2009b.

Table 3 Control of secretion of glucagon in domestic birds

Stimulus	Chickens	Ducks	References
Fasting	+++		Christensen et al., 2012a
Low glucose	+++	+++	Honey et al., 1980; Laurent and Miahle, 1978
High glucose	–	–	Honey et al., 1980; Laurent and Miahle, 1978
Arginine	+	+	Honey et al., 1980; Laurent and Miahle, 1978
Insulin	–		Honey and Weir, 1979; Dupont et al., 2008
Somatostatin		++	Stroesser et al., 1980

concentrations of glucagon in migratory garden warblers (Totzke et al., 1998). What is not known in birds are effects of gastric hormones such as the incretins-glucose dependent insulin tropic peptide (GIP) and glucagon like peptides (GLP) 1, together with gastrin and cholecystokinin, other gastro-intestinal peptides such as ghrelin, GLP-2, obestatin, and orexigen together with adipose hormones such as the ligand for the avian leptin receptor and adiponectin. Moreover, there is a need to investigate the physiologic roles of these controlling circulating concentrations following a meal or in fasting in birds using glucagon antagonists. What is further unknown in birds is the extent that the assays in the studies where peripheral glucagon was determined (Laurent and Mialhe, 1978; Honey et al., 1979) also detected other glucagon gene products such as GLP1 and 2, glicentin or oxyntomodulin.

Insulin

Insulin appears to lack several of the roles it has in mammals:

- No effect on lipolysis at least in domestic birds (based on *in vitro* studies with chicken adipose explants (Langslow and Hales, 1969),
- No effect on hepatic glycogenolysis based on studies in chick embryo hepatocytes (Picardo and Dickson, 1982),
- No effect on glycolysis by either skeletal muscle or liver or gluconeogenesis by either liver or kidneys (Chida et al., 2000).

However, insulin does have some effects in birds based on studies where either insulin was administered or *in vitro* studies. Insulin administration increases muscle glycogen (Hazelwood and Lorenz, 1959) despite the absence of the insulin dependent glucose transporter 4 (GLUT 4) in birds (chicken: Kono et al., 2005; sparrow: Sweazea and Braun, 2006a). Insulin enhances glucose entry into kidney, brain and muscle tissue but not adipose tissue in birds. This is supported by the decreased circulating concentrations of glucose following insulin administration (Hazelwood and Lorenz,1959), the increased uptake of 2-deoxy-D-[1-(3)H] glucose ([(3)H]2DG) by skeletal muscles (*soleus, extensor-digitorum longus* and *pectoralis superficialis* muscles) *in vivo* (Tokushima et al., 2005) and *in vitro* (Rudas and Scanes, 1983). Moreover, insulin does increase uptake of fatty acids by sparrow muscle (Sweazea and Braun, 2006b).

Insulin increases expression of the liver form of phospho-fructokinase in chicken breast muscle (*pectoralis*) (Seki et al., 2006). In addition, insulin *in vitro* has a modest effect on the synthesis of fatty acids; insulin synergizing with T_3 to stimulate the synthesis of fatty acid synthase in the chicken liver (Wilson et al., 1986) but has no discernible effect on lipogenesis by duck hepatocytes (Bedu et al., 2002).

There is strong evidence for insulin having a physiological role in the control of glucose metabolism in birds. For instance, circulating concentrations of glucose in fed chickens rise to extremely high levels when endogenous insulin is selectively removed using insulin antibodies (Simon et al., 2000; Dupont et al., 2008). Moreover, despite the elevated ambient glucose concentrations, there are very high circulating concentrations of glucagon (Dupont et al., 2008). These data are consistent with insulin *per se* acting in a tonic manner to depress circulating concentrations of glucose. Alternatively, insulin antibodies can be envisioned to be removing insulin's tonic suppression of glucagon secretion (Table 3) which in turn elevates circulating concentrations of glucose. What is not clear is whether blocking glucagon's effect with an antagonist can influence circulating concentrations of glucose in the hyperglycemic and hyperglucagonemic state following administration of antisera to insulin. Furthermore, it is not known the extent that insulin is mediating the increases in circulating of T_3 and hepatic GH binding and the decreases in hepatic deiodinase type III activity following re-feeding fasted chickens (Buyse et al., 2002). This could be approached by examining *in vivo* using antisera to insulin.

Insulin also downregulates insulin receptor expression in the chicken hypothalamus and probably other tissues (Shiraishi et al., 2011). Insulin influences release of insulin like growth factors; stimulating *per se* secretion of IGF-I by chicken hepatocytes *in vitro* and acts synergistically with GH to increase IGF-I release (Houston and O'Neill, 1991). Insulin also depresses hepatic IGF binding protein 2 expression in fasted chickens (Nagao et al., 2001).

Table 4 summarizes the factors controlling insulin secretion in birds. What is not known in birds are effects of gastric hormones such as the incretins-GIP and GLP 1, together with gastrin and cholecystokinin, other gastro-intestinal peptides such as ghrelin, GLP-2, obestatin, and orexigen together with adipose hormones such as the ligand for the avian leptin receptor and adiponectin. Moreover, there is a need to investigate the physiological roles of these controlling circulating concentrations of gastro-intestinal and pancreatic

Table 4 Control of insulin secretion in domestic birds

Stimulus	Chickens	Ducks	References
Fasting	–		Christensen et al., 2012a
High glucose	++	++	King and Hazelwood 1976; Laurent and Miahle, 1978
Arginine	+	+	Honey et al., 1980; Laurent and Miahle, 1978
Glucagon	+		King and Hazelwood, 1976
Somatostatin		–	Stroesser et al., 1980
Epinephrine	–		Langslow et al., 1970
Growth hormone[a]		–	Foltzer and Miahle, 1976.
Fatty acids	–	–	Laurent and Miahle, 1978
Glucocorticoids	++		Zhao et al., 2009b; Song et al., 2011

hormones following a meal or in fasting in birds using administration of specific antagonists orantisera.

In turkey poults, hypophysectomy decreases circulating concentrations of insulin with the effect partially overcome by GH replacement therapy (Proudman et al., 1994).

Other pancreatic hormones

There are effects of other pancreatic hormones on metabolism. For instance, pancreatic polypeptide stimulates both basal and glucagon stimulated lipolysis by chicken adipocytes (Oscar, 1993). There is scant information on the physiologic role for pancreatic polypeptide in birds. The metabolic effects of SRIF will be discussed under gastro-intestinal hormones (below).

Pituitary, thyroid hormones, adrenal hormones and metabolism

Glucocorticoid—corticosterone

Avian metabolism is profoundly influenced by either corticosterone, the major glucocorticoid in birds, or dexamethasone acting as a surrogate. Administration of glucocorticoids to chickens is followed by decreased growth, particularly of skeletal muscle with marked increases in adiposity and liver weight (Bartov, 1985; Siegel et al., 1989; Jiang et al., 2008; Yuan et al., 2008). Corticosterone decreases skeletal muscle and nitrogen retention in chickens (Bartov, 1985). This is not apparently due to decreases in the rate of protein synthesis (Hayashi et al., 1994). Rather, corticosterone is increasing degradation of both myofibrillar and non-myofibrillar muscle proteins (Hayashi et al., 1994; Ohtsuka et al., 1998; Dong et al., 2007). Moreover, there are increases in the circulating concentrations of glucose, insulin, triglyceride and non-esterified fatty acids (NEFA) with glucocorticoid administration (Yuan et al., 2008). There are also increases in adipose lipoprotein lipase (Jiang et al., 2008) and *pectoralis* muscle glycogen (Lin et al., 2007; Gao et al., 2008). Glucocorticoids decrease expression of IGF1 and increase that of myostatin in chicken muscle (Song et al., 2011). It is unknown whether effects of the effects of glucocorticoid on avian metabolism are physiological or do they represent supra-physiological or pharmacological effects.

Glucocorticoids increase hepatic glycogen and circulating concentrations of glucose (Kobayashi et al., 1989). There is evidence that glucocorticoids stimulate gluconeogenesis in the liver (Watford, 1985; Niwa et al., 1986) and kidneys of chickens (Watford, 1989). There is clearly a need to examine whether or not physiological concentrations of corticosterone stimulate gluconeogenesis in the liver (Niwa et al., 1986) and kidneys of birds. This is particularly germane to carnivorous birds where gluconeogenesis would be anticipated to be more important. Moreover, it is be important to determine quantitatively the importance of liver and kidney to overall gluconeogenesis under different physiologic states and hormonal milieu. Glucocorticoids are thought to act by inducing insulin resistance in chickens (Dupont et al., 1999; Yuan et al., 2008). There are reductions in hepatic insulin binding and insulin receptor substrate-1 levels (Dupont et al., 1999) together with decreased insulin stimulated glucose uptake in skeletal muscle (Zhao et al., 2009a).

Growth hormone

Components of the hypothalamic pituitary growth hormone axis influence lipid metabolism. Ghrelin and SRIF are discussed under gastro-intestinal hormones (below). Lipolysis is increased by GH as indicated by elevated non-esterified fatty acids (hypophysectomized chickens: Scanes et al., 1987; acutely in chickens: Scanes, 1992; chronically in turkeys: Bacon et al., 1995). Moreover, GH stimulates lipolysis *in vitro* with chicken adipose explants (Harvey et al., 1977; Campbell and Scanes, 1985). GH from birds, mammals and reptiles is effective while that from lower vertebrates is not (Campbell and Scanes, 1985; Campbell et al., 1990, 1991). The effects of GH on lipolysis are blocked by a specific GH antagonist (Campbell et al., 1993), by protein synthesis inhibitors and low calcium in the incubation media (Campbell and Scanes, 1988a) and by either SRIF or insulin (Campbell and Scanes, 1988b). In addition, GH has an anti-lipolytic effect with the lipolytic effect of glucagon *in vitro* being reduced in the presence of GH (Campbell and Scanes, 1987). The anti-lipolytic effect is observed with mammalian, avian

GH together with both lower vertebrate GH (Campbell et al., 1991) and the GH antagonist (Campbell et al., 1993); the later not evoking a lipolytic effect. It is not known whether GH acts via direct effects on the adipocytes or by acting on fibroblasts or other cells found in adipose explants. In addition, GH depresses lipogenesis (Harvey et al., 1977; Rosebrough et al., 1991). There is a strong case to re-examine the effects of GH *in vitro* determining effects on gene expression, protein synthesis, post-translational changes (particular phosphorylation) and employing a comprehensive metabolomics approach.

Growth hormone also influences metabolism indirectly by increasing circulating concentrations of IGF-1 (Houston and O'Neill, 1991) and T_3 (Darras et al., 1993).

Prolactin

Prolactin increases feeding and hence elevates the quantity of energy stored in adipose tissue in birds. This is supported by the ability of intra-cerebroventricular administration of prolactin to stimulate food consumption and increase bodyweight in ring doves (Buntin et al., 1999). The effect is independent of glucocorticoids as prolactin induced hyperphagia is not blocked by a glucocorticoid antagonist (Koch et al., 2004). It is not clear whether this is an effect of pituitary prolactin *per se* or of the recently described prolactin-like protein (PLP) (Wang et al., 2010); PLP being expressed in the brain of chickens and also zebra fish (Wang et al., 2010).

Thyroid hormones

The active thyroid hormone, T_3, has marked effects on metabolism in birds based on albeit relatively small number of studies in poultry species. Fasting results in decreases in body temperature (Christensen et al., 2012b), presumably reflecting decreased metabolic rate, and reductions in circulating concentrations of T_3 (Buyse et al., 2002). Refeeding fasted chickens is followed by increased circulating concentrations of T_3 due to decreased hepatic deiodinase type III activity and elevated metabolic rate (Buyse et al., 2002). It is reasonable to propose that the increased T_3 is mediating the shift in metabolism. However, definitive studies are required to examine this hypothesis.

The transition from fasting to the fed state is accompanied by a shift from lipolysis to lipogenesis (Buyse et al., 2002). It is unknown the extent to which shifts in the circulating concentrations of T_3 mediate the changes in lipid metabolism. There is evidence that T_3 enhances both lipolysis and lipogenesis in birds. Pre incubation of chicken adipocytes with T_3 increases basal and glucagon stimulated lipolysis (Suniga and Oscar, 1994). Lipogenesis in the chicken liver is stimulated by T_3 with increases in both the expression and synthesis of fatty acid synthase particularly in the presence of insulin (Wilson et al., 1986).

Adrenocorticotropic hormone, β lipotropin and other products of proopiomelanocortin (POMC)

The avian pituitary gland expresses proopiomelanocortin (POMC), the precursor for ACTH, β-lipotropin, β endorphin and α, β and γ melanocyte stimulating hormone (MSH) (chicken: Berghman et al., 1998; Takeuchi et al., 1999; ostrich: Naudé et al., 2006). The primary structure of ostrich β-lipotropin has been characterized (Naudé et al., 1981). What is not known is the extent to which POMC products other than ACTH such as α, β and γ MSH and β-lipotropin are released from the avian pituitary gland. Both glucagon and ACTH stimulate lipolysis by chicken adipose tissue *in vitro* (Langslow and Hales, 1969; Strosser et al., 1983). What is also not known is whether these hormones stimulate lipolysis in all avian species, whether the effects are physiological and whether other products of the POMC gene such as α, β and γ MSH or β-lipotropin also influence lipolysis and metabolism in other peripheral organs.

Adipose hormones

Adiponectin There is high expression of the adiponectin gene in chicken adipose tissue and to a less extent in the liver. Expression in both tissues is increased in chickens fasted for 48 h (Maddineni et al., 2005). However, no changes in circulating concentrations of adiponectin were observed in fasted chickens (Hendricks et al., 2009). An increase in adiponectin expression is reported in protein restricted chickens (Tahmoorespur et al., 2010). In the chicken, there are two genes for the adiponectin receptor, namely AdipoR1 and AdipoR2. Both receptors are expressed in the adipose tissue together with skeletal muscle and liver with increased expression of AdipoR2 in adipose tissue in chickens fasted for 48 h (Ramachandran et al., 2007). What is not known includes whether adiponectin has a physiologic role in either influencing carbohydrate or lipid metabolism directly or indirectly via effects on the secretion of insulin, glucagon or other hormones that control metabolism in birds.

Leptin There are marked effects of leptin reported on metabolism in birds. For instance, administration of leptin increases hepatic expression of fatty acid synthase in chickens (Dridi et al., 2005). The leptin receptor has been characterized (chicken: Liu et al., 2007; goose: Wang et al., 2011; turkey: Richards and Poch, 2003). There is evidence for a physiological role of the avian leptin receptors. Oleic acid increases expression of leptin receptors in goose adipocytes and expression of genes related to adipocyte differentiation are downregulated in adipocytes in which leptin receptor is knocked down (Wang et al., 2011). There is high expression of the leptin receptor in the chicken brain (Wang et al., 2011) with changes in hypothalamic expression during development (Huang et al., 2010). The chicken leptin receptor activates the JAK-STAT pathway (Adachi et al., 2008). The

endogenous ligand for the leptin receptor is, perhaps surprisingly, not conclusively established in chickens or other species of birds (Adachi et al., 2008). A bioassay for leptin failed to detect any leptin activity in chicken serum (Hen et al., 2008). It has been argued that the chicken leptin structure deposited in Genbank is erroneous and that leptin has been lost in birds (Sharp et al., 2008; Pitel et al., 2010). Clarification is required as to the very existence of leptin in birds and to potential alternative ligands for the leptin receptor.

Gastro-intestinal Hormones

Ghrelin There is evidence for effects of ghrelin on avian lipid metabolism. Ghrelin decreases hepatic expression of fatty acid synthase (Buyse et al., 2009). Ghrelin presumably acting via the GH secretagogue receptor (GHSR) influences metabolism in birds. It is unknown whether other products of the ghrelin gene namely unacylated ghrelin or obestatin have physiologic roles in birds.

Somatostatin There is evidence for direct effects of SRIF on metabolism in birds. Somatostatin suppresses glucagon stimulated lipolysis with chicken adipose tissue *in vitro* (Di Scala-Guenot et al., 1985; Oscar, 1996b). In turkeys, SRIF has been demonstrated to decrease glucagon induced lipolysis *in vivo* (Kurima et al., 1994). Similarly, SRIF inhibits GH stimulated lipolysis by chicken adipose tissue explants *in vitro* (Campbell and Scanes, 1988b). It is noted that SRIF is without any discernible effect on carbohydrate metabolism (Kurima et al., 1994).What is not known whether avian lipolysis is physiologically influenced by SRIF. Moreover, it is questioned whether cortistatin which binds to SRIF receptors is also an anti-lipolytic hormone in birds.

Other intestinal hormones It is not clear whether there are effects of gastro-intestinal peptides such as ghrelin, motilin or gastrin releasing peptide on avian lipolysis. It is further unknown whether growth factors influence avian lipolysis in an analogous manner to the effects of fibroblast growth factor 21 (FGF21) on human adipocytes (Arner et al., 2008).

Control of carbohydrate metabolism in wild birds

Circulating concentrations of glucose and their control

The physiologic relevance of the comparative high plasma glucose concentrations exhibited by birds is not clear. The results of a number of studies have demonstrated these concentrations do not change significantly during or as result of long distance migration (Jenni and Jenni-Eiermann, 1998; Maillet and Weber, 2006) and that migrants "burn" primarily fatty acids. For example, Warblers migrating from Northern Europe to sub-Saharan Africa do so in "hop-Scottish" manner (Schaub and Jenni, 2001).That is the tend to accumulate large fat depots before departing the summer feeding and breeding grounds, fly until the fat deposits are depleted, come to rest and replenish fat deposits (Schaub and Jenni, 2001). This pattern is repeated several times until they reach their wintering territories. A second example is that of the Plovers (*Calidris pusilla*) that are summer resident in Eastern Canada. These birds feed on the amphipod (*Corophium volutator*) that contains high concentrations of n-3 polyunsaturated fatty acids. Once conditions are correct, they fly non-stop to New Zealand and their plasma glucose concentrations on arrival are not significantly different from that of departure levels (Maillet and Weber, 2006). Thus, it remains somewhat of an open question as to why this condition has evolved in birds and how their tissues withstand plasma glucose concentrations that would be lethal to mammals and to humans in particular.

The results of some interesting recent work demonstrated that small birds, Swainson's thrushes (*Catharus ustulatu*), flown in a wind tunnel at low relative humidity metabolized protein to produce water to prevent dehydration while sparing glucose (Gerson and Guglielmo, 2011). These results add another intriguing dimension to the as yet not completely understood complex metabolism of birds.

Another interesting aspect of avian glucose homeostasis is that this group appears to lack Glut 4, the primary insulin responsive glucose transport protein on muscle (skeletal and cardiac) and adipose tissue (Sweazea and Braun, 2006a). Moreover, birds appear to store very little glucose as glycogen in their tissues (Ferguson and Braun, 2010). So why do birds maintain relatively high plasma glucose concentrations?

Metabolism related to flight and migration

The prevailing view is that high energetic needs or "fuel" for flight by birds are met predominantly by oxidation of fatty acids.

Short-term flights

The view that birds use fatty acids to "fuel" flight is supported by a relative small number of reports on short-term flights of less than 50 km. For instance, immediately following flight in homing pigeons, there are marked increases in the circulating levels of glucose, lactate, non-esterified fatty acids, epinephrine, glucagon and norepinephrine but no change in those of corticosterone and decreases in those of both T_3 and T_4 (Viswanathan et al., 1987; George et al., 1989). The view that flight is powered by fatty acids is supported by the observed

respiratory quotient of 0.7 in fasted hummingbirds (Suarez et al., 2011). However, glucose also can be the source of energy for flight as indicated by the respiratory quotient of 1.0 in nectar feeding hummingbirds (Suarez et al., 2011). Moreover in pigeons, there is a high capacity for glycolysis in the type 1 red muscle fibers in the pectoralis flight muscles (Meléndez-Morales et al., 2009).

Extended flights in migrations

The energetic needs for extended migrations are confounded by the absence of feeding during the period. Fatty acids are the major source of energy for flight during migration of birds (Jenni and Jenni-Eiermann, 1998). This is not surprising given the energy density of triglyceride in adipose tissue:

- Glycogen in skeletal muscle and liver 3.5 – 4.4 MJ per gram wet weight
- Protein in skeletal muscle 5.3 MJ per gram wet weight
- Triglyceride in adipose tissue 37.6 MJ per gram wet weight

(calculated from Jenni and Jenni-Eiermann, 1998).

In migratory birds, there is a seasonal fattening prior to migration to provide stored energy for during the rigors of migration. Prior to migration, birds prepare for the anticipated energetic requirements by laying down adipose fat stores (e.g. Landys et al., 2004). The hormonal basis for this is only partially understood. During and prior to migration, there are increases in circulating concentrations of the major avian glucocorticoid, corticosterone (Landys et al., 2004; Falsone et al., 2009). This is accompanying hyperphagia due at least in part to increased circulating concentrations of corticosterone based on studies with glucocorticoid antagonist (Landys et al., 2004). There are shifts in the glucagon:insulin ratio (Totzke et al., 2000). Circulating concentrations of glucagon are somewhat depressed during pre-migratory fat deposition in red-winged blackbirds (Hintz, 2000). There are likely to be also reductions in circulating concentrations of T_3. Flight is associated with a reduction in basal metabolic rate in birds (Speakman and Selman, 2003).

In addition in preparation for migration, there are changes in the expression of metabolic enzymes to prepare for the rigors of long distant flight. For instance, there is upregulation of both enzymes for fatty acid oxidation and the fatty acid transporters (membrane and intra-cellular) in flight muscles (e.g. Bishop et al., 1995; Pelsers et al., 1999; Guglielmo et al., 2002; McFarlan et al., 2009; Guglielmo, 2010). Moreover, as might be expected, fatty acid synthase expression is decreased immediately prior to migration (Zajac et al., 2011).

Birds use fatty acids as the major energy source for flight during migration (e.g. Sweazea and Braun, 2006a; Vaillancourt and Weber, 2007). The corollary to this is that there should be the following:

- Adequate stores of triglyceride in adipose tissue,
- High rates of lipolysis and consequently elevated circulating concentrations of non-esterified fatty acids,
- High capacity for muscles to transport fatty acids and for β fatty acid oxidation
- Gluconeogenesis using amino-acids from protein degradation to supply glucose.

In migrating birds, there are very high rates of lipolysis (e.g. Vaillancourt and Weber, 2007). Similarly at the end of migration of a shorebird, circulating concentrations of triglyceride, non-esterified fatty acids and glycerol are elevated; the latter two indicating high lipolytic activity (Landys et al., 2005). Moreover, high circulating concentrations of uric acid suggesting elevated protein degradation presumably to supply gluconeogenic precursors (Landys et al., 2005).

Responses in extended periods of fasting

King penguins and other species of penguins will fast for periods of five months in the winter losing about two thirds of their bodyweight (Cherel and Le Maho, 1985). There are three metabolic phases in response to prolonged fasting in birds:

- Phase 1: Adaptation with catabolism of fat stores,
- Phase II: Lower metabolism (economy) with slow but steady body mass loss using adipose lipid stores but with protein sparing,
- Phase III: More rapid bodyweight loss with elevated circulating uric acid indicating protein (muscle) degradation induced by the elevated circulating concentrations of corticosterone (Spée et al., 2011).

During phase II, there are reductions in metabolic rate as indicated decreases in plasma $_PCO_2$ in studies in geese (Le Maho et al., 1981). Moreover, plasma concentrations of the gluconeogenic amino-acid, alanine, are not changed (0.4 mM) (Le Maho et al., 1981). This would indicate protein sparing. There are increases in lipolysis and fatty acid oxidation. Plasma concentrations of beta-hydroxybutyrate are considerably elevated by prolonged fasting in geese (Le Maho et al., 1981) and king penguins (Cherel and Le Maho, 1985). Perhaps surprisingly, glucagon is not maximally stimulating lipolysis and gluconeogenesis in fasted penguins as glucagon infusion increases lipolysis further (Bernard et al., 2003). Moreover, glucagon infusion is accompanied by elevated circulating concentrations of glucose, beta-hydroxybutyrate and insulin in fasted king penguins (Bernard et al., 2003).

During phase III of fasting, there are further shifts in the circulating concentrations of nutrients and metabolites. Prolonged fasting is accompanied by some decrease in the circulating concentrations of glucose and the gluconeogenic amino-acid, alanine (Cherel and Le Maho, 1985).This is explicable by increases in protein (muscle) degradation generating alanine and other gluconeogenic amino-acids but a relatively larger increase in the rate of gluconeogenesis in

the penguins. Similarly, circulating concentrations of glucose are maintained in the range 144–180 mg/dL (8–10 mM) in long-term fasted geese (Le Maho et al., 1981). These changes would appear to be mediated induced by the elevated circulating concentrations of corticosterone (Spée et al., 2011).

Control of metabolism in poultry

Plasma concentrations of glucose in poultry

There is a marked variation in the reported circulating concentrations of glucose in chickens even in the same physiological state. For instance, in an analysis of 15 studies of plasma concentration of glucose in chickens of a limited age range with similar nutrition and genetics, mean plasma concentration of glucose were reported to vary between 156 and 330 mg/dL (Scanes, 2008). In chick embryos, the disparity between studies/investigators is even more apparent with circulating concentrations of glucose being reported at 200 mg/dL on days 18 of embryonic development (Lu et al., 2007) but at 111 mg/dL, when glucose was determined by isotope dilution gas chromatography mass spectrometry (Sunny and Bequette, 2010). The basis for the disparities between reported glucose concentrations requires attention and the use of common standards. An issue that should be addressed is the capability of avian red blood cells to metabolize glucose. Unlike mammalian erythrocytes, avian red blood cells contain a nucleus and mitochondria. If avian erythrocytes utilize glucose for their energy needs, it is readily apparent that failure to separate red blood cells from plasma or to cool blood samples rapidly might result in erroneously low circulating concentrations of glucose.

Circulating concentrations of glucose rise during development of the chicken embryo; increasing from 120 mg/dL on days 10 to 12 to about 200 mg/dL on days 18 to 20 of embryonic development in the (Lu et al., 2007). There are changes in circulating concentrations of glucagon but these temporally lagging those of glucose in chick embryo development (Lu et al., 2007). Circulating concentrations of glucose increase markedly in the first 2 days of post hatching life in chickens rising from 140 mg/dL to 220 mg/dL with marked decrease in circulating concentrations of glucagon (Richards et al., 2010). The circulating concentrations of glucose were reported to decline during growth in three populations of chickens (mean at 3 weeks old – 260 mg/dL; 6 weeks old – 243 mg/dL; 9 weeks old – 178 mg/dL; 12 weeks old – 162 mg/dL (Sinsigalli et al., 1987). Moreover, the incremental change in circulating concentrations of glucose declines 20 min after glucose load (2 g per kg intubated into the crop); the Δ glucose being at 3 weeks old-104 mg/dL; 6 weeks old – 91 mg/dL; 9 weeks old – 60 mg/dL; 12 weeks old – 25 mg/dL (Sinsigalli et al., 1987).

It is not clear as to what are the relative contributions of glucose, lactate and fatty acids to avian metabolism. Based on *in vivo* studies where radioactive glucose was placed into a duodenal loop, about 37% of the glucose is converted to lactate by the wall of the small intestine during absorption (Riesenfeld et al., 1982). Moreover, there is fermentation of starch to lactate in the crop of gallinaceous birds. This is illustrated in Table 6 for turkeys with similar levels of lactate in the chicken crop (Moore et al., 2004). Circulating concentrations of lactate are reported at 43 mg/dL and muscle tissue levels of 3.6 mg/g (Savenije et al., 2002). There is a need to determine the importance to overall avian metabolism of lactate either generated in the crop or small intestine wall. Moreover, if avian erythrocytes utilize glycolysis for their energy needs, it is readily apparent that failure to separate red blood cells from plasma or to cool blood samples rapidly might result in erroneously high circulating concentrations of lactate.

The role of liver and muscle glycogen in glucose metabolism

It is suggested that both liver and muscle glycogen play an important role supplying energy in birds during embryonic development and during the transition from *in ovo* to independent life. During hatching of chicks, the concentration of glycogen in the liver declines (Christensen et al., 2001). There are also decreases in the liver glycogen concentrations between days 15 and 19 of embryonic development (Pulikanti et al., 2010). Glycogen in skeletal muscles declines during the process of hatching (Christensen et al., 2001) presumably due to the energy needs for the physical process of hatching.

Glycogen is a readily available store of energy for times of feed interruption. There are reports that liver levels of glycogen decline during a fast. However, the available data exhibit a marked inconsistency in the rate of decline (> 80% lost in 6 h – Warriss et al., 1988; 77% in 24 h – Edwards et al., 1999; 37% in 12 h – Trampel et al., 2005). Moreover, levels of liver glycogen reported in the literature show marked variation between studies: 14 mg and 50 mg glycogen respectively prior to and following feeding in meal fed chickens (Ekmay et al., 2010) and 1.2 and 2.6 g glycogen respectively prior to and following feeding in meal fed chickens (de Beer et al., 2007). These differences may be explicable by the levels in the first study being a concentration (mg/g liver weight). There are decreases in muscle glycogen in chickens that had been subjected to feed withdrawal for 5 h; glycogen in the *pectoralis* reported to decline from 15.5 to 8.6 μmoles per g (Savenije et al., 2002). It is not clear whether this is μmoles glycogen or μmoles glucose generated by hydrolysis. Assuming that the glycogen concentrations reported are in glucose equivalents (Savenije et al., 2002), then the net rate of muscle glycogenolysis during fasting would be 246 μg per g per hour (Table 10) which is consistent to the blood glucose concentration. There is a need for studies on glycogen levels, synthesis and degradation in the liver and

skeletal muscle in fed and fasted adult birds and during growth. Moreover, *post mortem* increases in muscle glycogen were reported (Savenije et al., 2002). It is therefore essential to ensure tissues are rapidly frozen following sampling.

The role of liver fat in metabolism

The liver is a major site of fatty acid synthesis (Table 5). Hatching is accompanied by marked shifts in metabolism. With the transition from very high lipid ingested from the yolk to a starch based diet, there is a large increase in lipogenesis and in the expression of key enzymes in the lipogenic pathways (e.g. malic enzyme, fatty acid synthase and stearoyl coenzyme A desaturase) in the first few days of post hatching life in chickens (Richards et al., 2010).

There are changes in liver fat and hepatic lipogenesis following feeding in adult chickens. The amount of fat in the liver is increased (from 3 g to 5.2 g) 12 h after feeding in adult female chickens fed daily (Ekmay et al., 2010). A larger increase in liver fat (from 2.1 to 6.0 g) is reported in in birds fed on alternate days (Ekmay et al., 2010). It is reasonable to suggest that these are due to lipogenesis from glucose and consequent triglyceride formation. Synthesis of fatty acids from ^{14}C-acetate *in vivo* is reported to be increased following feeding (Silpananta and Goodridge, 1971). Hepatic expression of both fatty acid synthase and malic enzyme are also increased after feeding (Ekmay et al., 2010).

A model for metabolism

Table 5 summarizes metabolism in fed and fasted adult chickens. Fasting reduces whole body glucose utilization (Belo et al., 1976) reflecting decreases in lipogenesis, triglyceride formation, muscle and hepatic glycogenesis and glucose oxidation. In meal fed chickens, there is net glycogen formation after a meal with much higher rate (170 mg/hour/kg bodyweight) in chickens fed on alternate days (de Beer et al., 2007). Twelve hours following meal feeding, net glycogenolysis occurs with again a higher rate (250 mg/hours/kg) in birds fed on alternate days (de Beer et al., 2007). Glycogenolysis is insufficient to maintain circulating concentrations of glucose during fasting. Given the estimates for glycogenolysis and glucose utilization, rates of gluconeogenesis are likely to be very high during fasting (Rate of gluconeogenesis = Whole body glucose utilization – Rate of Glycogenolysis).

Although there is not information on glucose oxidation by different organs, fatty acid synthesis *in vivo* drops by 90% within 2 h of fasting (Yeh and Leveille, 1970; Goodridge et al., 1986). Decreases in glucose utilization by muscle tissue during fasting are supported by the reduction in arterial-venous glucose difference in glucose concentration in fasted 8 week old chickens (Tinker et al., 1986). Similarly, there is a decrease in the metabolic rate in fasted growing chickens based on the reduced circulating bicarbonate concentration (Christensen et al., 2012b). Moreover although the rates of lipolysis or triglyceride formation are not established, circulating concentrations of free fatty acids were elevated within 30 min of fasting indicating increased lipolysis and decreased triglyceride formation (Yeh and Leveille, 1970). It is noted that there is substantial storage of lipid in the liver (Table 5). During fasting, liver lipid is mobilized rapidly. On a weight basis, the rate of liver lipid breakdown is similar to that of whole body glycogenolysis (Table 5). However on an energetic basis, it would seem that lipid breakdown in the liver alone contributes considerable more than glycogenolysis.

Along with the limited information on metabolism in adult

Table 5 Quantitative estimates of metabolic flows in adult chickens[a] (mg/hour/kg)

	Fed	Fasted	Delta	Calculated from references
Whole body glucose utilization	833	521	~322	Belo et al., 1976
Hepatic net glycogen synthesis	62.5[b]	0	~62.5	De Beer et al., 2007
Hepatic net glycogenolysis	0	50[2]	+ 50	De Beer et al., 2007
Muscle net glycogenolysis[c]	0	110	+ 110	Savenije et al., 2002
Glucose oxidation	NA	NA		
Gluconeogenesis	NA	NA but calculated as 370		
Energy needs for protein synthesis	NA	NA		
Hepatic triglyceride net formation	92	0	~92	Ekmay et al., 2010
	83			De Beer et al., 2007
Hepatic triglyceride net loss	0	117	+ 117	Ekmay et al., 2010
	0	250	+ 250	De Beer et al., 2007
Lipogenesis - Fatty acid synthesis from glucose[d][4]	44.1	4.5	~39.6	Yeh and Leveille, 1970
Fatty acid oxidation	NA	NA		
Lipolysis	NA	NA		
Adipose triglyceride formation	NA	NA		

NA: No information; [a]: There is little quantitative information on metabolism in young growing chickens; [b]: Study employed 16 week old females; [c]: Assuming 45% of body weight is muscle based on Havenstein et al., 2003; [d]: Assuming lipogenesis from glucose to fatty acids is 33% efficient.

chickens, there is a surprising dearth of quantitative information on metabolism in young rapidly growing chickens. To model metabolism fully in birds, it will be necessary to quantify carbohydrate, lipids and protein. This should include the following:

- Characterizing carbohydrate metabolism, determining changes in amount of glycogen in the liver and muscles with time during fasting and following feeding together with rates of glycogenolysis, glycogenesis and glyconeogenesis throughout growth.
- Characterizing lipid metabolism, determining changes in amount of triglyceride in the liver and adipose tissue with time during fasting and following feeding together with rates of fatty acid synthesis, fatty acid oxidation, triglyceride formation and breakdown throughout growth.
- Characterization protein metabolism, determining changes in amount of protein in liver, muscles and gastro-intestinal tract with time during fasting and following feeding together with rates of protein synthesis and degradation throughout growth.

Responses to fasting

Feed deprivation can be addressed by a series of strategies:

- Mobilization of energy from chemical storage
- Glucose from glycogen
- Fatty acids together with glycerol from triglyceride
- Amino-acids from proteins as gluconeogenic precursors
- Reduced metabolic rate with potentially a consequent reduction in core body temperature
- Mechanic storage of feed including slower gut transit time
- Reduced locomotory activity and other behavioral changes.

The role of mobilization of energy from chemical storage

The effects of fasting on metabolism are summarized in Table 5. Fasting has a relatively small effect on circulating concentrations of glucose in chickens perhaps explaining inconsistency between different studies. No effects of fasting on circulating concentrations of glucose have been reported in some studies (e.g. Belo et al., 1976; Brady et al., 1978). In contrast, decreases in circulating concentrations of glucose were in chickens were reported to be depressed by fasting (Langslow et al., 1970; Harvey et al., 1978; Simon et al., 2011; Christensen et al., 2012a) (Table 2). Fasting in chickens is followed by decreases in both the concentration of glycogen in the liver (Hazelwood and Lorenz, 1959) and in glucose replacement rate (Belo et al., 1976). Moreover, there are increases in the circulating concentrations of free fatty acids (Langslow et al., 1970). Fasting is associated with increases in circulating concentrations of amino-acids (Belo et al., 1976; Brady et al., 1978) reflecting protein degradation and providing a substrate for gluconeogenesis. There is evidence for increased gluconeogenesis in fasting in chickens with elevated kidney phosphoenolpyruvate carboxykinase (Bisbis et al., 1994). Fasting reduces lipogenesis and increases lipolysis (Buyse et al., 2002). In meat type chickens, fasting results in reductions in circulating concentrations of triglyceride and increases in circulating concentrations of fatty acids (Nijdam et al., 2005; Delezie et al., 2007). In an analogous manner, there is a large decline ($>50\%$) in NEFA 20 min after start of meal (Buyse et al., 2002).

Endocrine responses to fasting

In meat type chickens, fasting for as little as 12 h results in marked reductions in circulating concentrations of insulin (Shiraishi et al., 2011; Simon et al., 2011; Christensen et al., 2012a) (Table 2) and T_3 (Buyse et al., 2002). Although circulating concentrations of insulin are depressed in fasted chickens, there are increases in insulin receptors in liver (Simon et al., 1986) and kidney (Bisbis et al., 1994). There appear to be no changes in circulating concentrations of corticosterone with fasting (Nijdam et al., 2005; Delezie et al., 2007). Fasting increases circulating concentrations of both glucagon (Christensen et al., 2012a) and GH (Harvey et al., 1978). Fasting increases hepatic IGF binding protein 2 expression in chickens (Nagao et al., 2001). What is not precisely known are the roles of glucagon, insulin and T_3 in fasted poultry?

Metabolic rate and body temperature responses to fasting

Nocturnal period of fasting In birds active during the day, core body temperatures peak during the day and are low at night (pigeons: Graf et al., 1989; chickens: Christensen et al., 2012b). In nocturnally active species, core body temperatures peak during the scotophase (rats: Yoda et al. 2000). There is obvious selective value to reduce energy consumption during the period of inactivity, sleep and fasting. There are circadian changes in core body temperatures with lower temperatures during the period of inactivity (Aschoff, 1983).The nocturnal fast is accompanied by reduced energy expenditures in humans (Holmbäck et al., 2003) and chickens with the metabolic rate declining rapidly by 26% at night (Buyse et al., 1993).

Short-term fasting Fasted pigeons show reductions in both heat production and core body temperature with declines in both the zenith and nadir in the daily cycle of temperatures (Graf et al., 1989; Ostheim, 1992). Similarly in fasted chickens, there are marked decreased in core body temperatures (Christensen et al., 2012b). Moreover, there is a nocturnal decrease in the metabolic rate in chickens with the rate at night being 26% lower than during the day (Buyse et al., 1993).

Mechanical storage of energy

There is a unique capability for storage of feed in the crop and gizzard/proventriculus studied in gallinaceous birds such as chickens and turkeys; the crop being a blind sac in the lower esophagus; the gizzard being the equivalent of the muscular component of the mammalian stomach and the proventriculus being the equivalent of the glandular stomach. There is storage of largely or entirely undigested ingesta in the crop and also gizzard during the night when feeding activity is very low in chickens and turkeys (Tables 6 and 7) (laying chickens: Scanes et al., 1987; young broiler chickens: Buyse et al., 1993; turkeys: Cutler et al., 2005).The role of the gizzard in food storage is supported by the increased fill in both chickens and quail in which the crop has been surgically removed (Savory, 1985).

Ingesta stored in the superior gastro-intestinal tract accounts for more than a half of the nocturnal energy needs of the poultry (Scanes et al., 1987) (assuming metabolism is constant throughout the day and night):

- Crop storage accounting for 43% of the energy requirements of the laying chicken during the night,
- Storage of ingesta in the gizzard accounts for a further 14% of the energy requirements (Scanes et al., 1987).

However, this does not take into account the nocturnal decrease in the metabolic rate in chickens (Buyse et al., 1993). If we combine the decrease in metabolic rate and the feed/ingesta stored in the crop and gizzard, we can account for 77% of nocturnal energy needs.

Crop filling seems to depend on the amount of feed consumed. For instance, the crop is filled with feed in meal fed chickens and completely engorged in chickens meal fed on alternate days (DeBeer et al., 2008). Moreover, the crop is similarly filled in meal fed turkeys (Cutler et al., 2005; Scanes, 2008). There is increased passage of feed into crop rather than the gizzard prior to the night in turkeys (Jackson and Duke, 1995). The filled crop at the beginning of the period of night may be related to the high feed intake prior to lights off (Savory, 1985). Surgical removal of the crop in Japanese quail and chickens influences feeding behavior with more frequent meals (Savory, 1985). The rate of emptying of the crop (in g/hour) is similar in chickens meal fed daily or on alternate days (DeBeer et al., 2008). This suggests an inherent mechanical process for voiding the crop of its contents. In addition, crop emptying can be influenced by nervous innervation, neuropeptides and dietary constituents:

- Ghrelin stimulates the muscles of the crop to contract and thereby the crop empty (Kitazawa et al., 2009) while neuromedin C and bombesin, peripherally, depresses empting of the crop (Tachibana et al., 2010).
- GLP-1, neuromedins B, C and bombesin, administered intracerebrally, reduces crop emptying (Tachibana et al., 2003, 2010).
- Crop emptying is increased by tyrosine (Furuse et al.,

Table 6 Changes in the crop contents of ingesta and lactate during the period of night when young turkey poults are not feeding (data from or calculated from Johannsen et al., 2005)

Time (hours)	Crop ingesta wet weight	Crop lactate mM	Crop lactate (mM)	Crop lactate (mg)
+ 1	22.2 ± 2.4^{xy}	13.4 ± 4.47^{x}	0.30	26.7
+ 3	25.6 ± 4.7^{x}	38.0 ± 9.6^{x}	0.97	88
+ 5	22.4 ± 3.9^{xy}	93.3 ± 17.4^{y}	2.11	190
+ 7	13.2 ± 2.3^{xy}	87.6 ± 15.7^{y}	1.16	104
+ 9	10.2 ± 1.8^{y}	98.4 ± 11.4^{y}	1.00	90

$^{x, y}$: Different superscript letter indicate difference $P < 0.05$

Table 7 Changes in the wet ingesta (grams) in the gastro-intestinal tract crop during a day night cycle (14L: 10D)

Region	Day/night	Time (hours)	Young broiler chickens (32 day old)	Laying hens
Crop				
	Photophase	+7	2.0 ± 1.9^{ab}	4.5 ± 2.8^{b}
	Photophase	+11-12	2.5 ± 1.6^{ab}	15.5 ± 7.7^{b}
	Scotophase	+0-1	28.4 ± 6.9^{c}	44.7 ± 5.0^{c}
	Scotophase	+5	11.6 ± 3.5^{b}	20.0 ± 4.8^{b}
	Scotophase	+9	0.2 ± 0.1^{a}	1.6 ± 0.8^{a}
Proventriculus + gizzard				
	Photophase	+7	15.1 ± 2.0^{b}	22.0 ± 2.8^{b}
	Photophase	+11-12	10.3 ± 1.0^{ab}	26.2 ± 3.0^{bc}
	Scotophase	+0-1	22.2 ± 3.0^{c}	30.4 ± 2.8^{c}
	Scotophase	+5	11.0 ± 1.9^{ab}	23.0 ± 1.6^{b}
	Scotophase	+9	7.4 ± 1.5^{a}	15.5 ± 1.6^{a}
References			Buyse et al., 1993	Scanes et al., 1987

$^{a, b, c}$: Different superscript letter indicate difference $P < 0.05$

1991) or long-chain triacylglycerols (Mabayo et al., 1992) but decreased by phenylalanine (Furuse et al., 1991) and beta-hydroxybutyrate (Furuse et al., 1997).

Nocturnal gut transit time represents another form of mechanical storage of feed. Indeed, gut transit time is reported to be markedly longer at night than during the day (Buyse et al., 1993). It is not possible to different between this and crop/gizzard storage of ingesta. Gut transit time is closely related to filling and emptying of both the crop and the gizzard (May et al., 1990, 1998).

Other responses to fasting

The fat mass and obesity-associated gene (FTO) has been characterized in poultry (Jia et al., 2011). It is expressed in muscle, liver, adipose tissue, pituitary gland and the hypothalamus (Jia et al., 2011). Fasting increases expression of the FTO together with that of the gene peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) in muscle, liver and adipose tissue but deceases expression of both genes in the pituitary gland (Jia et al., 2011). The role of the protein translated from transcript of the FTO gene in poultry and wild birds remains to be elucidated. Moreover, what is not clear whether all cells in the anterior pituitary gland express FTO transcripts and/or PGC-1α.

Overfeeding and metabolism

Ducks and geese are used for fatty liver as pate *foie gras*. This is achieved by overfeeding. Overfeeding ducks with a high carbohydrate corn diet is accompanied by large, about 7 fold, in increases in liver weight in Pekin ducks, Muscovy ducks and hybrids (Chartrin et al., 2006). There are increases in circulating concentrations of both glucose and insulin (Berradi et al., 2007) and elevated hepatic specific activities of malic enzyme, acetyl coenzyme A carboxylase and glucose 6 phosphate dehydrogenase (Chartrin et al., 2006). In addition overfeeding increases hepatic specific activity and expression of glucokinase in Muscovy and hybrids but not Pekin ducks (Chartrin et al., 2006; Berradi et al., 2007).

In ovo feeding

Increasing the availability of nutrients to the developing avian embryo influences both metabolism and post-hatching growth and development. In poultry, this is performed by inserting the nutrient solution into the amniotic sac and is referred to as *in ovo* feeding. For example, *in ovo* feeding with carbohydrate and β-hydroxy-β-methylbutyrate accelerates gastro-intestinal development and improves growth post-hatching in chickens (Tako et al., 2004). Moreover, *in ovo* supplementation with β-hydroxy-β-methylbutyrate increases both liver and muscle glycogen in turkey embryos (Foye et al., 2006). Similarly, *in ovo* feeding with dextrin and β-hydroxy-β-methylbutyrate increases hepatic glycogen, embryonic myoblast proliferation and post-hatch growth rate in chickens (Kornasio et al., 2011).

Energetic needs for Immunity

It is assumed that there are energetic costs to both the innate and adaptive immunity with the costs greater when an animal is being challenged by the presence of a pathogenic or immune challenge (e.g. Råberg et al., 2002). A corollary is that there will be trade-offs between the energetics needs for reproduction or growth and energetic needs of immunity.

Is there an energetic cost for the existence of innate and adaptive immunity per se?

Surprisingly, there is evidence against for this conjecture at least for adaptive immunity. Transgenic mice lacking both B and T lymphocytes have a higher basal metabolic rate than controls in a controlled but not germ-free environment (Råberg et al., 2002). Råberg and colleagues (2002) concluded that "*energy saving is another plausible factor favoring the evolution of adaptive immunity.*" In contrast, evidence for the existance of innate and adaptive immunity having some energetic costs include the protein synthetic and maintenance requirements of primary and secondary immune organs; these representing in aggregate about 1% of body-weight (Table 10). What is not known is the energetic requirements in the face of an immune challenge.

What are the energetic costs for innate and adaptive immunity when challenged?

The available evidence generally supports there being increased energetic demands when immune challenged (Table 8). For instance, the metabolic cost of the cell mediated immune response to phytohemogglutinin was estimated as 4.2 kJ per day or 29% of resting or basal

Table 8 Effect of an immune challenge (adaptive) on basal metabolic rate in birds

Species	Change in basal metabolic rate	References
House sparrows (*Passer domesticus*)	+ 29%	Martin et al., 2003
Great tits (*Parus major*)	+ 9%	Ots et al., 2001
Blue tits (*Parus caeruleus*)	+ 8% – 13% n.s.	Swensson et al., 1998
Japanese quail (*Coturnix coturnix*)	-~7%	Boughton et al., 2007

n.s.: Non-significant

metabolic rate in house sparrows (*Passer domesticus*) (Martin et al., 2006). In other passerine birds, the metabolic cost of the humoral immune responses (primary and secondary) was estimated as 8% – 13% of basal metabolic rate with a 2.8% decrease in body weight following challenge (Swensson et al., 1998; Ots et al., 2001) (Table 8). In contrast, no increase in basal metabolic rate wasobserved in intact Japanese quail (*Coturnix coturnix*) challenged with phytohemagglutinin (Boughton et al., 2007). Basal metabolic rate tends to be further depressed in castrated quail following phytohemagglutinin challenge (Boughton et al., 2007). Innate immunity will have significant he energetic demands. For instance, early host responses to an oral challenge with *Salmonella enteritidis* include increases in macrophage number in the ceca and upregulation of expression of the inflammatory chemokines CXCLi1 and CXCLi2 (Cheeseman et al., 2008a); these being ligands for the chicken CXCR1 (Poh et al., 2008). Chicken macrophages produce nitric oxide (NO) with increased inducible nitric oxide synthase expression in response to interferon-γ (Cheeseman et al., 2008b).

Is there a required trade-off for growth due to the energetic costs for innate and adaptive immunity when challenged?

There is substantial evidence that a trade-off is required with growth due to the energetic costs for innate and adaptive immunity when challenged. First, decreases in growth correlate with increases in the constitutive innate humoral immune system in Leach's Storm-Petrel (*Oceanodroma leucorhoa*) (Mauck et al., 2005) and in tree sparrows (*Spizella arborea*) (Stambaugh et al., 2011). Secondly, chickens raised in a germ-free environment exhibit a markedly greater growth rate (23.4% calculated from review by Lochmiller and Deerenberg, 2000). Thirdly, poultry selected for growth have depressed immune functioning. A meta-analysis has been conducted of immune-related responses in lines of chickens and turkeys selected for growth (van der Most et al., 2011). This provides strong evidence that for a trade-off between utilizing energy for immune functioning and for growth. The meta-analysis excluded data from commercial lines, from "*articles presenting least-square means only and no raw means*" and from *in vitro* immune parameters. Moreover, mortality, antibody titers and a measure of cell mediated immunity were combined. In Table 9, combined data on mortality and morbidity from six of the studies in the meta-analysis are presented. Clearly, in both chickens and turkeys, there was greater mortality following infectious challenge in the high growth selected lines; by 3.4 fold in fast growing chickens (compared to a line selected for low growth) and by 1.94 fold in fast growing turkeys (compared to random bred line). Moreover, morbidity, as indicated by paralysis, was increased by 6.0 fold in the high growth rate chickens. Mortality and/or morbidity differences are presumed to reflect those of innate and adaptive immunity. It is not possible to preclude other factors such as tolerance of the disease organism(s) favoring the survival of the slower growing poultry.

Studies on differences in adaptive immunity between poultry selected for high growth and either random bred or slow growth line do not consistently support for the trade-off model. Data from a series of comparisons is summarized in Table 10. The weights of immune organs (thymus, bursa Fabricius and spleen) are greater in fast growing poultry but their relative weights tend to be lower. There are not consistently higher antibody titers in response to challenges. There are increased numbers of $CD4^+/CD8^-$ peripheral blood lymphocytes in fast growing turkeys (Li et al., 2000).

Another support for a trade-off between immunity and growth comes from the decrease in growth rate in chickens after a challenge to the adaptive immune system using a foreign protein (sheep red blood cells) or activation of the innate immune system in the acute inflammatory response to *Escherichia coli* lipopolysaccharide (LPS) (Klasing et al., 1987; Mireles et al., 2005; Zhang et al., 2011).

Are there trade-offs between the energetic needs for reproduction and for innate and adaptive immunity?

There is evidence supporting trade-offs between reproduction and immunity. There are marked seasonal changes both in reproduction and cell mediated immunity in house sparrows (*Passer domesticus*). These are consistent with the view that there are trade-off between energy needs of reproduction and those of immunity with maximal immunity not being maintained throughout the year (Martin et al., 2006). Moreover, castrated Japanese quail have a greater immune response than intact quail but a lower basal metabolic rate (Boughton et al., 2007). Lipopolysaccharide (LPS) induces weight loss and reductions in feed intake in white-crowned sparrow (*Zonotrichia leucophrys*) with the response greater in birds on long than short day lengths depending on body

Table 9 Effect of selection for growth on ability growing poultry to withstand challenge by infectious organisms

Species	Challenge	Mortality/morbidity	High growth % (n =)	Low growth % (n =)	References
Chicken†	Marek's Disease virus	Mortality	25.5 (302)[a]	7.6 (302)[b]	Han and Smyth, 1972, 1973
Chicken†	Marek's Disease virus	Paralysis	31.2 (160) [a]	5.2 (173) [b]	Han and Smyth 1972
Turkeys††	*Pasteurella multocida* or Newcastle disease virus	Mortality	49.3 (207) [a]	25.4 (54) [b]	Nestor et al., 1996a,b; 1999a,b

[ab]: Different superscript indicates difference $P < 0.05$; †: Chickens were selected either for high growth or low grow; ††: Turkeys were selected for high growth and comparisons made to random bred controls.

Table 10 Comparison of immune parameters in poultry selected for fast growth with either random bred controls or with lines selected for low growth

		Bursa weight in g (% of body weight)	Thymus weight in g (% of body weight)	Spleen weight in g (% of body weight)	Antibody response[b] (after second challenge[c])	References
Chicken	Random bred[a]	0.89	0.49	0.33	1.01	Cheema et al., 2003
Male		(0.40)	(0.22)	(0.15)	(4.7)	
	Fast growing	2.00*	1.69*	1.00*	0.56	Cheema et al., 2003
	Commercial breed	(0.26*)	(0.22)	(0.13)	(3.9)	
Chicken	Random bred[a]	1.03	0.97	0.33	0.86	Cheema et al., 2003
Female		(0.50)	(0.47)	(0.26)	(4.2)	
	Fast growing Commercial breed	2.02* (0.27*)	2.24* (0.30*)	0.82* (0.11*)	0.42 (4.3)	Cheema et al., 2003
Turkey	Random bred[a]	0.72	N.A.	N.A.	6.9	Cheema et al., 2007
Male		(0.34)			(5.6)	
	Fast growing	2.58*	N.A.	N.A.	6.5	Cheema et al., 2007
	Commercial breed	(0.66*)			(5.3)	
Turkey	Random bred[a]	0.61	N.A.	N.A.	6.6	Cheema et al., 2007
Female		(0.36)			(4.9)	
	Fast growing	2.47*	N.A.	N.A.	7.2	Cheema et al., 2007
	Commercial breed	(0.65*)			(4.6)	
Turkey	Random bred[a]	27.4	N.A.	26.6	1.6	Li et al., 2001
Mixed		(1.14)		(1.11)		
	Growth selected line	47.0*	N.A.	63.5*	1.5	Li et al., 2001
		(0.94*)		(1.27*)		

[a]: Equivalent to breeds 40 years ago; [b]: Titer after 10/11 days in chickens and 7 days (Cheema et al., 2007) and 5 weeks (Li et al., 2001) in turkeys; [c]: Titer after 4/5 days in chickens and 7 days in turkeys (Cheema et al., 2007); N. A.: Information not available; *: Different from slow growing lines $P < 0.05$.

condition (Owen-Ashley et al., 2008).

Are there trade-offs between the energetic requirements for responding to stressors and to the needs for innate and adaptive immunity?

There is abundant evidence that the avian glucocorticoid stress hormone, corticosterone, depresses immune functioning. In chickens, administration of corticosterone exerts the following effects:

- Decreased weight and weight relative to body weight of the bursa Fabricius (Davison et al., 1983; 1985; Donker and Beuving, 1989).),
- Decreased weight and weight relative to body weight of the thymus (Donker and Beuving, 1989) with increased apoptosis and expression of IL-1alpha, IL-6 and TNF-alpha (Franchini et al., 2004),
- Decreased weight of the spleen (Davison et al., 1985; Donker and Beuving, 1989; Post et al., 2003),
- Reduced antibody formation (Post et al., 2003),
- Antibody to infectious bronchitis virus (IBV) vaccination initially stimulated but thereafter titers decreased (Shini et al., 2008),
- Depressed production of IgM while increasing that of IgG following challenge with West Nile virus (Jankowski et al., 2010),
- Increased heterophil to lymphocyte (H/L) ratios (Shini et al., 2008),
- Increased heterophils in circulation (Post et al., 2003) but with reduced expression pro-inflammatory cytokines in heterophils (Shini et al., 2010),
- Decreased number of lymphocytes in the circulation but with increased expression of interleukin (IL)-1beta, IL-6, IL-18, transforming growth factor (TGF)-beta4 and of chemokines CCLi2, CCL5, CCL16 and CXCLi1 in both peripheral and splenic lymphocytes (Shini and Kaiser, 2009),
- Extended viremia following challenge with West Nile virus (Jankowski et al., 2010),

In wild birds, corticosterone has similar effects. For instance, corticosterone reduces the antibody response but increases the innate immune response (red blood cell lysis) in owls (Stier et al., 2009). Stress induced reduction in the immune response allows reallocation of resources to other critical physiologic functions.

Lipopolysaccharide (LPS) challenge

Lipopolysaccharide (LPS) challenge is accompanied after 6 h with initially hypothermia (core body temperatures reduced by 0.5°C) with reduced blood pressure followed by a rebound increase in body temperature (by 0.4°C compared to pre-challenge) (Cheng et al., 2004; De Boever et al., 2008, 2009). Along with the LPS-induced inflammatory response in inducing fever, there is increased circulating concentrations of nitric oxide and corticosterone together with elevated expression of inflammatory response genes: TNF-like factor

(TL)1A, Interleukin (IL)-1beta and IL-6 inducible NO synthase and toll-like receptor (TLR) 4 in the spleen and other lymphocytes (Klasing et al., 1987; De Boever et al., 2008,2009; Takahashi et al., 2008). What is not known are the temporal changes in basal metabolic rate in birds challenged with LPS and the extent to which corticosterone (whose secretion is increased by LPS) reduces the inflammatory response to LPS.

Glutamine and immune function

Glutamine is utilized by rapidly proliferating immune and gastro-intestinal cells (Calder and Yaqoob, 1999). It is not known the extent to which glutamine is utilized by avian lymphocytes following challenge or by the gastro-intestinal tract when undergoing regeneration following nutritional restriction and flight. Glutamine supplementation has little effect of the development of the small intestine during growth or following fasting in young chickens (Yi et al., 2005).

Conclusions on the control of the control of circulating glucose in wild and domesticated birds including evolutionary aspects

When the plasma glucose concentrations of birds are compared to a closely related phylogenetic group of vertebrates, reptiles one might expect to observe similar plasma concentrations. Quite the opposite appears to be the case. In a data set compiled for 55 reptilian species by Dessauer (1970), the mean plasma glucose concentration was 80 mg/dL (Table 11), a value similar to that of mammals as phylogenetic group. Thus, the ability of birds to maintain and tolerate comparatively high plasma glucose concentrations appears to have evolved independent of other vertebrate groups.

Table 11 Plasma glucose concentrations (mg/dL) of reptiles*

Order	*n*	Plasma glucose concentration
Squamata (Sauria)	17	121
Squamata (Ophidia)	26	59
Testudines	10	64
Crocodilia	2	87
Grand totals	55	80

*: Data condensed from Dessauer, 1970

Figure 2 summarizes the circulating concentration of glucose and the evolutionary relationship between birds, mammals and the major groups of living reptiles. Circulating concentrations of glucose in free living reptiles are increasingly found to be very low compared to mammals. Circulating glucose in caught sea-turtles was reported as 18 mg/dL (1 mM) with lactate being higher at 3.4 mM (Lutz

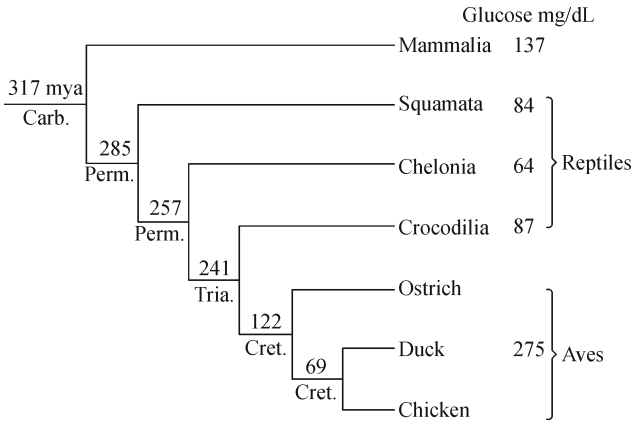

Figure 2 Comparison of the mean glucose concentrations in mammals, birds and reptiles with their evolutionary relationships and estimated separation dates of common ancestors. Bold lines indicate identical structures for insulin. Phylogeny and separation dates are based on Shen et al., 2011. Similar phylogenies are reported by Hedges and Poling (1999) and Sanders and Lee (2007).

and Dunbar-Cooper, 1987). Circulating concentrations of glucose in birds are normally held within tight range about a set point. For instance in ducks, there is little difference between the plasma concentrations of glucose in fed or fasted birds (Table 2). However, they are elevated by 15% by overfeeding (Berradi et al., 2007) but are increased, by 2 fold, 30 min after an intramuscular glucose challenge in ducks (Applegate et al., 1999). There are increasing circulating concentrations of glucose with age in pigeons (Prinzinger and Misovic, 2010).

The circulating concentrations of glucose were even lower in recent studies where plasma concentrations of glucose were determined in free living reptiles immediately after capture (Table 1). Not only are circulating concentrations of glucose high in birds, but they are only modestly decreased by insulin challenge in birds being, for instance, decreased by 19% doves (Sweazea et al., 2006) and 25%–30% in chickens (e.g. Langslow et al., 1970; Harvey et al., 1978; Zhao et al., 2009a). In contrast in both mammals and the very limited studies in reptiles, exogenous insulin reduced circulating concentrations of glucose to extremely low levels. In alligators, administration of insulin (either bovine or alligator insulin at dose of 400 μg per kg) is followed by a steady decline over 12 h in circulating concentrations of glucose to less than 35 mg/dL (Lance et al., 1993).

It might be speculated that the high circulating concentrations in birds are a requirement for the energetic requirements of flight. Militating against this intuitively obvious but probably wrong assumption are the following. The circulating concentrations of glucose for flightless birds, including ostriches and penguins are well within the avian range (Table 1). Moreover, in the other flying vertebrates, namely bats, circulating concentrations of glucose are within but to the low end of the mammalian range being 54 mg/dL

(3.0 mM) in nectar-feeding bats (Kelm et al., 2011) and from an average of 15 to over 80 mg/dL in different months in insectivorous bats depending on their physiology (Roy and Krishna, 2011). Very high circulating concentrations of glucose (450 mg/dL) are reported in nectar-feeding bats after feeding with rapid decreases when the animals fly following eating (Kelm et al., 2011).

Evolution of insulin

It is reasonable to propose that the structure of chicken insulin is that of the common ancestor of birds and at least of two major groups of reptiles (Fig. 3). Chicken insulin (Perler et al., 1980) is identical to that from the ostrich (Evans et al., 1988) and species from 10 different orders of birds: (Spheniformes)

	A chain	B chain
Avian branch 1		
Chicken[1]	GIVEQ CCHNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKA
Avian branch 1A		
Hummingbird[2]	GIVEQ CCHNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKA
Sparrow[3]	GIVEQ CCHNT CSYLQ LENYCN	AVNQH LCGSH LVEAL YLVCG ERGFF YQPKA
Magpie[4]	GIVEQ CCHNT CSYLQ LENYCN	AVSQH LCGSH LVEAL YLVCG ERGFF YQPKA
Avian branch 1B		
Kestrel[5]	GIVEQ CCHNT CSYLQ LENYCN	AATQH LCGSH LVEAL YLVCG ERGFF YSPKA
Moorhen[6]	GIVEQ CCHNT CSYLQ LENYCN	VATQH LCGSH LVEAL YLVCG ERGFF YSPKA
Avian branch 1C		
Albatros[7]	GIVEQ CCSNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKA
Avian branch 1D		
Rhea[8]	GIVEQ CCHNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCR ERGFF YSPKA
Avian branch 2		
Stork[9]	GIVEQ CCHNP CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKT
Ducks[10]	GIVEQ CCENP CSYLQ LENYCN	AANQR LCGSH LVEAL YLVCG ERGFF YSPKT
Turtle	GIVEQ CCHNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKA
Alligator	GIVEQ CCHNT CSYLQ LENYCN	AANQR LCGSH LVDAL YLVCG ERGFF YSPKG
Human	GIVEQ CCT SI CSYLQ LENYCN	FVNQH LCGSH LVEAL YLVCG ERGFF YTPKT
Pig	GIVEQ CCT SI CSYLQ LENYCN	FVNQH LCGSH LVEAL YLVCG ERGFF YTPKA
Putative ancestral forms		
Birds	GIVEQ CCHNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKA
Reptiles	GIVEQ CCHNT CSYLQ LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YSPKA
Amphibians	GIVEQ CCHNT CSLYQ LENYCN	LANQH LCGSH LVEAL YLVCG ERGFF YSPKS
Lungfish	GIVEQ CCHNP CSLYQ LENYCN	ALVNQH LCGSH LVEAL YLVCG ERGFF Y?PKG
Boney fish	GIVEQ CCHSP CSLYD LENYCN	AANQH LCGSH LVEAL YLVCG ERGFF YTPKV
Elasmobranchs	GIVEQ CCHNT CSLYD LEGYCN	VPTQH LCGSH LVEAL YLVCG ERGFF YSPK?

Figure 3 Structure of insulin in birds. [1] Identical structures as characterized in species from 10 orders of birds: (Spheniformes) — Chickens (*Gallus gallus*), turkeys (*Meleagris gallopavo*) (order Galliformes); common pigeon (*Columbia livia*) (order Columbiformes); emperor penguin (*Aptenodytes forsteri*) (order Spheniformes); petrel (*Pagodroma nivea*), fulmar (*Fulmarus glacialis*) and booby (*Sula sula*) (order Procellariformes); kittiwake (*Rissa tridactyla*), murre (*Uria aalge*) (order Charadriiformes); owl (*Strix aluca*) (order Strigiformes); red billed tropicbird (*Phaethon aethereus*)(order Pelecaniformes); heron (*Nycticoraxnycti*)(order Ciconiiformes); ostrich (*struthiocamelus*) (order Struthioniformes) and emu (*Dromiceius novaehollandiae*); [2] Hummingbird (*Selasphorus rufus*) (order Trochiliformes); [3] Sparrow (*Passer domesticus*) and blackbird (*Turdus merula*) (order Passeriformes); [4] Magpie (*Pica pica*) (order Psittaciformes); [5] Kestel (*Faco tinnunculus*) (order Falconiformes) and budgerigar (*Melapsittacus undulates*) (order Psittaciformes); [6] Moorhen (*Gallinula chloropus*) (order Gruiformes); [7] Albatros (*Diomedea melanophris*) (order Procellariiformes); [8] American rhea (*Rhea Americana*) (order Rheiformes); [9] Stork (*Ciconia coconia*) (order Pelecaniformes). Note: placing storks in branch 2 bases on a single amino-acid substitution is arbitrary. Equally they could be placed in branch 1E. [10] Identical structures in all Anseriform species — domestic and wild ducks (*Anas platyrhynchos*), teal (*Anas crecca*), geese (*Anser anser* or *Anser cygnoides*), Shelduck (*Tadorna tadorna*) and Muscovy ducks (*Cairina moschata*). Based on avian insulin sequences in Simon et al., 2004.

— chickens (*Gallus gallus*), turkeys (*Meleagris gallopavo*) (order Galliformes); common pigeon (*Columbia livia*) (order Columbiformes); emperor penguin (*Aptenodytes forsteri*) (order Spheniformes); petrel (*Pagodroma nivea*), fulmar (*Fulmarus glacialis*) and booby (*Sula sula*)(order Procellariiformes); kittiwake (*Rissa tridactyla*), murre (*Uria aalge*) (order Charadriiformes); owl (*Strix aluca*)(order Strigiformes); red billed tropicbird (*Phaethon aethereus*)(order Pelecaniformes); heron (*Nycticoraxnycti*)(order Ciconiiformes); ostrich (*struthiocamelus*) (order Struthioniformes) and emu (*Dromiceius novaehollandiae*) (Simon et al., 2004). Moreover, insulins from other orders of birds (excluding the anseriformes — ducks and geese) have simple amino-acid residue substitutions compared to chicken insulin (Fig. 3). In contrast, duck and chicken insulin differ from each other by three amino-acid residues (Fig. 3) (reviewed: Conlon, 2000; chicken: Perler et al., 1980; duck: Markussen and Sundby, 1973; Chevalier et al., 1996; Simon et al., 2004).

Perhaps surprisingly, insulin from one group of reptiles, the turtles, is identical to that of chickens, and the putative avian model (turtles: Conlon and Hicks, 1990; Cascone et al., 1991). Moreover, alligator insulin has only 3 differences in the amino-acid sequence (Lance et al., 1984) while tortoise insulin differs from alligator insulin by 3 amino-acid residues (Wang et al., 1999). In contrast, python insulin has 18 substitutions compared with alligator and 20 substitutions compared with chicken (Conlon et al., 1997). Based on the identity of amino-acid sequences in both the A and B chains, it is suggested that the turtle/chicken/ostrich insulin represents an ancestral form dating back to the divergence of the ancestors of birds, crocodilians and turtles (Order Testudines, Super order Chelonida). The divergence between the ancestors of turtles/crocodiles and birds is over 225 million years ago being estimated at 228 million years ago (MYA)(Hedges and Poling, 1999), 247 MYA (Sanders and Lee, 2007) or 257 MYA (Shen et al., 2011). The common ancestors of birds/turtles and crocodiles diverged from that of snakes and lizards significantly earlier; estimated as 245 MYA (Hedges and Poling, 1999), 282 MYA (Sanders and Lee, 2007) or 285 MYA (Shen et al., 2011). The three amino-acid substitutions in ducks compared to the presumed ancestral form of insulin occurred presumably after the divergence of the ancestors of ducks and chickens (Figs. 2 and 3). While, duck insulin has a lower biologic activity compared to that of the chicken or mammal in mammalian systems, it has identical affinities to either chicken or duck insulin receptors (Constans et al., 1991; Chevalier et al., 1996). The conservatism of insulin in birds and two branches of reptiles argues for its critical importance to the biology in these groups.

Overall conclusions

Not only are the circulating concentrations of glucose are much higher in birds than in either mammals or reptiles, but also there are maintained with tight homeostatic control. The evolutionary basis for these high glucose concentrations is unclear. It does not appear to be a requirement for flight. Indeed, the principal fuel for avian flight is fatty acids. Moreover, the circulating concentrations of glucose are high in flightless birds and are not elevated in flying mammals, the bats. Recent studies that report on the circulating concentrations of glucose in reptiles indicate that its concentration is very low in the wild state but very labile to perturbations such as handling during capture. Circulating concentrations of glucose are greater in mammals than reptiles (Figs. 1 and 3) although not to the same extent as in birds. It is speculated that the increases are related in some way to homeothermy with body temperatures in birds markedly higher than those in mammals.

There is a profound need for quantitative studies on metabolism, and metabolomics, in both poultry and wild birds. Avian metabolism can be markedly influenced by hormones in a manner not identical to that in mammals. There is, however, a need to establish the extent to which these effects on physiologic.

Compliance with ethics guidelines

Colin G. Scanes and Eldon Braun declare that they have no conflict of interest. This article does not contain any studies with human subjects performed by any of the authors. All institutional and national guidelines for the care and use of laboratory animals were followed.

Acknowledgements

The authors express their appreciation to Dr. Sara Hoot (Department of Biologic Sciences, University of Wisconsin, Milwaukee, USA) for advice on phylogeny and for Fig. 2.

References

Adachi H, Takemoto Y, Bungo T, Ohkubo T (2008). Chicken leptin receptor is functional in activating JAK-STAT pathway *in vitro*. J Endocrinol, 197(2): 335–342

Algauhari A E I (1967). Experimental studies on the blood sugar in reptiles. Effect of fasting, temperature and insulin administration in *Psammophis sibilans*. J Comp Physiol A Neuroethol Sens Neural Behav Physiol, 54(3): 395–399

Arner P, Pettersson A, Mitchell P J, Dunbar J D, Kharitonenkov A, Rydén M (2008). FGF21 attenuates lipolysis in human adipocytes - a possible link to improved insulin sensitivity. FEBS Lett, 582(12): 1725–1730

Applegate T J, Ladwig E, Weissert L, Lilburn M S (1999). Effect of hen age on intestinal development and glucose tolerance of the Pekin duckling. Poult Sci, 78(11): 1485–1492

Aschoff J (1983). Circadian control of body temperature. J Therm Biol, 8

(1–2): 143–147

Bacon W L, Long D W, Vasilatos-Younken R (1995). Responses to exogenous pulsatile turkey growth hormone by growing 8-week-old female turkeys. Comp Biochem Physiol B Biochem Mol Biol, 111 (3): 471–482

Bartov I (1985). Effects of dietary protein concentration and corticosterone injections on energy and nitrogen balances and fat deposition in broiler chicks. Br PoultSci, 26(3): 311–324

Bedu E, Chainier F, Sibille B, Meister R, Dallevet G, Garin D, Duchamp C (2002). Increased lipogenesis in isolated hepatocytes from cold-acclimated ducklings. Am J Physiol Regul Intre Comp Physiol, 283 (5):R1245–R1253

Belo P S, Romsos D R, Leville G A (1976). Blood metabolites and glucose metabolism in the fed and fasted chicken. J Nutr, 106(8): 1135–1143

Berghman L R, Devreese B, Verhaert P, Gerets H, Arckens L, Vanden Broeck J, Van Beeumen J, Vaudry H, Vandesande F (1998). The molecular characterisation of chicken pituitary N-terminal pro-opiomelanocortin (POMC). Mol Cell Endocrinol, 142(1-2): 119–130

Bernard S F, Thil M A, Groscolas R (2003). Lipolytic and metabolic response to glucagon in fasting king penguins: phase II vs. phase III. Am J Physiol Regul Integr Comp Physiol, 284(2): R444–R454

Berradi H, Bernadet M D, Guy G, Rideau N (2007). Expression of the glucokinase gene in mule duck liver and glucokinase activities in chicken and mule duck livers. Poult Sci, 86(10): 2216–2220

Beuchat C A, Chong C R (1998). Hyperglycemia in hummingbirds and its consequences for hemoglobin glycation. Comp Biochem Physiol A Mol Integr Physiol, 120(3): 409–416

Bisbis S, Derouet M, Simon J (1994). Characterization of insulin receptors in chicken kidneys: effect of nutritional status. Gen Comp Endocrinol, 96(1): 37–49

Bishop C M, Butler P J, Egginton S, El Haj A J, Gabrielson G W (1995). Development of metabolic enzyme activity in locomotor and cardiac muscles of the migratory barnacle goose. Am J Physiol Regul Integr Comp Physiol, 269: 64–72

Boughton R K, Bridge E S, Schoech S J (2007). Energetic trade-offs between immunity and reproduction in male Japanese quail (*Coturnix coturnix*).J Exp Zool A Ecol Genet Physiol 307(9):479–487

Brady L J, Romsos D R, Brady P S, Bergen W G, Leveille G A (1978). The effects of fasting on body composition, glucose turnover, enzymes and metabolites in the chicken. J Nutr, 108(4): 648–657

Braun E J, Sweazea K L (2008). Glucose regulation in birds. Comp Biochem Physiol B Biochem Mol Biol, 151(1): 1–9

Buntin J D, Hnasko R M, Zuzick P H (1999). Role of the ventromedial hypothalamus in prolactin-induced hyperphagia in ring doves. Physiol Behav, 66(2): 255–261

Buyse J, Adelsohn D S, Decuypere E, Scanes C G (1993). Diurnal-nocturnal changes in food intake, gut storage of ingesta, food transit time and metabolism in growing broiler chickens: a model for temporal control of energy balance. Br Poult Sci, 34(4): 699–709

Buyse J, Janssens K, Van der Geyten S, Van As P, Decuypere E, Darras V M (2002). Pre- and postprandial changes in plasma hormone and metabolite levels and hepatic deiodinase activities in meal-fed broiler chickens. Br J Nutr, 88(06): 641–653

Buyse J, Janssen S, Geelissen S, Swennen Q, Kaiya H, Darras V M, Dridi S (2009). Ghrelin modulates fatty acid synthase and related transcription factor mRNA levels in a tissue-specific manner in neonatal broiler chicks. Peptides, 30(7): 1342–1347

Calder P C, Yaqoob P (1999). Glutamine and the immune system. Amino Acids, 17(3): 227–241

Campbell R M, Scanes C G (1985). Lipolytic activity of purified pituitary and bacterially derived growth hormone on chicken adipose tissue *in vitro*. Proc Soc Exp Biol Med, 180(3): 513–517

Campbell R M, Scanes C G (1987). Growth hormone inhibition of glucagon- and cAMP-induced lipolysis by chicken adipose tissue *in vitro*. Proc Soc Exp Biol Med, 184(4): 456–460

Campbell R M, Scanes C G (1988a). Pharmacological investigations on the lipolytic and antilipolytic effects of growth hormone (GH) in chicken adipose tissue *in vitro*: evidence for involvement of calcium and polyamines. Proc Soc Exp Biol Med, 188(2): 177–184

Campbell R M, Scanes C G (1988b). Inhibition of growth hormone-stimulated lipolysis by somatostatin, insulin, and insulin-like growth factors (somatomedins) *in vitro*. Proc Soc Exp Biol Med, 189(3): 362–366

Campbell R M, Kostyo J L, Scanes C G (1990). Lipolytic and antilipolytic effects of human growth hormone, its 20-kilodalton variant, a reduced and carboxymethylated derivative, and human placental lactogen on chicken adipose tissue *in vitro*. Proc Soc Exp Biol Med, 193(4): 269–273

Campbell R M, Kawauchi H, Lewis U J, Papkoff H, Scanes C G (1991). Comparison of lipolytic and antilipolytic activities of lower vertebrate growth hormones on chicken adipose tissue *in vitro*. Proc Soc Exp Biol Med, 197(4): 409–415

Campbell R M, Chen W Y, Wiehl P, Kelder B, Kopchick J J, Scanes C G (1993). A growth hormone (GH) analog that antagonizes the lipolytic effect but retains full insulin-like (antilipolytic) activity of GH. Proc Soc Exp Biol Med, 203(3): 311–316

Cascone O, Turyn D, Dellacha J M, Machado V L, Marques M, Vita N, Cassan C, Ferrara P, Guillemot J C (1991). Isolation, purification and primary structure of insulin from the turtle *Chrysemys dorbigni*. Gen Comp Endocrinol, 84(3): 355–359

Chandavar V R, Naik P R (2008). Immunocytochemical detection of glucagon and insulin cells in endocrine pancreas and cyclic disparity of plasma glucose in the turtle *Melanochelys trijuga*. J Biosci, 33(2): 239–247

Chartrin P, Bernadet M D, Guy G, Mourot J, Hocquette J F, Rideau N, Duclos M J, Baéza E (2006). Does overfeeding enhance genotype effects on liver ability for lipogenesis and lipid secretion in ducks? Comp Biochem Physiol A Mol Integr Physiol, 145(3): 390–396

Cheema M A, Qureshi M A, Havenstein G B (2003). A comparison of the immune response of a 2001 commercial broiler with a 1957 randombred broiler strain when fed representative 1957 and 2001 broiler diets. Poult Sci, 82(10): 1519–1529

Cheema M A, Qureshi M A, Havenstein G B, Ferket P R, Nestor K E (2007). A comparison of the immune response of 2003 commercial turkeys and a 1966 randombred strain when fed representative 2003 and 1966 turkey diets. Poult Sci, 86(2): 241–248

Cheeseman J H, Levy N A, Kaiser P, Lillehoj H S, Lamont S J (2008a). *Salmonella* enteritidis-induced alteration of inflammatory CXCL chemokine messenger-RNA expression and histologic changes in the ceca of infected chicks. Avian Dis, 52(2): 229–234

Cheeseman J H, Lillehoj H S, Lamont S J (2008b). Reduced nitric oxide production and iNOS mRNA expression in IFN-gamma-stimulated

chicken macrophages transfected with iNOS siRNAs. Vet Immunol Immunopathol, 125(3–4): 375–380

Cheng H W, Freire R, Pajor E A (2004). Endotoxin stress responses in chickens from different genetic lines. 1. Sickness, behavioral, and physical responses. Poult Sci, 83(5): 707–715

Cherel Y, Le Maho Y (1985). Five months of fasting in king penguin chicks: body mass loss and fuel metabolism. Am J Physiol, 249(4 Pt 2): R387–R392

Chevalier B, Anglade P, Derouet M, Mollé D, Simon J (1996). Isolation and characterization of Muscovy (*Cairna moschata)* duck insulin. Comp Biochem Physiol B Biochem Mol Biol, 114(1): 19–26

Chida Y, Ohtsu H, Takahashi K, Sato K, Toyomizu M, Akiba Y (2000). Carbohydrate metabolism in temporal and persistent hypoglycemic chickens induced by insulin infusion. Comp Biochem Physiol C Toxicol Pharmacol, 126(2): 187–193

Christensen K, McMurtry J P, Vizzier Thaxton Y, Thaxton J P, Corzo A, McDaniel C, Scanes C G (2012a). Metabolic and hormonal responses of modern meat type chickens to fasting. Br Poult Sci, (submitted)

Christensen K, Vizzier Thaxton Y, Thaxton J P, Scanes C G (2012b). Changes in body temperature during growth and in response to fasting in modern meat type chickens. Br Poult Sci, (in press)

Christensen R A, Malinowski K, Massenzio A M, Hafs H D, Scanes C G (1997). Acute effects of short-term feed deprivation and refeeding on circulating concentrations of metabolites, insulin-like growth factor I, insulin-like growth factor binding proteins, somatotropin, and thyroid hormones in adult geldings. J Anim Sci, 75(5): 1351–1358

Christensen V L, Wineland M J, Fasenko G M, Donaldson W E (2001). Egg storage effects on plasma glucose and supply and demand tissue glycogen concentrations of broiler embryos. Poult Sci, 80(12): 1729–1735

Constans T, Chevalier B, Derouet M, Simon J (1991). Insulin sensitivity and liver insulin receptor structure in ducks from two genera. Am J Physiol, 261(4 Pt 2): R882–R890

Conlon J M (2000). Molecular evolution of insulin in non-mammalian vertebrates. Am Zool, 40(2): 200–212

Conlon J M, Hicks J W (1990). Isolation and structural characterization of insulin, glucagon and somatostatin from the turtle, *Pseudemys scripta*. Peptides, 11(3): 461–466

Conlon J M, Secor S M, Adrian T E, Mynarcik D C, Whittaker J (1997). Purification and characterization of islet hormones (insulin, glucagon, pancreatic, polypeptide and somatostatin) from the *Burmese python*, *Python molurus*. Regul Pept, 71(3): 191–198

Cutler S A, Rasmussen M A, Hensley M J, Wilhelms K W, Griffith R W, Scanes C G (2005). Effects of lactobacilli and lactose on *Salmonella typhimurium* colonisation and microbial fermentation in the crop of the young turkey. Br Poult Sci, 46(6): 708–716

Darras V M, Rudas P, Visser T J, Hall T R, Huybrechts L M, Vanderpooten A, Berghman L R, Decuypere E, Kühn E R (1993). Endogenous growth hormone controls high plasma levels of 3,3′,5-triiodothyronine (T3) in growing chickens by decreasing the T3-degrading type III deiodinase activity. Domest Anim Endocrinol, 10 (1): 55–65

Davison T F, Rea J, Rowell J G (1983). Effects of dietary corticosterone on the growth and metabolism of immature *Gallus domesticus*. Gen Comp Endocrinol, 50(3): 463–468

Davison T F, Freeman B M, Rea J (1985). Effects of continuous treatment with synthetic ACTH1-24 or corticosterone on immature *Gallus domesticus*. Gen Comp Endocrinol, 59(3): 416–423

de Beer M, Rosebrough R W, Russell B A, Poch S M, Richards M P, Coon C N (2007). An examination of the role of feeding regimens in regulating metabolism during the broiler breeder grower period. 1. Hepatic lipid metabolism. Poult Sci, 86(8): 1726–1738

de Beer M, McMurtry J P, Brocht D M, Coon C N (2008). An examination of the role of feeding regimens in regulating metabolism during the broiler breeder grower period. 2. Plasma hormones and metabolites. Poult Sci, 87(2): 264–275

De Boever S, Beyaert R, Vandemaele F, Baert K, Duchateau L, Goddeeris B, De Backer P, Croubels S (2008). The influence of age and repeated lipopolysaccharide administration on body temperature and the concentration of interleukin-6 and IgM antibodies against lipopolysaccharide in broiler chickens. Avian Pathol, 37(1): 39–44

de Boever S, Croubels S, Meyer E, Sys S, Beyaert R, Ducatelle R, De Backer P (2009). Characterization of an intravenous lipopolysaccharide inflammation model in broiler chickens. Avian Pathol, 38(5): 403–411

Delezie E, Swennen Q, Buyse J, Decuypere E (2007). The effect of feed withdrawal and crating density in transit on metabolism and meat quality of broilers at slaughter weight. Poult Sci, 86(7): 1414–1423

Dessauer H (1970). Blood chemistry of reptiles: physiological and evolutionary aspects. In: Biology of the reptilia. Vol. 3 Ed C. Gans and T.S. Parsons pp 1–72, Academic Press, New York.

Di Scala-Guenot D, Strosser M T, Mialhe P (1985). The biological activity of duck 'big' somatostatin on chicken adipose tissue. Biochim Biophys Acta, 845(2): 261–264

Donker R A, Beuving G (1989). Effect of corticosterone infusion on plasma corticosterone concentration, antibody production, circulating leukocytes and growth in chicken lines selected for humoral immune responsiveness. Br Poult Sci, 30(2): 361–369

Dridi S, Buyse J, Decuypere E, Taouis M (2005). Potential role of leptin in increase of fatty acid synthase gene expression in chicken liver. Domest Anim Endocrinol, 29(4): 646–660

Dupont J, Derouet M, Simon J, Taouis M (1999). Corticosterone alters insulin signaling in chicken muscle and liver at different steps. J Endocrinol, 162(1): 67–76

Dupont J, Tesseraud S, Derouet M, Collin A, Rideau N, Crochet S, Godet E, Cailleau-Audouin E, Métayer-Coustard S, Duclos M J, Gespach C, Porter T E, Cogburn L A, Simon J (2008). Insulin immuno-neutralization in chicken: effects on insulin signaling and gene expression in liver and muscle. J Endocrinol, 197(3): 531–542

Dong H, Lin H, Jiao H C, Song C M, ZhaoJ P, Jiang K J (2007). Altered development and protein metabolism in skeletal muscles of broiler chickens (*Gallus gallus domesticus*) by corticosterone. Comp Biochem Physiol A Mol Integr Physiol, 147(1): 189–195

Edwards C M, Stanley S A, Davis R, Brynes A E, Frost G S, Seal L J, Ghatei M A, Bloom S R (2001). Exendin-4 reduces fasting and postprandial glucose and decreases energy intake in healthy volunteers. Am J Physiol Endocrinol Metab, 281(1): E155–E161

Edwards M R, McMurtry J P, Vasilatos-Younken R (1999). Relative insensitivity of avian skeletal muscle glycogen to nutritive status. Domest Anim Endocrinol, 16(4): 239–247

Ekmay R D, de Beer M, Rosebrough R W, Richards M P, McMurtry J P, Coon C N (2010). The role of feeding regimens in regulating metabolism of sexually mature broiler breeders. Poult Sci, 89(6): 1171–1181

Evans T K, Litthauer D, Oelofsen W (1988). Purification and primary structure of ostrich insulin. Int J Pept Protein Res, 31(5): 454–462

Falsone K, Jenni-Eiermann S, Jenni L (2009). Corticosterone in migrating songbirds during endurance flight. Horm Behav, 56(5): 548–556

Farhat A, Chavez E R (2001). Metabolic studies on lean and fat Pekin ducks selected for breast muscle thickness measured by ultrasound scanning. Poult Sci, 80(5): 585–591

Ferguson D, Braun EJ (2010). Skeletal muscle and hepatic glycogen content in birds. FASEB J, 24: 1055.14.

Foltzer C, Mialhe P (1976). Pituitary and adrenal control of pancreatic endocrine function in the duck. II. Plasma free fatty acids, aminoacids, and insulin variations following hypophysectomy and replacement therapy with growth hormone and corticosterone. Diabete Metab, 2(3): 101–105

Foye O T, Uni Z, Ferket P R (2006). Effect of in ovo feeding egg white protein, beta-hydroxy-beta-methylbutyrate, and carbohydrates on glycogen status and neonatal growth of turkeys. Poult Sci, 85(7): 1185–1192

Franchini A, Marchesini E, Ottaviani E (2004). Corticosterone 21-acetate *in vivo* induces acute stress in chicken thymus: cell proliferation, apoptosis and cytokine responses. Histol Histopathol, 19(3): 693–699

Furuse M, Chol Y H, Yang S I, Kita K, Okumura J (1991). Enhanced release of cholecystokinin in chickens fed diets high in phenylalanine or tyrosine. Comp Biochem Physiol A, 99(3): 449–451

Furuse M, Mabayo R T, Miyachi Y, Okumura J (1997). Effect of ketone bodies on crop emptying in the chicken. Br Poult Sci, 38(4): 432–435

Gao J, Lin H, Song Z G, Jiao H C (2008). Corticosterone alters meat quality by changing pre-and postslaughter muscle metabolism. Poult Sci, 87(8): 1609–1617

George J C, John T M, Mitchell M A (1989). Flight effects on plasma levels of lipid, glucagon and thyroid hormones in homing pigeons. Horm Metab Res, 21(10): 542–545

Gerson A R, Guglielmo C G (2011). Flight at low ambient humidity increases protein catabolism in migratory birds. Science, 333(6048): 1434–1436

Goodridge A G (1973). Regulation of fatty acid synthesis in isolated hepatocytes prepared from the livers of neonatal chicks. J Biol Chem, 248(6): 1924–1931

Goodridge A G, Back D W, Wilson S B, Goldman M J (1986). Regulation of genes for enzymes involved in fatty acid synthesis. Ann N Y Acad Sci, 478(1 Metabolic Reg): 46–62

Graf R, Krishna S, Heller H C (1989). Regulated nocturnal hypothermia induced in pigeons by food deprivation. Am J Physiol, 256(3 Pt 2): R733–R738

Guglielmo C G (2010). Move that fatty acid: fuel selection and transport in migratory birds and bats. Integr Comp Biol, 50(3): 336–345

Guglielmo C G, Haunerland N H, Hochachka P W, Williams T D (2002). Seasonal dynamics of flight muscle fatty acid binding protein and catabolic enzymes in a migratory shorebird. Am J Physiol Regul Integr Comp Physiol, 282(5): R1405–R1413

Han P F S, Smyth J R Jr (1972). The influence of growth rate on the development of Marek's disease in chickens. Poult Sci, 51(3): 975–985

Han P F S, Smyth J R Jr (1973). The influence of maternal effects on the response of fast and slow growing chickens to a Marek's disease virus. Poult Sci, 52(3): 909–915

Harvey S, Scanes C G, Howe T (1977). Growth hormone effects on *in vitro* metabolism of avian adipose and liver tissue. Gen Comp Endocrinol, 33(3): 322–328

Harvey S, Scanes C G, Chadwick A, Bolton N J (1978). Influence of fasting, glucose and insulin on the levels of growth hormone and prolactin in the plasma of the domestic fowl (*Gallus domesticus*). J Endocrinol, 76(3): 501–506

Havenstein G B, Ferket P R, Qureshi M A (2003). Carcass composition and yield of 1957 versus 2001 broilers when fed representative 1957 and 2001 broiler diets. Poult Sci, 82(10): 1509–1518

Hayashi K, Nagai Y, OhtsukaA, TomitaY(1994). Effects of dietary corticosterone and trilostane on growth and skeletal muscle protein turnover in broiler cockerels. Br Poult Sci, 35(5): 789–798

Hazelwood R L (1986). Carbohydrate Metabolism. In: Avian Physiology Ed. P.D.Sturkie pp.303–325, Springer-Verlag, New York

Hazelwood R L, Lorenz F W (1959). Effects of fasting and insulin on carbohydrate metabolism of the domestic fowl. Am J Physiol, 197(1): 47–51

Hedges S B, Poling L L (1999). A molecular phylogeny of reptiles. Science, 283(5404): 998–1001

Hen G, Yosefi S, Ronin A, Einat P, Rosenblum C I, Denver R J, Friedman-Einat M (2008). Monitoring leptin activity using the chicken leptin receptor. J Endocrinol, 197(2): 325–333

Hendricks G L 3rd, Hadley J A, Krzysik-Walker S M, Prabhu K S, Vasilatos-Younken R, Ramachandran R (2009). Unique profile of chicken adiponectin, a predominantly heavy molecular weight multimer, and relationship to visceral adiposity. Endocrinology, 150(7): 3092–3100

Hidalgo-Vila J, Díaz-Paniagua C, Pérez-Santigosa N, Laza A, Camacho I, Recio F (2007). Hematologic and biochemical reference intervals of free-living Mediterranean pond turtles (*Mauremys leprosa*). J Wildl Dis, 43(4): 798–801

Hintz J V (2000). The hormonal regulation of premigratory fat deposition and winter fattening in red-winged blackbirds. Comp Biochem Physiol A Mol Integr Physiol, 125(2): 239–249

Holmbäck U, Lowden A, Akerfeldt T, Lennernäs M, Hambraeus L, Forslund J, Akerstedt T, Stridsberg M, Forslund A (2003). The human body may buffer small differences in meal size and timing during a 24-h wake period provided energy balance is maintained. J Nutr, 133(9): 2748–2755

Honey R N, Weir G C (1979). Insulin stimulates somatostatin and inhibits glucagon secretion from the perfused chicken pancreas-duodenum. Life Sci, 24(19): 1747–1750

Honey R N, Schwarz J A, Mathe C J, Weir G C (1980). Insulin, glucagon, and somatostatin secretion from isolated perfused rat and chicken pancreas-duodenum. Am J Physiol, 238(2): E150–E156

Houston B, O'Neill I E (1991). Insulin and growth hormone act synergistically to stimulate insulin-like growth factor-I production by cultured chicken hepatocytes. J Endocrinol, 128(3): 389–393

Huang J X, Lu L, Xi L, Luo X G, Liu B (2010). Effects of age and strain on the expression of leptin receptor, neuropeptide Y and pro-opiomelanocortin in the hypothalamus of young chickens. Br Poult Sci, 51(5): 696–702

Jackson S, Duke G E (1995). Intestine fullness influences feeding behaviour and crop filling in the domestic turkey. Physiol Behav, 58 (5): 1027–1034

Jankowski M D, Franson J C, Möstl E, Porter W P, Hofmeister E K (2010). Testing independent and interactive effects of corticosterone and synergized resmethrin on the immune response to West Nile virus in chickens. Toxicology, 269(1): 81–88

Jenni L, Jenni-Eiermann S (1998). Fuel supply and metabolic constraints in migrating birds. J Avian Biol, 29(4): 521–528

Jia X, Nie Q, Lamont S J, Zhang X (2011). Variation in Sequence and Expression of the Avian FTO, and Association with Glucose Metabolism, Body Weight, Fatness and Body Composition in Chickens. Int J Obes (Lond)

Jiang K J, Jiao H C, Song Z G, Yuan L, Zhao J P, Lin H (2008). Corticosterone administration and dietary glucose supplementation enhance fat accumulation in broiler chickens. Br Poult Sci, 49(5): 625–631

Kelm DH, Simon R, Kuhlow D, Voigt CC, Ristow M (2011). High activity enables life on a high-sugar diet: blood glucose regulation in nectar-feeding bats. Proc Biol Sci, 278(1724): 3490–3466

Klasing K C, Laurin D E, Peng R K, Fry D M (1987). Immunologically mediated growth depression in chicks: influence of feed intake, corticosterone and interleukin-1. J Nutr, 117(9): 1629–1637

King D L, Hazelwood R L (1976). Regulation of avian insulin secretion by isolated perfused chicken pancreas. Am J Physiol, 231(6): 1830–1839

Kitazawa T, Maeda Y, Kaiya H (2009). Molecular cloning of growth hormone secretagogue-receptor and effect of quail ghrelin on gastrointestinal motility in Japanese quail. Regul Pept, 158(1-3): 132–142

Kobayashi T, Iwai H, Uchimoto R, Ohta M, Shiota M, Sugano T (1989). Gluconeogenesis in perfused livers from dexamethasone-treated chickens. Am J Physiol, 256(4 Pt 2): R907–R914

Koch K A, Wingfield J C, Buntin J D (2004). Prolactin-induced parental hyperphagia in ring doves: are glucocorticoids involved? Horm Behav, 46(4): 498–505

Kono T, Nishida M, Nishiki Y, Seki Y, Sato K, Akiba Y (2005). Characterisation of glucose transporter (GLUT) gene expression in broiler chickens. Br Poult Sci, 46(4): 510–515

Kornasio R, Halevy O, Kedar O, Uni Z (2011). Effect of *in ovo* feeding and its interaction with timing of first feed on glycogen reserves, muscle growth, and body weight. Poult Sci, 90(7): 1467–1477

Kurima K, Bacon W L, Vasilatos-Younken R (1994). Effects of glucagon infusion, alone or in combination with somatostatin, on plasma growth hormone and metabolite levels in young female turkeys under different feeding regimens. Poult Sci, 73(5): 704–713

Lance V, Hamilton J W, Rouse J B, Kimmel J R, Pollock H G (1984). Isolation and characterization of reptilian insulin, glucagon, and pancreatic polypeptide: complete amino acid sequence of alligator (*Alligator mississippiensis*) insulin and pancreatic polypeptide. Gen Comp Endocrinol, 55(1): 112–124

Lance V A, Elsey R M, Coulson R A (1993). Biological activity of alligator, avian, and mammalian insulin in juvenile alligators: plasma glucose and amino acids. Gen Comp Endocrinol, 89(2): 267–275

Landys M M, Ramenofsky M, Guglielmo C G, Wingfield J C (2004). The low-affinity glucocorticoid receptor regulates feeding and lipid breakdown in the migratory Gambel's white-crowned sparrow *Zonotrichia leucophrys gambelii*. J Exp Biol, 207(1): 143–154

Landys M M, Piersma T, Guglielmo C G, Jukema J, Ramenofsky M, Wingfield J C (2005). Metabolic profile of long-distance migratory flight and stopover in a shorebird. Proc Biol Sci, 272(1560): 295–302

Langslow D R, Hales C N (1969). Lipolysis in chicken adipose tissue *in vitro*. J Endocrinol, 43(2): 285–294

Langslow D R, Butler E J, Hales C N, Pearson A W (1970). The response of plasma insulin, glucose and non-esterified fatty acids to various hormones, nutrients and drugs in the domestic fowl. J Endocrinol, 46(2): 243–260

Laurent F, Mialhe P (1976). Insulin and the glucose-glucagon feedback mechanism in the duck. Diabetologia, 12(1): 23–33

Laurent F, Mialhe P (1978). Effect of free fatty acids and amino acids on glucagon and insulin secretions in normal and diabetic ducks. Diabetologia, 15(4): 313–321

Le Maho Y, Vu Van Kha H, Koubi H, Dewasmes G, Girard J, Ferré P, Cagnard M (1981). Body composition, energy expenditure, and plasma metabolites in long-term fasting geese. Am J Physiol, 241(5): E342–E354

Li Z, Nestor K E, Saif Y M, Luhtala M (2000). Flow cytometric analysis of T lymphocyte subpopulations in large-bodied turkey lines and a random bred control population. Poult Sci, 79(2): 219–223

Li Z, Nestor K E, Saif Y M, Anderson J W, Patterson R A (2001). Effect of selection for increased body weight in turkeys on lymphoid organ weights, phagocytosis, and antibody responses to fowl cholera and Newcastle disease-inactivated vaccines. Poult Sci, 80(6): 689–694

Lin H, Sui S J, Jiao H C, Jiang K J, Zhao J P, Dong H (2007). Effects of diet and stress mimicked by corticosterone administration on early postmortem muscle metabolism of broiler chickens. Poult Sci, 86(3): 545–554

Liu X, Dunn I C, Sharp P J, Boswell T (2007). Molecular cloning and tissue distribution of a short form chicken leptin receptor mRNA. Domest Anim Endocrinol, 32(3): 155–166

Lochmiller R L, Deerenberg C (2000). Trade-offs in evolutionary immunology: just what are the costs of immunity? Oikos, 88(1): 87–98

Lu J W, McMurtry J P, Coon C N (2007). Developmental changes of plasma insulin, glucagon, insulin-like growth factors, thyroid hormones, and glucose concentrations in chick embryos and hatched chicks. Poult Sci, 86(4): 673–683

Lutz P J, Dunbar-Cooper A (1987). Variation in the blood chemistry of the loggerhead sea turtle, *Caretta caretta*. Fish Bull, 85(1): 37–43

Maddineni S, Metzger S, Ocón O, Hendricks G 3rd, Ramachandran R (2005). Adiponectin gene is expressed in multiple tissues in the chicken: food deprivation influences adiponectin messenger ribonucleic acid expression. Endocrinology, 146(10): 4250–4256

Maillet D, Weber J M (2006). Performance-enhancing role of dietary fatty acids in a long-distance migrant shorebird: the semipalmated sandpiper. J Exp Biol, 209(14): 2686–2695

Markussen J, Sundby F (1973). Duck insulin: isolation, crystallization and amino acid sequence. Int J Pept Protein Res, 5(1): 37–48

Martin L B 2nd, Scheuerlein A, Wikelski M (2003). Immune activity elevates energy expenditure of house sparrows: a link between direct and indirect costs? Proc Biol Sci, 270(1511): 153–158

Martin L B 2nd, Hasselquist D, Wikelski M (2006). Investment in immune defense is linked to pace of life in house sparrows. Oecologia, 147(4): 565–575

Mauck R A, Matson K D, Philipsborn J, Ricklefs R E (2005). Increase in the constitutive innate humoral immune system in Leach's Storm-Petrel (*Oceanodroma leucorhoa*) chicks is negatively correlated with

growth rate. Funct Ecol, 19(6): 1001–1007

May J D, Lott B D, Deaton J W (1990). The effect of light and environmental temperature on broiler digestive tract contents after feed withdrawal. Poult Sci, 69(10): 1681–1684

May J D, Lott B D, Simmons J D (1998). The effect of environmental temperature and body weight on growth rate and feed:gain of male broilers. Poult Sci, 77(4): 499–501

Mabayo R T, Furuse M, Yang S I, Okumura J (1992). Medium-chain triacylglycerols enhance release of cholecystokinin in chicks. J Nutr, 122(8): 1702–1705

McFarlan J T, Bonen A, Guglielmo C G (2009). Seasonal upregulation of fatty acid transporters in flight muscles of migratory white-throated sparrows *(Zonotrichia albicollis)*. J Exp Biol, 212(18): 2934–2940

Meléndez-Morales D, de Paz-Lugo P, Meléndez-Hevia E (2009). Glycolysis activity in flight muscles of birds according to their physiological function. An experimental model *in vitro* to study aerobic and anaerobic glycolysis activity separately. Mol Cell Biochem, 328(1–2): 127–135

Mireles A J, Kim S M, Klasing K C (2005). An acute inflammatory response alters bone homeostasis, body composition, and the humoral immune response of broiler chickens. Poult Sci, 84(4): 553–560

Moore R W, Park S Y, Kubena L F, Byrd J A, McReynolds J L, Burnham M R, Hume M E, Birkhold S G, Nisbet D J, Ricke S C (2004). Comparison of zinc acetate and propionate addition on gastrointestinal tract fermentation and susceptibility of laying hens to Salmonella enteritidis during forced molt. Poult Sci, 83(8): 1276–1286

Nadal M R, Thompson D L Jr, Kincaid L A (1997). Effect of feeding and feed deprivation on plasma concentrations of prolactin, insulin, growth hormone, and metabolites in horses. J Anim Sci, 75(3): 736–744

Nagao K, Aman Yaman M, Murai A, Sasaki T, Saito N, Okumura J, Kita K (2001). Insulin administration suppresses an increase in insulin-like growth factor binding protein-2 gene expression stimulated by fasting in the chicken. Br Poult Sci, 42(4): 501–504

Naudé R J, Chung D, Li C H, Oelofsen W (1981). Deta-Lipotropin: primary structure of the hormone from the ostrich pituitary gland. Int J Pept Protein Res, 18(2): 138–147

Naudé R, Oelofsen W, Takahashi A, Amano M, Kawauchi H (2006). Molecular cloning and characterization of preproopiomelanocortin (prePOMC) cDNA from the ostrich (*Struthio camelus*). Gen Comp Endocrinol, 146(3): 310–317

Nestor K E, Saif Y M, Zhu J, Noble D O (1996a). Influence of growth selection in turkeys on resistance to *Pasteurella multocida*. Poult Sci, 75(10): 1161–1163

Nestor K E, Saif Y M, Zhu J, Noble D O, Patterson R A (1996b). The influence of major histocompatibility complex genotypes on resistance to *Pasteurella multocida* and Newcastle disease virus in turkeys. Poult Sci, 75(1): 29–33

Nestor K E, Lilburn M S, Saif Y M, Anderson J W, Patterson R A, Li Z, Nixon J E (1999a). Influence of body weight restriction in a body-weight-selected line of turkeys on response to challenge with *Pasteurella multocida*. Poult Sci, 78(9): 1263–1267

Nestor K E, Saif Y M, Anderson J W, Patterson R A, Li Z (1999b). Variation in resistance to *Pasteurella multocida* among turkey lines. Poult Sci, 78(10): 1377–1379

Nijdam E, Delezie E, Lambooij E, Nabuurs M J, Decuypere E, Stegeman J A (2005). Feed withdrawal of broilers before transport changes plasma hormone and metabolite concentrations. Poult Sci, 84(7): 1146–1152

Niwa H, Yamano T, Sugano T, Harris R A (1986). Hormonal effects and the control of gluconeogenesis from sorbitol, xylitol and glycerol in perfused chicken liver. Comp Biochem Physiol B, 85(4): 739–745

Ohtsuka A, Tanaka H, Hizaki K, Hayashi K(1998). Chick skeletal muscle proteolysis *in vitro* increased by corticosterone. Biosci Biotechnol Biochem, 62(9): 1781–1783

Oscar T P (1992). Glucagon-induced desensitization of broiler adipocyte lipolysis. Poult Sci, 71(6): 1015–1021

Oscar T P (1993). Enhanced lipolysis from broiler adipocytes pretreated with pancreatic polypeptide. J Anim Sci, 71(10): 2639–2644

Oscar T P (1996a). Down-regulation of glucagon receptors on the surface of broiler adipocytes. Poult Sci, 75(8): 1027–1034

Oscar T P (1996b). Prolonged *in vitro* exposure of broiler adipocytes to somatostatin enhances lipolysis and induces desensitization of antilipolysis. Poult Sci, 75(3): 393–401

Ostheim J (1992). Coping with food-limited conditions: feeding behavior, temperature preference, and nocturnal hypothermia in pigeons. Physiol Behav, 51(2): 353–361

Ots I, Kerimov A B, Ivankina E V, Ilyina T A, Hõrak P (2001). Immune challenge affects basal metabolic activity in wintering great tits. Proc Biol Sci, 268(1472): 1175–1181

Owen-Ashley N T, Hasselquist D, Råberg L, Wingfield J C (2008). Latitudinal variation of immune defense and sickness behavior in the white-crowned sparrow (*Zonotrichia leucophrys*). Brain Behav Immun, 22(4): 614–625

Padilla S E, Weber M, Jacobson E R (2011). Hematologic and plasma biochemical reference intervals for Morelet's crocodiles (*Crocodylus moreletii*) in the northern wetlands of Campeche, Mexico. J Wildl Dis, 47(3): 511–522

Pelsers M M, Butler P J, Bishop C M, Glatz J F C (1999). Fatty acid binding protein in heart and skeletal muscles of the migratory barnacle goose throughout development. Am J Physiol, 276(3 Pt 2): R637–R643

Perler F, Efstratiadis A, Lomedico P, Gilbert W, Kolodner R, Dodgson J (1980). The evolution of genes: the chicken preproinsulin gene. Cell, 20(2): 555–566

Picardo M, Dickson A J (1982). Hormonal regulation of glycogen metabolism in hepatocyte suspensions isolated from chicken embryos. Comp Biochem Physiol B, 71(4): 689–693

Pitel F, Faraut T, Bruneau G, Monget P (2010). Is there a leptin gene in the chicken genome? Lessons from phylogenetics, bioinformatics and genomics. Gen Comp Endocrinol, 167(1): 1–5

Poh T Y, Pease J, Young J R, Bumstead N, Kaiser P (2008). Re-evaluation of chicken CXCR1 determines the true gene structure: CXCLi1 (K60) and CXCLi2 (CAF/interleukin-8) are ligands for this receptor. J Biol Chem, 283(24): 16408–16415

Post J, Rebel J M, ter Huurne A A (2003). Physiological effects of elevated plasma corticosterone concentrations in broiler chickens. An alternative means by which to assess the physiological effects of stress. Poult Sci, 82(8): 1313–1318

Prinzinger R, Misovic A (2010). Age-correlation of blood values in the rock pigeon (*Columba livia*). Comp Biochem Physiol A Mol Integr Physiol, 156(3): 351–356

Proudman J A, McGuinness M C, Krishnan K A, Cogburn L A (1994). Endocrine and metabolic responses of intact and hypophysectomized turkey poults given a daily injection of chicken growth hormone. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol, 109(1): 47–56

Pulikanti R, Peebles E D, Keirs R W, Bennett L W, Keralapurath M M, Gerard P D (2010). Pipping muscle and liver metabolic profile changes and relationships in broiler embryos on days 15 and 19 of incubation. Poult Sci, 89(5): 860–865

Råberg L, Vestberg M, Hasselquist D, Holmdahl R, Svensson E, Nilsson J A (2002). Basal metabolic rate and the evolution of the adaptive immune system. Proc Biol Sci, 269(1493): 817–821

Ramachandran R, Ocón-Grove O M, Metzger S L (2007). Molecular cloning and tissue expression of chicken AdipoR1 and AdipoR2 complementary deoxyribonucleic acids. Domest Anim Endocrinol, 33(1): 19–31

Richards M P, Poch S M (2003). Molecular cloning and expression of the turkey leptin receptor gene. Comp Biochem Physiol B Biochem Mol Biol, 136(4): 833–847

Richards M P, Proszkowiec-Weglarz M, Rosebrough R W, McMurtry J P, Angel R (2010). Effects of early neonatal development and delayed feeding immediately post-hatch on the hepatic lipogenic program in broiler chicks. Comp Biochem Physiol B Biochem Mol Biol, 157(4): 374–388

Riesenfeld G, Geva A, Hurwitz S (1982). Glucose homeostasis in the chicken. J Nutr, 112(12): 2261–2266

Rosebrough R W, McMurtry J P, Vasilatos-Younken R(1991). Effect of pulsatile or continuous administration of pituitary-derived chicken growth hormone (p-cGH) on lipid metabolism in broiler pullets. Comp Biochem Physiol A Comp Physiol, 99(1–2): 207–214

Rubin C J, Zody M C, Eriksson J, Meadows J R, Sherwood E, Webster M T, Jiang L, Ingman M, Sharpe T, Ka S, Hallböök F, Besnier F, Carlborg O, Bed'hom B, Tixier-Boichard M, Jensen P, Siegel P, Lindblad-Toh K, Andersson L (2010). Whole-genome resequencing reveals loci under selection during chicken domestication. Nature, 464(7288): 587–591

Roy V K, Krishna A (2011). Regulation of leptin synthesis during adipogenesis in males of a vespertilionid bat, *Scotophilus heathi*. J Exp Biol, 214(9): 1599–1606

Rudas P, Scanes C G (1983). Influences of growth hormone on glucose uptake by avian adipose tissue. Poult Sci, 62(9): 1838–1845

Sanders K L, Lee M S (2007). Evaluating molecular clock calibrations using Bayesian analyses with soft and hard bounds. Biol Lett, 3(3): 275–279

Savenije B, Lambooij E, Gerritzen M A, Venema K, Korf J (2002). Effects of feed deprivation and transport on preslaughter blood metabolites, early postmortem muscle metabolites, and meat quality. Poult Sci, 81(5): 699–708

Savory C J (1985). An investigation into the role of the crop in control of feeding in Japanese quail and domestic fowls. Physiol Behav, 35(6): 917–928

Scanes C G (1992). Lipolytic and diabetogenic effects of native and biosynthetic growth hormone in the chicken: a re-evaluation. Comp Biochem Physiol Comp Physiol, 101(4): 871–878

Scanes C G (2008). Perspectives on analytical techniques and standardization. Poult Sci, 87(11): 2175–2177

Scanes C G, Campbell R, Griminger P (1987). Control of energy balance during egg production in the laying hen. J Nutr, 117(3): 605–611

Schaub M, Jenni L (2001). Stopover durations of three warbler species along their autumn migration route. Oecologia, 128(2): 217–227

Seki Y, Sato K, Kono T, Akiba Y (2006). Two types of phosphofructokinase-1 differentially regulate the glycolytic pathway in insulin-stimulated chicken skeletal muscle. Comp Biochem Physiol B Biochem Mol Biol, 143(3): 344–350

Sharp P J, Dunn I C, Waddington D, Boswell T (2008). Chicken leptin. Gen Comp Endocrinol, 158(1): 2–4

Shen X X, Liang D, Wen J Z, Zhang P (2011). Multiple genome alignments facilitate development of NPCL markers: a case study of tetrapod phylogeny focusing on the position of turtles. Mol Biol Evol, 28(12): 3237–3252

Shini S, Kaiser P (2009). Effects of stress, mimicked by administration of corticosterone in drinking water, on the expression of chicken cytokine and chemokine genes in lymphocytes. Stress, 12(5): 388–399

Shini S, Kaiser P, Shini A, Bryden W L (2008). Biological response of chickens (*Gallus gallus domesticus*) induced by corticosterone and a bacterial endotoxin. Comp Biochem Physiol B Biochem Mol Biol, 149(2): 324–333

Shini S, Shini A, Kaiser P (2010). Cytokine and chemokine gene expression profiles in heterophils from chickens treated with corticosterone. Stress, 13(3): 185–194

Shiraishi J, Yanagita K, Fukumori R, Sugino T, Fujita M, Kawakami S, McMurtry J P, Bungo T (2011). Comparisons of insulin related parameters in commercial-type chicks: Evidence for insulin resistance in broiler chicks. Physiol Behav, 103(2): 233–239

Siegel P B, Gross W B, Dunnington E A (1989). Effects of dietary corticosterone in young Leghorn and meat-type cockerels. Br Poult Sci, 30(1): 185–192

Silpananta P, Goodridge A G (1971). Synthesis and degradation of malic enzyme in chick liver. J Biol Chem, 246(18): 5754–5761

Silva L F, Riani-Costa C C, Ramos P R, Takahira R K (2011). Seasonal influence on biochemical profile and serum protein electrophoresis for *Boa constrictor amarali* in captivity. Braz J Biol, 71(2): 517–520

Simon J, Rosebrough R W, McMurtry J P, Steele N C, Roth J, Adamo M, LeRoith D (1986). Fasting and refeeding alter the insulin receptor tyrosine kinase in chicken liver but fail to affect brain insulin receptors. J Biol Chem, 261(36): 17081–17088

Simon J, Derouet M, Gespach C (2000). An anti-insulin serum, but not a glucagon antagonist, alters glycemia in fed chickens. Horm Metab Res, 32(04): 139–141

Simon J, Laurent S, Grolleau G, Thoraval P, Soubieux D, Rasschaert D (2004). Evolution of preproinsulin gene in birds. Mol Phylogenet Evol, 30(3): 755–766

Simon J, Rideau N, Taouis M, Dupont J (2011). Plasma insulin levels are rather similar in chicken and rat. Gen Comp Endocrinol, 171(3): 267–268

Sinsigalli N A, McMurtry J P, Cherry J A, Siegel P B (1987). Glucose tolerance, plasma insulin and immunoreactive glucagon in chickens selected for high and low body weight. J Nutr, 117(5): 941–947

Song Z G, Zhang X H, Zhu L X, Jiao H C, Lin H (2011). Dexamethasone alters the expression of genes related to the growth of skeletal muscle in chickens (*Gallus gallus domesticus*). J Mol Endocrinol, 46(3): 217–225

Speakman J R, Selman C (2003). Physical activity and resting metabolic

rate. Proc Nutr Soc, 62(03): 621–634

Spée M, Marchal L, Thierry A M, Chastel O, Enstipp M, Le Maho Y, Beaulieu M, Raclot T (2011). Exogenous corticosterone mimics a late fasting stage in captive Adelie penguins (*Pygoscelis adeliae*). Am J Physiol Regul Integr Comp Physiol, 300(5): R1241–R1249

Stambaugh T, Houdek B J, Lombardo M P, Thorpe P A, Hahn D C (2011). Innate immune response development in nestling tree swallows. Wilson Journal of Ornithology, 123(4): 779–787

Stier K S, Almasi B, Gasparini J, Piault R, Roulin A, Jenni L (2009). Effects of corticosterone on innate and humoral immune functions and oxidative stress in barn owl nestlings. J Exp Biol, 212(13): 2085–2091

Stroesser M, Cohen T L, Harvey S, Mialhe P (1980). Somatostatin stimulates glucagon secretion in ducks. Diabetogia, 18(4): 319–322

Strosser M T, Di Scala-Guenot D, Koch B, Mialhe P (1983). Inhibitory effect and mode of action of somatostatin on lipolysis in chicken adipocytes. Biochim Biophys Acta, 763(2): 191–196

Suarez R K, Herrera M L G, Welch K C Jr (2011). The sugar oxidation cascade: aerial refueling in hummingbirds and nectar bats. J Exp Biol, 214(2): 172–178

Suniga R G, Oscar T P (1994). Triiodothyronine attenuates somatostatin inhibition of broiler adipocyte lipolysis. Poult Sci, 73(4): 564–570

Sunny N E, Bequette B J (2010). Gluconeogenesis differs in developing chick embryos derived from small compared with typical size broiler breeder eggs. J Anim Sci, 88(3): 912–921

Sweazea K L, Braun E J (2006a). Glucose transporter expression in English sparrows (*Passer domesticus*). Comp Biochem Physiol B Biochem Mol Biol, 144(3): 263–270

Sweazea K L, Braun E J (2006b). Oleic acid uptake by *in vitro* English sparrow skeletal muscle. J Exp Zool A Comp. Exp Biol, 305(3): 268–276

Sweazea K L, McMurtry J P, Braun E J (2006). Inhibition of lipolysis does not affect insulin sensitivity to glucose uptake in the mourning dove. Comp Biochem Physiol B Biochem Mol Biol, 144(3): 387–394

Swensson E, Råberg L, Koch C, Hasselquist D (1998). Energetic stress, immune-suppression and the cost of an antibody response. Funct Ecol, 12(6): 912–919

Tachibana T, Matsumoto M, Furuse M, Hasegawa S, Yoshizawa F, Sugahara K (2003). Central, but not peripheral, glucagon-like peptide-1 inhibits crop emptying in chicks. Comp Biochem Physiol A Mol Integr Physiol, 134(4): 777–781

Tachibana T, Matsuda K, Sawa H, Mikami A, Ueda H, Cline M A (2010). Differential thresholds of neuromedins B-, C-, and bombesin-induced anorexia and crop-emptying rate in chicks. Gen Comp Endocrinol, 169(2): 144–150

Tahmoorespur M, Ghazanfari S, Nobari K (2010). Evaluation of adiponectin gene expression in the abdominal adipose tissue of broiler chickens: feed restriction, dietary energy, and protein influences adiponectin messenger ribonucleic acid expression. Poult Sci, 89(10): 2092–2100

Takahashi K, Aoki A, Takimoto T, Akiba Y (2008). Dietary supplementation of glycine modulates inflammatory response indicators in broiler chickens. Br J Nutr, 100(5): 1019–1028

Takeuchi S, Teshigawara K, Takahashi S (1999). Molecular cloning and characterization of the chicken pro-opiomelanocortin (POMC) gene. Biochim Biophys Acta, 1450(3): 452–459

Tako E, Ferket P R, Uni Z (2004). Effects of *in ovo* feeding of carbohydrates and beta-hydroxy-beta-methylbutyrate on the development of chicken intestine. Poult Sci, 83(12): 2023–2028

Tinker D A, Brosnan J T, Herzberg G R (1986). Interorgan metabolism of amino acids, glucose, lactate, glycerol and uric acid in the domestic fowl (*Gallus domesticus*). Biochem J, 240(3): 829–836

Tokushima Y, Takahashi K, Sato K, Akiba Y (2005). Glucose uptake *in vivo* in skeletal muscles of insulin-injected chicks. Comp Biochem Physiol B Biochem Mol Biol, 141(1): 43–48

Totzke U, Hübinger A, Bairlein F (1998). Glucose utilization rate and pancreatic hormone response to oral glucose loads are influenced by the migratory condition and fasting in the garden warbler (*Sylvia borin*). J Endocrinol, 158(2): 191–196

Totzke U, Hübinger A, Dittami J, Bairlein F (2000). The autumnal fattening of the long-distance migratory garden warbler (*Sylvia borin*) is stimulated by intermittent fasting. J Comp Physiol B, 170 (8): 627–631

Trampel D W, Sell J L, Ahn D U, Sebranek J G (2005). Preharvest feed withdrawal affects liver lipid and liver color in broiler chickens. Poult Sci, 84(1): 137–142

Turk E, Wright E M (1997). Membrane topology motifs in the SGLT cotransporter family. J Membr Biol, 159(1): 1–20

Vaillancourt E, Weber J M (2007). Lipid mobilization of long-distance migrant birds *in vivo*: the high lipolytic rate of ruff sandpipers is not stimulated during shivering. J Exp Biol, 210(7): 1161–1169

van der Most P J, de Jong B, Parmentier H K, Verhulst S (2011). Trade-off between growth and immune function: ameta-analysis of selection experiments. Functional Ecology 25(1): 74–80

Verstappen F A, Lumeij J T, Bronneberg R G (2002). Plasma chemistry reference values in ostriches. J Wildl Dis, 38(1): 154–159

Viswanathan M, John T M, George J C, Etches R J (1987). Flight effects on plasma glucose, lactate, catecholamines and corticosterone in homing pigeons. Horm Metab Res, 19(09): 400–402

Wang F, Lu L, Yuan H, Tian Y, Li J, Shen J, Tao Z, Fu Y (2011). Molecular cloning, expression, and regulation of goose leptin receptor gene in adipocytes. Mol Cell Biochem, 353(1-2): 267–274

Wang Y, Lance V A, Nielsen P F, Conlon J M (1999). Neuroendocrine peptides (insulin, pancreatic polypeptide, neuropeptide Y, galanin, somatostatin, substance P, and neuropeptide gamma) from the desert tortoise, *Gopherus agassizii*. Peptides, 20(6): 713–722

Wang Y, Li J, Yan Kwok A H, Ge W, Leung F C (2010). A novel prolactin-like protein (PRL-L) gene in chickens and zebrafish: cloning and characterization of its tissue expression. Gen Comp Endocrinol, 166(1): 200–210

Warriss P D, Kestin S C, Brown S N, Bevis E A (1988). Depletion of glycogen reserves in fasting broiler chickens. Br Poult Sci, 29(1): 149–154

Watford M (1985). Gluconeogenesis in the chicken: regulation of phosphoenolpyruvate carboxykinase gene expression. Fed Proc, 44 (8): 2469–2474

Watford M (1989). Hormonal and nutritional regulation of phosphoenolpyruvate carboxykinase mRNA levels in chicken kidney. J Nutr, 119(2): 319–322

West B, Zhou B X (1988). Did chickens go north? New evidence for domestication. J Archaeol Sci, 14(5): 515–533

Wilson S B, Back D W, Morris S M Jr, Swierczynski J, Goodridge A G (1986). Hormonal regulation of lipogenic enzymes in chick embryo hepatocytes in culture. Expression of the fatty acid synthase gene is

regulated at both translational and pretranslational steps. J Biol Chem, 261(32): 15179–15182

Yeh Y Y, Leveille G A (1970). Hepatic fatty acid synthesis and plasma free fatty acid levels in chicks subjected to short periods of food restriction and refeeding. J Nutr, 100(12): 1389–1397

Yi G F, Allee G L, Knight C D, Dibner J J (2005). Impact of glutamine and Oasis hatchling supplement on growth performance, small intestinal morphology, and immune response of broilers vaccinated and challenged with Eimeria maxima. Poult Sci, 84(2): 283–293

Yoda T, Crawshaw L I, Yoshida K, Su L, Hosono T, Shido O, Sakurada S, Fukuda Y, Kanosue K (2000). Effects of food deprivation on daily changes in body temperature and behavioral thermoregulation in rats. Am J Physiol Regul Integr Comp Physiol, 278(1): R134–R139

Yokota S D, Benyajati S, Dantzler W H (1985). Comparative aspects of glomerular filtration in vertebrates. Ren Physiol, 8(4–5): 193–221

Yuan L, Lin H, Jiang K J, Jiao H C, Song Z G (2008). Corticosterone administration and high-energy feed results in enhanced fat accumulation and insulin resistance in broiler chickens. Br Poult Sci, 49(4): 487–495

Zajac D M, Cerasale D J, Landman S, Guglielmo C G (2011). Behavioral and physiological effects of photoperiod-induced migratory state and leptin on *Zonotrichia albicollis*3: II. Effects on fatty acid metabolism. Gen Comp Endocrinol, 174(3): 269–275

Zhang W H, Jiang Y, Zhu Q F, Gao F, Dai S F, Chen J, Zhou G H (2011). Sodium butyrate maintains growth performance by regulating the immune response in broiler chickens. Br Poult Sci, 52(3): 292–301

Zhao J P, Lin H, Jiao H C, Song Z G (2009a). Corticosterone suppresses insulin- and NO-stimulated muscle glucose uptake in broiler chickens (*Gallus gallus domesticus*). Comp Biochem Physiol C Toxicol Pharmacol, 149(3): 448–454

Zhao J P, Jiao H C, Song Z G, Lin H (2009b). Effects of L-arginine supplementation on glucose and nitric oxide (NO) levels and activity of NO synthase in corticosterone-challenged broiler chickens (*Gallus gallus*). Comp Biochem Physiol C Toxicol Pharmacol, 150(4): 474–480