

Review

Production and growth related disorders and other metabolic diseases of poultry – A review

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Abstract

In humans, metabolic complaints may be associated with a failure in one of the body hormone or enzyme systems, a storage disease related to lack of metabolism of secretory products because of the lack of production of a specific enzyme, or the breakdown or reduced activity of some metabolic function. Some of these disorders also occur in poultry, as do other important conditions such as those associated with increased metabolism, rapid growth or high egg production that result in the failure of a body system because of the increased work-load on an organ or system. These make up the largest group of poultry diseases classified as metabolic disorders and cause more economic loss than infectious agents.

Poultry metabolic diseases occur primarily in two body systems: (1) cardiovascular ailments, which in broiler chickens and turkeys are responsible for a major portion of the flock mortality; (2) musculoskeletal disorders, which account for less mortality, but in broilers and turkeys slow down growth (thereby reducing profit), and cause lameness, which remains a major welfare concern. In addition, conditions such as osteoporosis and hypocalcaemia in table-egg chickens reduce egg production and can kill.

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1. Introduction

Metabolic disorders may be classed as illness associated with a failure in one of the body hormone or enzyme systems, storage disease related to lack of metabolism of secretory products because of the lack of production of a specific enzyme, or the failure or reduced activity of some metabolic function. In humans these conditions frequently have a genetic cause (Stanbury et al., 1983). Known classical genetic loci in poultry have been included in a recent article by Romanov et al. (2004). There are numerous genetic, metabolic disorders in poultry (Migaki, 1982) but these are rare in commercial poultry.

In poultry it is usual to include under the heading of ‘metabolic disorders’ those conditions associated

with increased metabolism, rapid growth rate or high egg production that result in the failure of a body system because of the increased work-load on that organ or system. A broad interpretation of metabolic disorders within the general areas shown below, will be used for this review, but because of the extensive literature on some of the disorders not all of the references will be listed.

- (1) Metabolic disorders that result from an increase production of, or deficiency of or failure in the production, synthesis, or transport of an enzyme, hormone or secretory mechanism.
- (2) Metabolic disorders that result from high nutrient intake, rapid growth, high metabolic rate, pulmonary or systemic hypertension, and high egg production or a rapid increase in egg production.
- (3) Other conditions that could be classed as metabolic disorders related to: (a) management defects; (b) nutritional deficiency or excess; (c) infectious agents; (d) toxins.

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2. Metabolic disorders that result from the failure or deficiency in the production, synthesis or transport of an enzyme, hormone or secretory mechanism

Migaki (1982) listed 17 inherited metabolic diseases of birds including pigeons, quail and 'pet birds'. In poultry he reported two defects of amino acid metabolism in chickens, tyrosinase-positive albinism and protein binding riboflavinuria; one defect of lipid metabolism, hyperlipidaemia in chickens; two defects in connective tissue, muscle and bone, inherited muscular dystrophy in both chickens and turkeys; two defects in transport, ADH-responsive (kidney) nephrogenic diabetes and uric acid hyperuricaemia, both in chickens. He also reported four defects in circulating enzymes and plasma proteins: C₁ deficiency in chickens; dysgamma-globinaemia in chickens; α_1 -antitrypsin deficiency in turkeys and catalase acatalasaemia in ducks. Other researchers have also reported some of these defects in chickens: Benoff and Buss (1976) described hereditary diabetes, Cole and Austic (1980) hereditary uricaemia, and Wilson et al. (1988a,b) inherited muscular dystrophy.

Other defects reported include high density lipoprotein deficiency (Poernama et al., 1990); thyroiditis in obese strain chickens (Wick et al., 1989; Brown et al., 1991); trimethylamine taint in eggs (Butler et al., 1984) caused by an inherited inability to synthesize adequate amounts of trimethylamine oxidase; an enzymatic abnormality in the skin of Sebright roosters causing an increased conversion of androgens to oestrogens in the skin resulting in a female feather pattern (George and Wilson, 1980); ascorbic acid diabetogenesis (Meglasson and Hazelwood, 1982), and a genetic defect in hens that were unable to deposit riboflavin in their eggs. The embryos died at about day 13 because of impaired fatty acid oxidation (Abrams et al., 1995). There was decreased activity of flavin adenine dinucleotide (FAD)-dependant medium-chain acyl CoA dehydrogenase in liver and heart.

2.1. Fatty liver and kidney syndrome (FLKS) in broilers

FLKS is a biotin deficiency-related metabolic disease in broiler chicks, 2–3 weeks of age, resulting in impaired hepatic gluconeogenesis and increased fat deposition. The problem is caused by low activity of the biotin dependent enzyme pyruvate carboxylase. Birds die from hypoglycaemia and the clinical signs and death are related to hypoglycaemia (Whitehead et al., 1978). The condition usually occurs suddenly, as an outbreak, associated with some management, feed (perhaps fat level) or environmental change that affects feeding. Affected broilers are usually well grown. Clinical signs include aphagia, lethargy and weakness with uncoordinated behaviour and head movement (sometimes classed as

nervous signs). The chicks may lie on their breast with their neck and legs extended (Butler, 1976). Mortality can vary from 5% to 35%. At necropsy the liver and kidneys are markedly enlarged, pale and fatty. Adequate dietary biotin will prevent FLKS and the condition is no longer seen in broilers on commercial rations.

2.2. Fatty liver and kidney syndrome in turkeys

Fatty liver and kidney syndrome has been produced experimentally in young turkeys (Whitehead and Siller, 1983).

2.3. Spiking mortality syndrome in broiler chickens

Spiking mortality is the name given to a metabolic disorder of previously healthy, normal appearing, broiler chickens that experience a sudden increase in mortality between 12 and 18 days of age. Live chicks are found recumbent and uncoordinated, frequently lying on their breasts with legs extended. Reported nervous signs are related to the inability to rise and head movement. The clinical signs and death are caused by hypoglycaemia (Davis and Vasilatos-Younken, 1995). This hypoglycaemia is a metabolic disorder that may be related to melatonin deficiency caused by lack of a long dark period. Melatonin does have an effect on metabolism (Apeldoorn et al., 1999) and the use of a long daily dark period will usually prevent this problem. There are several reports of spiking mortality caused by infectious viral agents such as arenaviruses (Davis, 2003). It is unlikely that infectious agents cause this condition, but sub-clinical infection by a variety of biological organisms, or other stresses, could be a predisposing cause.

What has been called 'spiking mortality' in turkey poults may now be referred to as 'poult enteritis-mortality syndrome' (Barns and Guy, 2003).

2.4. Tip-over in turkey poults

Over the past 18 years there has been an increase in the percentage of newly hatched turkey poults that are found on their backs in the litter, unable to right themselves. When righted they may recover or they may tip over again. Various aetiologies have been postulated, such as a large yolk sac, but the cause is not clear. Friedman and Pantanowitz (1994) have reported that the poults have ketosis that may cause the disorientation. The incidence is reported to be higher in poults from younger breeder flocks (P. Gazdzinski, personal communication).

2.5. Dwarfism

Using dwarf female breeders may affect growth rate of progeny but there is no evidence that it causes

significant metabolic disorders in the progeny (Merat, 1984; Proudfoot et al., 1985).

2.6. *Fatty liver and hepatic steatosis in laying hens*

Hepatic steatosis, usually described as fatty liver syndrome, occurs as the result of feeding a low protein, high calorie ration to hens that are not laying enough eggs to require that level of energy. It was much more frequent in the past before the smaller, high-producing White Leghorn hybrids were introduced and layer nutrition became more advanced. It is frequently confused with fatty liver-haemorrhagic syndrome (FLHS), but these two conditions are different (Simpson and Harms, 1983; Diaz et al., 1994b). Hepatic steatosis causes a drop in egg production as hens become increasingly obese, but little increase in mortality, whereas FLHS causes increased mortality with little drop in egg production, since affected hens die from hypovolaemic shock because of liver haemorrhage and hens that die are in full production. Some of the fat in the liver in FLHS, which may result in increased fragility and rupture of the liver, may be the result of the high requirement for lipid in the egg yolk of hens in high production, and hens that do not die also have fatty livers. The two disorders have frequently been confused in the literature (Butler, 1976; Squires and Leeson, 1988).

2.7. *Fatty liver and hepatic lipidosis in turkey hens*

Hepatic steatosis in turkey hens associated with the introduction of a low protein 'holding' ration and a reduced lighting programme at about 16 weeks, designed to slow growth rate and maturity, has caused mortality in turkey breeder hens. Mortality was elevated for 12 days and affected hens were found recumbent or dead with 0.7–1.7% mortality. The hens died from liver failure (Gazdzinski et al., 1994). Cases have continued to occur in Canada and in other countries where turkey breeders are raised.

2.8. *Hepatic steatosis in waterfowl*

Fatty liver, as a commercial product, is produced deliberately in ducks and geese (Bogin et al., 1984; Chen and Chiou, 2001).

2.9. *Fatty liver-haemorrhagic syndrome*

Fatty liver-haemorrhagic syndrome occurs in commercial layers in high production and is frequently the major cause of death in healthy flocks causing up to 5% mortality during the laying cycle. Haemorrhage occurs from a ruptured liver. The liver capsule frequently ruptures as well so that a large blood clot is found in the ventral hepatoperitoneal sac of the affected lobe. The

liver in high production hens is fragile because of the large amount of lipid present to supply lipid for the developing ova. Rupture and death frequently occur during the increased abdominal pressure of egg-laying. If the liver capsule does not rupture the hen may survive and a large haematoma remains in the liver. These hens may cease production, at least temporarily. There has been extensive research into the cause and prevention of FLHS, with a higher incidence being reported in birds on a high-energy ration in hot weather (Butler, 1976; Squires and Leeson, 1988; Diaz et al., 1994b; Crespo and Shivaprasad, 2003) that could increase the fat content of the liver. Analysis of the fatty acid composition of plasma phospholipids showed a difference between normal and FLHS-susceptible laying hens. However the composition of dietary lipids may be more important than total dietary lipids (Thomson et al., 2003). This could influence the structural properties and integrity of cell membranes or have an anti-inflammatory effect. The coagulation profile is also different. High levels of plasma oestradiol increase the risk of FLHS (Haghighi-Rad and Polin, 1981) and hens in high production have high levels of oestradiol. Rapeseed meal in the ration increases the incidence of FLHS because erucic acid or other toxic products affect the strength of the connective tissue in the liver (Bhatnagar et al., 1980; Wight et al., 1986). FLHS has also been reported in quail (Spurlock and Savage, 1993).

2.10. *Necrotic, haemorrhagic hepatitis; hepatitis liver-haemorrhage syndrome; hepatitis-splenomegaly syndrome*

Necrotic, haemorrhagic hepatitis is a disease of egg laying chickens that occurs after the hens come into full egg production. It has been recognized as a specific disease since the early 1980s (Ritchie and Riddell, 1991; Dibner et al., 1994; Shivaprasad and Woolcock, 1995). The mortality is usually low, <1% per week, and may continue for several weeks or months. It is occasionally the most significant cause of death in caged layer flocks. Hens die from hepatitis or haemorrhage from the liver that appears to be caused by an immune-mediated vasculitis and hepatitis (Tablante et al., 1994; Julian, 1995). There are sub-acute and chronic hepatitis forms of the condition that are only seen at processing or necropsy (Julian, 1998a). This disease has only been reported from North America but similar conditions have been reported under a variety of names from many countries with several suggested aetiologies (Julian, 1995). The author has identified the condition on four continents.

In the acute form, hens are usually found dead. These hens have been in full egg production, and the ova show 3–6 days atrophy indicating the length of illness. There is often unclotted blood in the hepato-peritoneal space. The liver is enlarged and firm. It may be dark or pale,

depending on presence of blood. There are red and white foci and haemorrhages on the surface and in the parenchyma. The spleen is frequently enlarged.

In the sub-acute and chronic form the hens have pale, shrunken combs and are in poor body condition. They have been out of egg production for several weeks. Hepatitis is the primary gross lesion. The liver is enlarged, hard, mottled green, brown or red with white foci on the surface and throughout the parenchyma (Julian, 1998a).

In the acute form the microscopic picture is one of necrosis, haemorrhage, pools of pink-staining, amorphous material, focal granulomas and inflammatory cells, typical of a bacterial infection, but no consistent pathogens have been isolated from this condition. The focal granulomas appear to have formed around foci of dead hepatocytes or amyloid. Careful examination of interlobular veins shows vasculitis and thrombosis that probably is the significant lesion and the cause of the haemorrhage and hepatitis. Amyloid is present in the perihepatocellular (Disse) space and in vessel walls (Tablante et al., 1994).

In the chronic form there is a prominent lymphoplasmacytic cellular infiltrate in the liver. Clusters of heterophils are also present. There is a prominent fibrosis with bile duct hyperplasia. There is usually marked glomerulopathy in the kidney (Julian, 1998a).

3. Metabolic disease resulting from rapid growth, high nutrient intake or high metabolic rate

3.1. Cardiovascular disease in broilers

3.1.1. Ascites

Ascites is not a disease, it is a sign or lesion that may result from one or more of four physiological changes that cause an increased production or decreased removal of peritoneal lymph. Ascites may be associated with obstruction of lymph drainage as occurs in peritoneal carcinosis secondary to carcinoma of the oviduct; ascites may result from decreased plasma oncotic pressure, as occurs in anaemia or hypoproteinaemia. Ascites or oedema may result from fluid leakage secondary to increased vascular permeability following oxidative or chemical damage but by far the most frequent cause of ascites in birds is increased portal pressure, secondary to right ventricular failure (RVF) or liver damage. Since RVF also causes liver damage, the heart should always be examined carefully for evidence of RVF to separate the two causes of ascites that occur because of increased portal pressure. At post-mortem the fluid and fibrin is found primarily in the two ventral hepato-peritoneal spaces (Julian, 1993). Live birds may present with a swollen abdomen and respiratory distress.

3.1.2. Ascites syndrome (AS); pulmonary hypertension syndrome (PHS)

Ascites caused by valvular insufficiency (VI) and RVF following right ventricular hypertrophy (RVH) and dilation secondary to pulmonary hypertension (PH) has been recognized in poultry for many years at high altitude (Burton and Smith, 1967; Olander et al., 1967; Cueva et al., 1974; Lopez-Coello et al., 1982; Lopez-Coello, 1985; Huchzermeyer and de Ruyck, 1986; Hernandez, 1987; Monge and León-Velarde, 1991). The term ‘pulmonary hypertension syndrome’ appears to have been first used by Huchzermeyer and de Ruyck (1986). Julian and Wilson (1986) recognized that ascites at low altitude was also caused by PH resulting in RVH followed by RVF and ascites. PHS and ascites syndrome (AS) have been the terms used to describe ascites, secondary to PH. PHS has become prominent in many low or moderate altitude countries since the early 1980s (Julian, 1983, 1993). A variety of factors that increase metabolic rate, oxygen requirement or heat production (which raise blood flow and cardiac output) (Julian, 1987a,b; Julian et al., 1992b; Scheele et al., 1992; Wiernusz and Teeter, 1995), or secondary factors which increase resistance to blood flow in the lung, can markedly increase the incidence of PHS (Julian, 1987a,b, 1993, 2000; Decuyperé et al., 1994; Wideman and Kirby, 1995). Increased blood-flow or increase blood viscosity result in PH and high workload on the RV resulting in RVH (Burton and Smith, 1967; Reid, 1986; Maxwell et al., 1990; Mirsalimi and Julian, 1991; Monge and León-Velarde, 1991).

In fast-growing, meat-type chickens at low altitude, PH results from insufficient space for the increased blood flow through the lung required to supply the organs and tissues with oxygen (Julian, 1987a, 1993; Wideman, 2000, 2001; Wideman and French, 2000; Wideman et al., 1996, 1997). This is primary or spontaneous pulmonary hypertension (Peacock et al., 1990; Julian and Mirsalimi, 1992). There is no evidence that low pen oxygen concentration is a cause of PHS at low altitude (Julian and Wilson, 1992)

There are several experimental models that increase the incidence of PH-induced RVF. These cause either increased blood flow because of a higher metabolic rate: cold (Julian et al., 1989b), certain nutrients (Julian et al., 1992b), chemicals that increase metabolism (Hatch, 1988; Bartov, 1989; Toyomizu et al., 1992; Decuyperé et al., 1994), or they cause increased resistance to flow as a result of increased blood viscosity because of polycythaemia (Mirsalimi et al., 1993; Diaz et al., 1994a), increased red blood cell rigidity from high sodium (Mirsalimi et al., 1992; Mirsalimi and Julian, 1991) or reduced vascular capacity in the lung (Julian and Goryo, 1990; Julian, 1993). Some additive factors such as high sodium may cause both increased flow and increased resistance to flow (Julian et al., 1992a). Primary lung

pathology alone, however, can result in PH and RVF in broilers as it does in humans (Julian et al., 1989a; Julian and Goryo, 1990; Julian, 1993; Tottori et al., 1997). In the model used by Tankson et al. (2001) no evidence of PH was demonstrated. There is evidence of a genetic susceptibility to the PHS, probably related to rate of growth and vascular lung capacity (Wideman and French, 2000; Moghadam et al., 2001).

Hypoxia is a major secondary cause of PHS at moderate, >750 m (Bond et al., 1999) and high, altitude but hypoxia-induced AS can also be reduced by slowing metabolic rate (Arce et al., 1992; Hassanzadeh et al., 2003). Hypoxia results in hypoxaemia stimulating polycythaemia and increasing blood viscosity causing an increased resistance to flow (Burton and Smith, 1967; Monge and León-Velarde, 1991; Mirsalimi et al., 1993). Intermittent hypoxia will cause polycythaemia and PHS (Julian and Squires, 1994). Cobalt and other transition metals (e.g. Ni, Mn) increase polycythaemia (Diaz et al., 1994a; Martinez and Diaz, 1996) and cause PH. At high altitude low temperature at night is also a major contributing factor. Hypoxia (and to a lesser extent hypoxemia) can cause pulmonary arteriolar vasoconstriction (Meyrick, 1991).

In the acute form of PHS, broilers die from lung oedema secondary to PH. If these birds are seen alive they are of normal size. They may be cyanotic and mouth breathing (in respiratory distress). They are frequently found dead on their backs. Examination of the heart will show marked RVH. When broilers develop RVF they stop growing so may be smaller than their pen-mates. If they survive more than a few days they develop ascites and have a distended abdomen. The more liquid portion of the fluid in the hepato-peritoneal spaces can return to the vena cava via the lymphatics and thoracic duct until venous pressure caused by RVF becomes too high. Affected broilers become dull, depressed, inactive, cyanotic and may be in respiratory distress. The gross lesions vary depending on how long birds survive in RVF (Julian, 1993, 2000).

The only lesion that is specific for PH is hypertrophy of the right ventricular wall. There may also be dilation of the chamber if there is valvular leakage producing a volume overload in addition to the pressure load. The cause of the problem is PH, which produces RVH. All of the other signs, lesions, physiological and biochemical changes described for PHS are the result of VI, RVF and hypoxaemia, and are all secondary to PH (Wilson et al., 1988a,b). They are not part of the pathogenesis. Even pulmonary arteriolar hypertrophy, that may result from hypoxia at high altitude and be part of the cause of PH, may also be the result of PH similar to RVH. Much of the published literature on PHS focuses on the physiological, biochemical and physical changes that occur following RVF, and report those changes as the cause of RVF and ascites. In PHS the RVF is the result

of PH not the cause. RVF from causes other than PH will result in the same clinical, biochemical and post-mortem results. Ascites is the most prominent result of RVF although it is not always present in broilers that die suddenly from PH. To confirm a diagnosis of PHS the heart should be cut across in the mid-section and thickening of the right ventricular wall (hypertrophy) looked for. To weigh the right ventricular wall, all the fat, the atria and the vessels should be cut off and the right ventricle cut carefully away from the rest of the heart before doing a RV:TV weight ratio (Julian et al., 1987). A ratio above 0.25 (>25% RV) indicates RVH.

Not all researchers agree that the ascites caused by RVF is the result of PH. Olkowski et al. (1998, 1999) and Olkowski and Classen (1998) have published papers that attempt to show that RVF is secondary to left ventricular failure.

In broilers that have been in RVF for several days, or longer, the RV is markedly dilated because of the volume overload caused by VI. There may be prominent thinning of the LV wall (Julian, 1987a; Julian et al., 1987). This is caused by loss of myocytes, the result of the hypoxaemia associated with RVF and the reduced workload on the LV because of VI and reduced cardiac output. The left AV valves in these hearts would show the lesions described by Olander et al. (1967) and Olkowski et al. (1998).

Reducing AS must address the primary genetic cause of insufficient vascular capacity in the lung (Julian, 1993; Wideman and French, 2000; Wideman, 2001), reduced oxygen-carrying ability of the blood and high oxygen requirement of rapid growth as well as the causes that increase flow and resistance to flow. Ascites caused by PH is a production-related disease at low altitude. It can be prevented easily by restricting feed intake. The restriction may be in the quantity of feed allowed each day, or in the length of time allowed for feeding (Shlosberg et al., 1991, 1992; Bendheim et al., 1992). Restricting protein and energy in the ration (Mirsalimi et al., 1993) or using mash feed while allowing free-choice feed may also be effective. Vitamin C may reduce metabolic rate (Ladmaki et al., 1997; Julian, 2000). Feedstuffs and temperatures that increase metabolic rate should be avoided (Julian et al., 1989b, 1992b). Sodium levels in feed or water must not be excessive (Julian et al., 1992a). PHS at moderate (>750 m) and high altitude is a much more severe problem because of the polycythaemia and vasoconstriction (resistance to flow) induced by hypoxia (Reid, 1986; Bond et al., 1999), but it too can be reduced by restricting feed intake (reducing oxygen requirement) (Hernandez, 1987; Julian et al., 1987; Arce et al., 1992; Mirsalimi et al., 1993; Hassanzadeh et al., 2003). Poor ventilation has been blamed as a cause of PHS but no controlled research has shown poor ventilation or ammonia fumes to be a significant factor in PHS. It is more important that broilers be kept

at the proper temperature rather than well ventilated (Shlosberg et al., 1992), unless open-flame brooders are being used in a closed room.

3.1.3. Sudden death syndrome; *morte subita*; acute death syndrome; dead in good condition; heart attack; flip-over disease

Sudden death syndrome (SDS) is the name given to death in healthy, fast-growing, commercial broilers that die suddenly. It has been recognized as a specific condition since the 1950s when broiler chickens began to be grown commercially in large numbers. SDS occurs in all countries where broilers are grown rapidly under intensive conditions (Jackson et al., 1972; Volk et al., 1974; Julian, 1996a). In healthy flocks it is the most frequent cause of death with up to 4% mortality in some all-male flocks (Julian and Bowes, 1984; Julian, 1986).

Young, healthy, fast-growing boiler chickens die suddenly while standing, walking, sparring or feeding. They die with a short terminal wing-beating convulsion and frequently are found on their back. SDS can start as early as day 3, and continues for 8–12 weeks with the highest losses between days 9–22. The faster-growing males make up approximately two-thirds of affected birds (Julian, 1986; Newberry et al., 1987).

There are no diagnostic lesions in broilers that have died from SDS, but the sudden death in a previously healthy broiler (Bowes and Julian, 1986, 1988) would suggest that death is the result of ventricular fibrillation (Julian and Bowes, 1987; Greenlees et al., 1989; Olkowski and Classen, 1997a; Blanchard et al., 2002). There is a specific association with feed intake. SDS can be prevented completely by restricting feed intake to 75% of what would be eaten free-choice (Bowes et al., 1988). There is some evidence that carbohydrate availability and type, rather than protein or fat are part of the pathogenesis (Julian and Bowes, 1984). Much of the published literature on SDS relates to feeding trials to try to induce or prevent SDS (Rotter et al., 1988; Olkowski and Classen, 1997b). Except for the use of mash feed or other methods that reduce feed intake or growth rate there is little evidence that feedstuffs or vitamins have an effect on the incidence of SDS in commercial broilers on the farm.

The confirmation of SDS at necropsy is difficult since there are no lesions that are pathognomonic. The condition was first reported as being caused by lung oedema (Hemsley, 1965) and the lungs are oedematous, except in freshly dead birds (Julian, 1996a). The bursa is large and normal, which again suggests that the bird was healthy immediately prior to death. Heart ventricles are contracted, and atria are dilated and filled with blood, a significant observation. There are no specific gross or histopathological lesions that would distinguish broilers that have died from SDS from a healthy broiler that had been euthanased. Changes that have been described

(Ononuwu et al., 1979a; Riddell and Orr, 1980; Greenlees et al., 1989; Riddell, 1993; Grashorn, 1994; Crespo and Shivaprasad, 2003) are artifact, post-mortem change or incidental findings (congestion, haemorrhage, lymphoid and myeloid foci) that might be present in any normal healthy broiler that has been euthanased or that dies suddenly from hypoxia or hyperthermia (Julian, 1996b). It is unlikely that broilers that are 'found dead on arrival' at the processing plant have died from SDS. SDS is probably a metabolic disease, in which an imbalance of metabolites or electrolytes results in ventricular fibrillation.

Lowering energy intake by changing feed texture or density (mash), or management methods such as feed restriction or long dark periods (Classen and Riddell, 1989) will reduce mortality from SDS. Increased mortality is associated with crowding, unusual activity or bright light (Ononuwu et al., 1979b), particularly sunlight, so low-intensity light is recommended and the flock should be disturbed as little as possible.

Sudden death syndrome in broiler breeders, reported from Australia, is a different condition occurring in hens at the commencement of production. It is associated with low dietary potassium and hypokalaemia (Hopkinson, 1991).

3.1.4. Sudden death in turkeys caused by hypertrophic cardiomyopathy; sudden death with perirenal haemorrhage; perirenal haemorrhage syndrome; acute hypertensive angiopathy

Sudden death with perirenal haemorrhage from hypertrophic cardiomyopathy occurs in turkeys with 2–10% mortality in heavy male (tom) turkeys. Mortality may start as early as week 6 but is more prominent at 8–18 weeks (Julian, 1996a,b). In many flocks it is the most important cause of death in this age group. The condition affects larger, more rapidly growing turkeys that have high blood pressure and occurs in both toms and hens in breeder flocks. Some affected turkeys survive for several hours and appear to be in circulatory collapse (shock). Turkeys die from lung congestion and oedema and it has been suggested that this is caused by hypertrophic cardiomyopathy secondary to systemic hypertension (Boulianne et al., 1993a)

In 'concentric hypertrophic cardiomyopathy' the heart does not enlarge but, as the LV muscle mass increases because of the pressure load caused by systemic hypertension, the LV chamber becomes smaller. Stroke volume may become so small that the heart is unable to supply the blood flow required by the body. As stroke volume decreases heart rate increases to supply the required blood flow, until the LV no longer has time to fill during systole and the bird dies (Boulianne et al., 1993a,b). Slowing growth rate and reducing activity may reduce mortality.

In turkeys <18 weeks the most prominent lesions are perirenal haemorrhage, a swollen, haemorrhagic spleen, a swollen firm liver and marked lung congestion and oedema (Julian and Pettit, 1983; Mutalib and Hansen, 1990). There may be LV hypertrophy (Larochelle et al., 1992). Perirenal haemorrhage is a non-specific lesion and may occur in other conditions (Neumann et al., 1973). Bird kidneys do not have a capsule and the blood pools on the ventral surface of the kidney and in the renal portal system, probably because of failure of forward flow through the kidney. There is usually food in the crop and throughout the digestive tract. The bird is in good body condition and well hydrated, indicating that the turkey was healthy prior to death (Crespo and Shivaprasad, 2003). All tissues and organs are congested and in birds that have been dead for several hours there may be oedema in the sub-cutaneous tissue.

Histologic lesions have been described and include generalised congestion/haemorrhage with marked congestion of kidney, liver, spleen and lung (Frank et al., 1991; Julian, 1996a,b). Oedema is reported in the lung and kidney. An increase in proliferative arterial and arteriolar lesions has also been described in this condition (Julian and Pettit, 1983; Julian, 1996b) but these lesions are probably the result of hypertension.

Diagnosis is based on no prior illness, marked lung congestion and oedema, blood on the surface of the kidney, liver congestion and no other obvious cause of death. Hypertrophy of the LV indicates that this sudden death condition is the result of cardiac death following concentric hypertrophic cardiomyopathy, secondary to systemic hypertension.

Sudden death in turkeys may also be caused by ruptured aorta, spontaneous turkey cardiomyopathy or granulomatous, obstructive pulmonary disease caused by aspergillosis. These conditions can be differentiated at necropsy.

3.1.5. *Spontaneous turkey cardiomyopathy (STC); dilated cardiomyopathy of turkeys; cardio-hepatic syndrome*

STC is a dilated cardiomyopathy that causes mortality in young turkeys most frequently between weeks 2–4. STC causing heart failure, was first described as ‘round-heart disease’ by Magwood and Bray (1962). STC is related to early rapid growth and the incidence may be increased by hypoxia in the embryo or young poults, high Na⁺ in feed or water, cold and other management, environmental or genetic factors (Julian et al., 1992c). Insufficient cardiac myoglobin may be part of the pathogenesis (O’Brien et al., 1992). Dilated cardiomyopathy describes a condition in which the ventricular chamber is enlarged and the ventricular wall is thinned. Because the heart is larger, the ventricular mass is usually increased even though the wall is thin. Dilatory cardiomyopathy is a degenerative condition in which

myocytes are lost because of anoxic (excessive workload, lack of myocyte myoglobin or hypoxia), toxic (furazolidone, heavy metal), inflammatory, autoimmune or other insults (Julian et al., 1992c) There appears to be a genetic predisposition as there is in Holstein cattle and Doberman dogs. In poults <2 weeks it is primarily a RV dilatation with RVF and ascites. If poults survive this stage, LV dilatation and failure also develop and the poults dies from lung oedema because of congestive left heart failure or biventricular failure or they may survive for several weeks or months if the ventricular dilation does not progress to heart failure.

Mortality may be >2% in some flocks, but because most deaths occur in young birds economic loss is not high. Round heart also occurs in older, genetically susceptible Bronze turkeys.

Turkeys may survive to processing and severe or mild to moderate STC may be present at processing. These birds are smaller than their pen-mates. When RVF is present, liver lesions may be prominent and the liver may be swollen or shrunken and fibrotic (cardio-hepatic syndrome). Ascites may or may not be present. There is a low incidence of STC in many turkey flocks.

Reported microscopic lesions are inconsistent. In early cases in young poults fibres may appear thin and long with many mitotic figures. The lesions are caused by anoxia, myocardial cell death, oedema and fibrosis, probably secondary to ventricular dilation and oedema. Degeneration of individual myocardial cells is present in the heart of poults with experimentally induced STC before dilation becomes prominent (Julian, 1996b). After four weeks of age, affected turkeys survive longer and develop increased fibroelastic and occasionally fibrocartilaginous tissue in the sub-epicardium and endocardium of the left ventricle. The changes of terminal myocardial exhaustion are a response to the circulatory failure and the hypoxia of dilated cardiomyopathy rather than the cause (Julian, 1996a,b; Crespo and Shivaprasad, 2003). Furazolidone-induced cardiomyopathy is similar to STC (Julian, 1993).

3.1.6. *Round heart disease in chickens*

The name ‘round heart’ has been used to describe a variety of unrelated cardiomyopathies in poultry. It has also been used to describe the right ventricular failure, discussed under PHS, and STC. In chickens, round heart disease affects birds >4 months and is characterized by sudden death. Hearts of affected chickens are pale and enlarged, with hypertrophy confined to the left ventricle. The apex of an affected heart may be dimpled. The diagnosis is based on the shape of the heart and prominent left ventricular hypertrophy (Wilson and Siller, 1954). Muscle fibres throughout the myocardium are swollen and granular and contain fine vacuoles. In severe lesions the vacuoles may coalesce, producing an apparent empty space (fat?) around the nucleus and

leaving a prominent cell membrane around the periphery of the fibre (Crespo and Shivaprasad, 2003). The histological changes may be caused by cardiac muscle hypoxia. There have been no reports of this condition for many years.

3.1.7. Ruptured aorta; dissecting aneurysm

Fast-growing tom turkeys >6 weeks of age bleed to death from a rupture of the aorta. Affected turkeys are healthy, in good condition and are not seen sick. They die suddenly in a wing-beating convulsion. They are usually found dead on their breast or side. The skin is pale and there may be blood from the mouth. A large clot of blood that has originated from a rupture in the aorta, usually between the external iliac and sciatic arteries, is present in the abdominal cavity (Julian, 1996a,b). The highest mortality usually occurs between 8 and 16 weeks and in most flocks would be <1%.

The pathogenesis of aortic rupture is poorly understood, but the lesion usually develops in the tunica media in an area of the aorta where there is no vasa vasorum (less elastic). The most significant cause may be systemic hypertension. Many turkeys are hypertensive and high-energy diets increase hypertension. The incidence of ruptured aorta can be affected by diethylstilbestrol, which affects the level of lipid in the blood and the development of intimal plaques (Miller et al., 1985; Krista et al., 1987). In many cases there is no aneurysm or plaque in the aorta. β -amino-propionitrile, which is believed to interfere with collagen formation, will increase the incidence of aortic aneurysm if added to the diet (Simpson and Taylor, 1984). There are unconfirmed reports of peas increasing the incidence of ruptured aorta. It has been shown that liver levels of copper are low in some turkeys dying from aortic aneurysm (Graham, 1977). Copper is important in collagen synthesis. Other chemicals and toxins also affect collagen strength (Simpson and Taylor, 1984). It is also possible that purely mechanical forces may cause ruptured aorta (and ruptured atria) that occurs occasionally in male and female turkeys and cause death by cardiac tamponade (Bolden et al., 1983; Julian, 1996a,b).

3.1.8. Atherosclerosis

Atherosclerotic lesions are reported in the blood vessels of a variety of birds and are most frequently found in the aorta (Denholm and Lewis, 1987; Krista and McQuire, 1988; Nakamura et al., 1992; Siegel et al., 1995; Crespo and Shivaprasad, 2003). Lesions have also been reported in coronary vessels in the left ventricle in broiler chickens (Masegi et al., 1993). Atherosclerotic lesions have been associated with systemic hypertension. The severity of the lesions of atherosclerosis in birds is influenced by diet and induced by chemicals, drugs, hormones, hyperlipaemia, and hypercholesterolaemia (Julian, 1996a,b; Crespo and Shivaprasad, 2003). There

is experimental evidence that chickens infected with Marek's disease herpesvirus have an increased incidence of lesions, more widely distributed lesions, and more severe lesions than uninfected chickens (Fabricant et al., 1978; Minick et al., 1979; Fabricant, 1985; Witter and Schat, 2003). The lesions of arteriosclerosis affect primarily the tunica intima of the aorta and major arteries. In domestic chickens and turkeys, plaques in the tunica intima develop as early as four weeks of age. These early plaques consist mainly of collagen and connective tissue. In older birds, foamy cells, extra-cellular lipid, cholesterol, and mineralisation become marked in the plaques, which then can be considered true atheromas (Crespo and Shivaprasad, 2003).

3.1.9. Epicardial fibrosis

Cardiomyopathy and disorders of connective tissue have been seen in humans and animals when the diet contained high levels of rapeseed and rapeseed oil or meal that is high in erucic acid. Myocarditis and ascites have been produced when rapeseed oil, containing erucic acid, was fed to poultry. Erucic acid accumulates in the heart of birds, resulting in fatty degeneration of the myofibres, necrosis and fibrosis. The associated oedema is presumably the result of heart failure, but it may also be due to hypoproteinaemia secondary to liver damage (Ratanasethakul et al., 1976; Corner et al., 1985).

Endocarditis, epicarditis and pericarditis with hydropericardium resulting in restrictive cardiomyopathy is seen in individual turkeys and less frequently in broilers, at processing and has occurred as flock problems with 1–3% of turkeys condemned (V. Bowes, personal communication; Julian, 1996a,b, 1999). No aetiological agent has been identified. There is an association with high fat in the ration, particularly canola or rapeseed oil and meal. Mild to severe epicardial fibrosis has been reported in turkeys fed high levels (10%) of Tower and Target varieties of rapeseed oil or soybean oil. Liver lesions are frequently present as well (Umamura et al., 1977; Corner et al., 1985). Now that the association with feedstuffs has been established, only the affected hearts, or occasionally the heart and liver are condemned at processing.

Sub-endocardial and epicardial fibrosis are the prominent histologic lesions and suggest that necrosis or a circulatory problem causing oedema has initiated the reaction (Julian, 1999).

A variety of other non-infectious agents or mechanical conditions may cause pericarditis and/or epicarditis (Julian, 1996a,b). High levels of monensin or polychlorinated biphenols may produce epicardial lesions in chickens. Pericarditis is frequently present in chickens and turkeys with hydropericardium secondary to RVF.

Focal fibrinous epicarditis, occasionally with pericardial adhesion, is a frequent lesion on the antero-ventral side of the left ventricle where it is close to the

sternum. This white area of fibrosis on the epicardium is made up of proliferating and mature fibroblasts with few inflammatory cells. It likely occurs secondary to localised epicardial oedema as the result of trauma when the beating heart contacts the sternum (Julian, 1996a,b, 1999).

3.2. *Musculoskeletal disease in meat-type poultry*

3.2.1. *Introduction*

Most of the non-infectious causes of lameness and leg deformities that affect broiler chickens are related to rapid growth (Riddell, 1975, 1992; Thorp, 1996; Santora et al., 2001; Whitehead et al., 2003) and can therefore be classed as metabolic bone disease. Lameness is most prominent in rapidly growing males. Slowing growth, particularly in the first 15–20 days of life (Classen and Riddell, 1989) will markedly reduce the incidence of angular bone deformity (valgus–varus), dyschondroplasia and spondylolisthesis (kinky back) which probably make up 65–80% of the non-infectious causes of leg deformity and lameness in broiler chickens on a high density, nutritionally adequate ration.

Broiler chickens have short, thick bones. Rapid growth in these bones results in a wide, thick growth plate that models bones with inadequate strength under the growth plate, in the metaphysis. Many skeletal lesions are the result of abnormalities in bone modelling (Bain and Watkins, 1993). Rapid growth results in tendon and bone that may not have sufficient strength to support the weight of heavy broilers. This may result in painful tearing of tissue in conditions such as spondylolisthesis, ruptured gastrocnemius tendon and separation of the proximal femoral epiphysis, backward bending of the proximal tibia in bones weakened by dyschondroplasia, epiphyseitis (osteochondrosis), and pressure-induced micro-fractures at the diaphyses of the proximal tibia, which cause pain when a heavy broiler stands and walks. For a recent review of lameness in broilers and its relation to welfare; see Bradshaw et al. (2002).

The articular cartilage of rapidly growing turkeys, broilers and broiler breeders is thick and, as in all birds, is not produced from an ossification centre in the epiphysis. Focal avascular or ischaemic necrosis (osteochondrosis) of this cartilage frequently results in joint lesions. Avulsion fractures and ligament damage at the intertarsal joint or femorotibial joints are frequently missed during a necropsy examination for lameness in turkeys. Spontaneous fracture of the femur occurs sporadically in heavy males, occasionally as a flock or farm problem.

3.2.2. *Spondylolisthesis (kinky-back)*

This is the name for ventral dislocation of the anterior end of the articulating fourth thoracic vertebra with

over-riding of the posterior end by the fifth to cause pinching of the spinal cord. Damage to the spinal cord causes leg weakness that is usually followed by partial posterior paralysis. Affected broilers are lame, sit on their tail with their feet extended or fall to one side. The lesion must be differentiated from scoliosis (which usually causes no clinical signs) and osteomyelitis or osteochondrosis of the vertebrae or growth plates (Riddell, 1996) that produce similar clinical signs. This can only be done at a post-mortem examination by cutting the vertebral column medially in the mid-line to show the lesion (Riddell, 1992; Julian, 1998b; Crespo and Shivaprasad, 2003). Dislocation may also occur between other cervical and thoracic vertebrae. Spondylolisthesis is a frequent lesion in broiler chickens, associated with rapid growth in genetically susceptible broilers (Riddell, 1993). It is more common in females.

Osteochondrosis/epiphyseolitis in the T4–T5 articulating cartilage and growth plates may cause cartilage to protrude into the vertebral canal causing similar clinical signs and is more frequent in males (Julian, 1994, 1998b).

3.2.3. *Tibial dyschondroplasia (TD)*

Failure of change of the proliferating avascular, prehypertrophying, growth plate cartilage to hypertrophying cartilage to allow it to be replaced by bone at the lower edge of the growth plate results in an abnormal mass of cartilage under the growth plate. This lesion is called dyschondroplasia (Farquharson and Jefferies, 2000). It is a specific form of growth plate abnormality found in commercial meat-type poultry. This mass of cartilage occurs most frequently in the proximal tibia, but may also be found at other growth plates such as the proximal metatarsal and femoral head. If the lesion is small, bony change is minimal. If the lesion is large, the end of the affected bone enlarges and becomes weakened, allowing abnormal modeling. The tibia may be bent backward by tension from the strong gastrocnemius muscle as the bone grows. If the backward bending is greater than a few degrees, the bird cannot stand and is down on its hocks (a creeper). Affected metatarsal bones may bow medially. The bone may fracture spontaneously or at processing or occasionally necrosis develops around the cartilage plug and a sequestrum forms (Julian, 1998b). This results in long bone necrosis or fracture and severe lameness. As bone growth slows with approaching maturity the lesion may be removed and the bone may be remodelled to appear normal. Thirty to 50% of male meat-type poultry may develop dyschondroplastic lesions but lameness only occurs if there is deformity or enlargement with loss of bone strength that results in weakness, fracture or necrosis. A post-mortem examination or radiograph would be required to diagnose dyschondroplasia. The lesion is seen as a white or discoloured mass of cartilage under the

growth plate when the medial side of the proximal tibia is cut away (Julian, 1998b).

The cause of dyschondroplasia is multi-factorial but rapid growth, particularly without a long daily rest period, a deficiency of growth factor, a high anion/cation ratio in the feed and genetic susceptibility are primary factors (Riddell, 1976, 1992, 1993; Halley et al., 1987; Thorp, 1992; Ruiz-Lopez et al., 1993; Thorp et al., 1993, 1995; Cook et al., 1994; Leach and Twal, 1994; Edwards, 2000; Rath et al., 2000; Reddi, 2000). Dyschondroplasia causes 5–25% of the lameness in broiler chickens. It caused up to 50% of the lameness in some flocks of broiler chickens in countries where animal protein (which may have a high anion/cation ratio because of high levels of chloride, sulphate, phosphate or other anions) is used in the ration. Alkalinizing the ration by removing 1 kg of NaCl and replacing it with 2 kg of NaHCO₃ per tonne will reduce the incidence of dyschondroplasia. The addition of 5–10 µg 1,25-dihydroxycholecalciferol/kg of feed may prevent TD (Rennie et al., 1993), but since vitamin D deficiency results in acidosis (Booth et al., 1977), the pH in the growth plate may be more significant than has been assumed previously.

3.2.4. *Valgus–varus deformity; angular bone deformity; twisted legs*

These are the terms used to describe lateral or medial deviation of the distal tibiotarsus, frequently with a corresponding deviation of the metatarsus and secondary displacement and sometimes complete slippage of the gastrocnemius tendon (Julian, 1984a; Riddell, 1992; Thorp, 1992). Affected birds are bow-legged (varus) or knock-kneed (valgus) until they go down (twisted legs). This deformity usually starts before day 10 as a modeling defect but may be caused by a lack of remodelling as the bone grows. It may not result in significant deformity until after day 21. Growth plates are normal in the distal tibiotarsus but the proximal metatarsus may be enlarged. Intertarsal ligaments become stretched and the joint is slack. Bone strength is normal but spontaneous fracture may occur through the growth plate between the tibia and attached tarsal bones when there is severe deformity (Julian, 1984a).

The aetiology is not clear although the defect is related to over-nutrition, rapid growth and management factors (Julian, 1984a; Classen, 1992). It may be caused by continuous bone growth, without a long daily rest period to allow the bones to correct the mis-alignment. It may have to do with uneven growth of the two attached tarsal bones or of the growth plate at the end of the distal tibia or asymmetrical tendon tension on fast growing bones. It is the most frequent cause of lameness in broiler chickens, causing up to 60% of the skeletal disease. Prevention involves slowing growth rate in

weeks one and two, or a long daily dark period (Classen and Riddell, 1989).

Deficiencies of various B vitamins and minerals (Ferguson et al., 1978; Riddell, 1992, 1996) may result in what has been called perosis or chondrodystrophy. The clinical signs are similar to valgus–varus deformity.

3.2.5. *Rotated tibia*

An outward rotation (torsion) of the shaft of the tibiotarsus that results in the foot pointing laterally is called rotated tibia. The hock joint is normal with neither displacement of the gastrocnemius tendon nor bending of the distal tibiotarsal bone. The bone is straight and strong. The lesion is unilateral and the affected leg is often abducted, giving a “straddle-legged” posture. Rotated tibia is reported in turkeys, broiler chickens, Guinea fowl and ratites. It is also seen occasionally in Leghorn pullets. It is usually present at a low incidence, but can affect up to 10% of the flock. It is not likely a condition caused by rapid growth. It appears to be associated with poor footing and slippery floors in the hatching trays, shipping boxes, brooding area or cages. Improper egg storage and hatchery temperature may also increase the incidence (Thorp, 1992; Julian and Gazdzinski, 1999; Crespo and Shivaprasad, 2003). Affected birds should be culled.

3.2.6. *Rupture of the gastrocnemius tendon*

This is a common problem in heavy broilers. It is rare in turkeys and other birds. The rupture occurs above the hock and is usually primary, caused by excessive weight on tendons that have inadequate tensile strength. Rupture of the tendon of one leg puts stress on the other tendon and bilateral rupture is frequent. Affected birds are lame or may be down on their hocks, using their wings to assist movement (creepers) (Julian, 1994, 1998b). The ruptured tendon and the fibrosis of attempted repair can be palpated as a hard mass on the back of the leg above the hock. The end of the broken tendon can be found dorsal to the hock joint and haemorrhage from the injury is visible as red, blue, or green discolouration in the tissue above the hock on the back of the leg at post-mortem, and results in condemnation of the affected part at processing (red-leg, green-leg). Viral arthritis (Reovirus infection) is rarely involved in ruptured tendon.

3.2.7. *Shaky-leg lameness, shaky-leg syndrome*

Shaky-leg is a severe lameness, mainly of male turkeys 8–18 weeks old, in which the turkeys are reluctant to rise and walk. This can be a major problem in some flocks. When forced to rise, turkeys stand with their bodies tipped forward and quiver with pain. The specific aetiology is not clear, but the pain is caused by tendonitis. It becomes most obvious at the time leg tendons begin to ossify. It is associated with wet or sticky litter

conditions that cause foot-pad dermatitis and ulcers that make walking painful. As a result the turkeys spend much of their time squatting. They become stiff, develop muscle and tendon pain, and are increasingly reluctant to move to feed and water. Once the cycle of inactivity has been initiated, the stiffness and pain are self-perpetuating. Most turkeys recover as bone growth slows, but the extended time spent squatting on the floor frequently induces secondary foot, hock, and hip lesions (Julian and Bhatnagar, 1985). Good litter conditions and management strategies such as lighting programs (Buyse et al., 1996) that promote activity are important in preventing turkey lameness and leg problems.

3.2.8. *Avulsion of ligaments and epicondylitis*

Avulsion fractures and ligament damage at the intertarsal joint or femorotibial joints have been reported for many years (Crespo and Shivaprasad, 2003). They may be missed during a necropsy examination for lameness. Normal or excessive physical stress on the intertarsal joint of growing turkeys frequently causes ligament and bone lesions with inflammation of the epicondyle and avulsion or rupture of the ligament at the distal tibia (Julian, 1984b). This is a very painful condition and affected birds are quite lame. Affected birds become bowlegged and sit on their hocks that become swollen and infected (5–10% of turkey lameness). This lesion is related to rapid growth and immature bones, or occasionally to unusual activity (catching poults for weighing or moving to the growing barns). Rupture of the common retinaculum has also been reported in turkeys (Crespo and Shivaprasad, 2003).

3.2.9. *Epiphyseal separation*

The articular cartilage of rapidly growing broiler chickens and turkeys is thicker than in slow-growing birds and is not as firmly attached to the diaphyses. In broiler chickens it is frequently torn off the head of the femur by the joint capsule when the hip is dislocated at necropsy (Julian, 1998b). When live broiler chickens are picked up and carried by one leg the proximal femoral cartilage may separate when the bird struggles, resulting in haemorrhage from the end of the bone (Mitchell and de Boom, 1986). In broiler breeders and turkeys, focal avascular or ischemic necrosis of thickened cartilage frequently results in joint lesions (Thorpe, 1992). Turkeys with osteochondrosis of the femoral head may have spontaneous epiphyseal separation of the head of the femur (Julian, 1985).

3.2.10. *Fracture*

Heavy turkeys may suffer from spontaneous, spiral fracture of the femur. If it occurs as a flock problem, feed should be checked for calcium level.

3.2.11. *Trembling syndrome (metabolic myopathy) in broiler breeder pullets*

Trembling syndrome is reported as a metabolic condition causing mortality in feed restricted broiler breeder pullets. The specific cause has not been found (Perlman and Avidar, 1994).

3.2.12. *Deep pectoral myopathy (DPM)*

Spontaneous DPM has been recognized in turkeys for many years. It has been reported with increasing frequency in broiler chickens from Australia, Brazil, Canada, Italy, Japan and other countries, particularly older broilers with heavy breast muscles, grown for 'cut-up'. DPM is an exertional myopathy involving the supracoracoideus muscle, which is the muscle that raises the wing. The lesion can be easily induced by holding the broiler by its legs and allowing it to flap its wings, which is how it is produced experimentally (Martindale et al., 1979; Wight et al., 1981; Crespo and Shivaprasad, 2003). Muscle activity increases the production of lactic acid, which if not carried away by the blood, results in damage to the muscle cells with swelling and oedema. The supracoracoideus muscle is held against the breastbone by a strong fascial sheath that prevents expansion of the muscle. When swelling causes pressure to rise within the muscle, the pressure restricts the blood flow into the muscle. All or part of the muscle may die.

Turkey leg oedema also occurs secondary to exertional myopathy and there is a variety of other muscle conditions reported in turkeys (Sosnicki and Wilson, 1991; Barbut, 1997a,b).

4. **Metabolic disorders associated with egg production**

4.1. *Sudden death syndrome of broiler breeders*

Layers and broiler breeder hens may die suddenly from hypocalcaemia while shelling an egg. In most cases these hens have already withdrawn much of the calcium from their bones and their bones are osteoporotic. Sudden death syndrome of broiler breeder hens, reported from Australia, is a different condition occurring in hens at the commencement of production. It is associated with low dietary potassium and hypokalaemia (Hopkinson, 1991). The heart lesions that have been described are probably related to the hypokalaemia (Pass, 1983).

4.2. *Osteoporosis; osteopenia; osteomalacia*

Osteoporosis in laying hens is a condition that involves the progressive loss of bone during the laying period (Whitehead and Wilson, 1992; Whitehead and Fleming, 2000; Whitehead et al., 2003). Layers in high

production may become Ca depleted and develop osteoporosis. This may be because of inability to metabolize sufficient Ca, or because of inadequate dietary Ca, vitamin D₃ or P. When hens come into production they stop producing skeletal bone and only produce medullary bone (Whitehead and Fleming, 2000). If medullary bone is depleted by egg shell formation and Ca is not available from the diet, the hen then starts to withdraw Ca from cortical bone. Skeletal fracture is a frequent cause of death in high production strains of layers (>90% production for the first 3–4 months).

Phosphorus deficiency-induced osteoporosis in high producing cage layers is called cage layer fatigue (Riddell et al., 1969). Phosphorus is required to rebuild medullary bone since both Ca and P are withdrawn and replaced during the shelling–non-shelling cycle. Hens on the floor pick up excreted P from their droppings, so more dietary P is required when hens are in cages. Signs and lesions are similar to Ca deficiency. Fractured backs are more common.

Vitamin D₃ deficiency will result in osteoporosis in laying hens because it affects Ca metabolism. It is usually seen as a flock problem and may be accompanied by poor shell quality.

4.3. Hypocalcaemia

Hens may become paralysed or die from acute hypocalcaemia while shelling an egg. These are healthy hens, in full production, found dead with a shelled or partly shelled egg in the shell gland. They may be diagnosed as “egg-bound”. To diagnose this condition cut across the femur, with scissors, at the mid-point. The femur will be fragile and there will be little or no medullary bone in hens that have died from hypocalcaemia.

4.3.1. Prevention of osteoporosis and hypocalcaemia

In most flocks osteoporosis is the result of the high production. To prevent osteoporosis, without reducing production, hens must absorb enough Ca from the digestive tract to provide for daily egg-shell formation. Egg-shell formation requires that 2 g of Ca be put in each shell over an 18–20 h period every 24 h. At the peak of egg shell production, the hen is removing all of the Ca in her total pool of circulation blood ever 15 min. This Ca must be replaced or the hen will die. Since the most intense shell production occurs during the dark period, it is important that enough easily available Ca is available to be absorbed from the digest tract while the shell is being formed. Large-particle size Ca that is retained in the gizzard and which is slowly dissolved by stomach acid will help prevent osteoporosis and hypocalcaemia.

5. Conditions that could be classed as metabolic disorders

5.1. Management defects

5.1.1. Cold

The effect of cold on metabolism affects all ages of poultry. The increase in metabolic rate at temperatures below the ‘comfort zone’ (the temperature below which metabolism is increased to maintain body temperature in homothermic species) is a significant cause of increased mortality from the pulmonary hypertension syndrome (ascites) in broilers (Julian et al., 1989b). Environmental temperature either below or above the comfort zone causes discomfort. Commercial poultry rarely die from hypothermia unless buildings are damaged by wind or snow-load, the birds are not properly protected during transportation to processing in cold climates or if young birds get wet. The lethal low body temperature is 60 °F (15.5 °C) on day of hatch and 72 °F (22.2 °C) in mature chickens (Moreng and Shaffner, 1951). Young birds cannot control their body temperature for the first few days of life and do become hypothermic when they are cold. Their metabolism slows, they crowd together and are inactive. Young birds that are hypothermic may not move to feed or water and they die from dehydration and/or starvation.

Older birds that are cold appear dull and uncomfortable. They may shiver. They may be dirty because a cold pen is usually a wet pen. Cold induces a ‘stress effect’ that can be measured (Freeman and Manning, 1984; Scott and Washburn, 1985). Increased air velocity increases the effect of cold.

5.1.2. Heat

High temperature is stressful for poultry and frequently causes death from hyperthermia. High temperature also affects the developing embryo, as it does in mammals, causing abnormalities or death (Ande and Wilson, 1981). Hyperthermia may occur in the incubator, hatchery, during transfer to the farm, in the pen or during transportation to processing. The effect of ambient temperature on body temperature varies with body heat production that is directly related to body mass and feed intake (metabolism). The upper critical ambient temperature varies from just below to just above body temperature in young birds (Ernst et al., 1984; van der Hel et al., 1991) to 8–10 °C below body temperature in heavy broilers (Moulsley, 1984) because of metabolic heat production. Lethality is determined by internal body temperature. The lethal high body temperature is 116 °F for chicks and 117 °F (47.2 °C) for adult birds (Moreng and Shaffner, 1951).

Body heat production increases with food intake because of increased metabolism (feed-induced thermogenesis). Protein increases metabolism more than carbohydrate or fat and protein from animal sources

increases metabolism more than plant protein (Julian et al., 1992b). Some drugs such as nicarbazin (Bartov, 1989; Wiernusz and Teeter, 1995), thyroid hormone (May, 1980), phytotoxins (Chowdhury, 1988) and other chemical compounds such as chlorophenols and nitrophenols that uncouple oxidative phosphorylation (Hatch, 1988; Toyomizu et al., 1992) also increase body heat production. There is a linear relationship between the proportion of birds that die in a closed room because of high ambient temperature and the calculated heat output of the birds (Moulsley, 1984). Survival time may be affected by plasma phosphate level (McCormick and Garlick, 1982). In older broilers high temperature will increase metabolic rate when broilers expend energy in an effort to lose heat by convection (standing with neck and wing extended) and evaporative cooling by panting (gular flutter). Water intake is increased. Air velocity reduces (Yahav et al., 2001) and humidity increases the effect of heat.

Hyperthermia increases until heat exhaustion and death occur. Millions of heavy birds die each year from hyperthermia usually because of high environmental temperature, but also because of electric power failure in closed buildings. Death from hyperthermia does not leave diagnostic lesions. Ambient temperature and bird behaviour are significant. A thermometer that gives a daily high–low reading would assist diagnosis of death from hyperthermia. Dead birds are usually found on their breast and may be in less well-ventilated parts of the pen. They are in good body condition and the intestine may contain fluid content. High internal body temperature in dead birds, or live birds in the same pen, suggest hyperthermia as a cause of death. Body temperature does not rise after death unless the ambient temperature is above the body temperature of the dead bird. Heat also increases water loss and can result in death from dehydration in young chicks (van der Hel et al., 1991).

In live birds the metabolic response to heat can be measured by cloacal temperature, changes in plasma glucose and total ketones and progressive development of alkalosis induced by thermal panting (McCormick and Garlick, 1982; Sandercock et al., 2001; Odom and Ono, 1991). Correcting the acid–base balance may be helpful in preventing mortality (Teeter and Smith, 1986). Prevention of hyperthermia is based mainly on ventilation and evaporation techniques that cool the pen and birds and removal of feed (raising the feeders) early in the day to reduce metabolic heat production, but vitamin C may also be beneficial.

5.1.3. Dehydration and starvation

The number of hatched chicks and poults that die because of failure to eat (starve-outs) and/or drink (dehydration) varies from 0.5% to 1.5% depending on hatchery and farm management conditions. Much

higher mortality has been reported if delivery to the farm is delayed (Crespo and Shivaprasad, 2003) and, in broilers, the surviving chicks appear to have a reduced metabolic rate since they do not grow as well as chicks that start to eat within 12–24 h of hatch. It is not known what metabolic dysfunction results in the failure of the stimulation to eat and drink. Ketosis results in anorexia in some species and ketosis could be the reason for failure to eat in these chicks that are in negative energy balance. Chicks that die of dehydration or starvation do not usually show other signs of illness and usually die before the fifth day. Affected chicks are often the smaller birds. Small birds hatch from the smaller eggs. Smaller eggs lose more moisture during incubation and hatch earlier than larger eggs. These smaller birds may be in the hatchery for 24–48 h before the hatch is pulled and may be dehydrated (van der Hel et al., 1991) before they leave the hatchery.

5.1.4. Hypoxia

Oxygen is required for metabolism and reduced oxygen levels affect the growth rate and health of the developing embryo, growing birds and adults (Moreng, 1984; Christensen and Bagley, 1988). Hypoxia has its greatest effect on rapidly growing broilers in which even a slight reduction in available oxygen will slow growth.

5.1.5. Light

Broilers are frequently grown on 23–24 h of daily light that reduces normal melatonin production. A normal light/dark cycle will increase melatonin production and improves broiler health and well-being (Gordon, 1994) as well as energy metabolism (Apeldoorn et al., 1999) and immune function.

Eye health may be affected by continuous dark or light (Cummings et al., 1986).

5.2. Nutritional deficiencies or excesses

All nutrients affect metabolism but many micronutrients are active in enzyme and hormone systems, so disease caused by a deficiency or excess of a specific nutrient could be classed as a nutritional, toxic or metabolic disorders (Kolb and Tegeler, 1992; McDowell, 2000; Bender, 2002). Vitamin D₃ deficiency, which causes rickets, a very painful skeletal disorder, frequently is classed a metabolic condition in poultry. Vitamin D toxicity may also act through the endocrine system (Vieth, 1990). Vitamin C appears to have a specific effect on metabolism by reducing metabolic rate (Ladmaki et al., 1997; Julian, 2000). Free radical-induced diseases (encephalomalacia, nutritional muscular dystrophy, transudative diathesis) may be associated with an excess of poly-unsaturated fatty acid or a deficiency of vitamin E or selenium antioxidant enzymes, so are nutritional metabolic disorders (Mezes et al., 1997).

Free radicals may damage cell membranes, causing cell death. In selenium/vitamin E-deficient birds, myopathy in skeletal, gizzard or intestinal muscle is generally more remarkable than that in the myocardium. Lesions in cardiac muscle that are responsive to vitamin E and selenium have been reported in turkeys and ducks. Heart lesions are recognized as white streaks or patches and associated with hydropericardium (Scott et al., 1967; Austic and Scott, 1997). The lesions result from focal hyaline degeneration and mineralisation of myofibres (Julian, 1996b). Damage to capillary endothelium followed by fibrin thrombi, haemorrhage and ischaemic necrosis are the lesions seen in encephalomalacia (Swayne, 1996).

Iodine is required for thyroid function. Phosphorus, zinc, chromium, manganese, copper and other mineral and vitamins, particularly the vitamin B complex, are required nutrients for enzyme function (McCormick, 2002). The clinical signs of riboflavin deficiency (peripheral neuropathy and paralysis) are caused by an enzyme deficiency (Jortner et al., 1987).

The acid–base balance (usually low pH) of the feed affects poultry health, egg-shell quality, kidney function and the incidence of leg problems in broilers (Austic, 1984; Wideman et al., 1985; Halley et al., 1987; Ruiz-Lopez and Austic, 1993). The problem is usually caused by chloride, a strong ion or sulphate, but other negative ions (anions) may also increase the anion/cation ratio.

Lack of fibre in the ration results in hypoplasia of gizzard muscle, causing a back up of feed in the proventriculus and proventricular dilation, after daily feed consumption becomes high.

5.2.1. Urolithiasis

Nutritional factors (the anion/cation ratio, in this case usually high cations) that affect urine pH may result in concretions in the kidney tubules and ureters (Wideman et al., 1985; Wideman, 1987; Fitz-Coy et al., 1988; Crespo and Shivaprasad, 2003). If both ureters are blocked birds will die from hyperuricaemia. These birds have visceral urate deposits on their serous membranes. Because birds excrete semisolid urine, high calcium in young birds may also block tubules and ureters with calcium as the excess is excreted in the urine. Feed intended for layers is toxic for young broilers. High sodium also causes kidney disease (Siller, 1981; Mirsalimi and Julian, 1993), probably because high sodium increases blood viscosity by reducing red blood cell deformability (Mirsalimi and Julian, 1991) that may interfere with blood-flow through the capillaries in the glomerulus.

5.3. Infectious agents

The host response to infectious disease alters metabolism (Colditz, 2002) but rarely produces what might be

classified as specific metabolic disease in poultry. However the systemic stress response to infection or trauma contributes to the expression of metabolic disorders (Klasing, 2003) and the immune response to infectious agents has a profound effect on general metabolic processes (Humphrey and Klasing, 2004). The monokines, acute phase proteins and other mediators released by macrophages, lymphocytes and other leucocytes increase body temperature and decrease feed consumption. The bird shifts its emphasis from growth and production to defence (Klasing and Johnstone, 1991; Klasing, 2003).

Amyloid may be produced in response to inflammation and may cause chronic arthritis in chickens, but is more frequent in waterfowl (Landman et al., 1998; Landman, 1999; Crespo and Shivaprasad, 2003). Amyloidosis has been reported in the liver and spleen of young, healthy meat-type ducks that do not have evidence of other disease (Julian, 1988; Crespo and Shivaprasad, 2003).

A condition with many names but known as ‘stunting syndrome’ is caused by an infectious agent or combination of agents resulting in maldigestion and malabsorption (Shapiro and Nir, 1995; McNulty, 1998). Damage to the pancreas and enterocytes in the small intestine result in lack of digestive enzymes, reduced absorption of nutrients and poor growth. Affected broilers fail to thrive, but appear bright and active.

Some infectious agents utilise nutrients required by the bird and cause nutritional deficiency as when *Mycoplasma meliagridis* and other mycoplasma cause chondrodystrophy (turkey syndrome 65) in turkey poults by causing biotin deficiency (Thorpe, 1994).

5.4. Toxins

Many heavy metals and other toxins such as cyanide exert their effect by disabling enzyme systems. The toxic effect of most mycotoxins is also mediated through enzyme systems (Leeson et al., 1995) and some cause storage disease (Warren and Hamilton, 1981). Sulphaquinoxaline, an anti-coccidial drug, interferes with vitamin K synthesis by inhibiting epoxide reductase, which converts vitamin K to its active form. Low levels of biogenic amines may increase broiler growth, but high levels of some are toxic (Smith et al., 1996). Gizzerozine is of particular significance in countries where fishmeal is used to supplement the protein part of the ration (Sugahara, 1995). Gizzerozine either directly or by stimulating histamine production causes ulceration and damage to the proventriculus and results in haemorrhage into the digestive tract (vomito negro).

Some feedstuffs have toxin elements and many contain anti-nutrients (Julian and Brown, 1997). Rapeseed and some low erucic acid rapeseed varieties can cause heart and liver problems in broiler chickens, layers and

turkeys (Gough and Weber, 1978; Corner et al., 1985; Julian and Brown, 1997). Some *Lathyrus* species contain toxins that affect metabolism (Chowdhury, 1988).

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