

Review article

Responses of domestic fowl to excess iodine: a review

P. D. Lewis*

Animal and Poultry Science, School of Agricultural Sciences and Agribusiness, University of Natal,
Private Bag X01, Scottsville 3209, South Africa

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Typically, poultry diets contain 1–2 mg I/kg, but higher concentrations are sometimes used to enhance the I content of eggs. In addition to an increased deposition of I in the yolk, other often adverse responses occur, especially at exceptionally high concentrations. Excess I in grower diets can prevent sexual maturation in male and female fowl, and in layer diets will progressively reduce egg production until, by about 2500 mg I/kg diet, ovulation is inhibited and egg production ceases. Most I accumulates in the thyroid gland, and it is likely that the mechanism responsible for these reproductive disorders involves a modification of thyroid hormone activity. Simultaneous with the declining rate of lay, feed intake declines, egg weight and yolk-cholesterol contents decrease and body weight increases. Whereas fertility is unaffected in female breeders, hatch of fertile eggs is reduced, hatch time extended and embryonic mortality and dead-in-shell proportions increased. In contrast, male fertility is decreased because of an increased incidence of dead spermatozoa, although hatchability of eggs from normally fed hens is unaffected. All reproductive variables, together with feed intake and body weight, are normalised within about 7 d of returning to a diet with normal I levels. Excess I suppresses growth in meat-type chickens, but does not affect feed conversion efficiency. There are transient increases in plasma I and cholesterol concentration during excess I intake in all types of bird. The evidence for varying responses to different I sources is equivocal, but the consensus is that source is probably not important.

Cholesterol: Iodine: Minerals

I occurs in poultry diets in its free form, or as an iodate or iodide. A poultry diet typically contains 1–2 mg I/kg, most of which will be contributed by supplementation, with the most likely form being $\text{Ca}(\text{IO}_3)_2$ or KI within a mineral premix, or iodised salt (3 g KI/kg NaCl). Raw materials commonly used to formulate a poultry diet probably contribute <0.15 mg I/kg, unless they are included specifically for their high I content, e.g. kelp. The recommendation for egg-laying stock is about 0.35 mg I/kg (Leeson & Summers, 2001).

Free I and iodates are reduced to iodide in the intestines before absorption, and once in the circulatory system, iodide diffuses into the extracellular fluid (Leeson & Summers, 2001). Although most of the iodide is trapped in the thyroid gland, lesser quantities accumulate in the ovary, kidney, salivary glands, small intestine and skin (Pena *et al.* 1967; Ringer, 1976). Within the thyroid gland, and to a minimal extent within the ovary, iodide is rapidly oxidised and combined with tyrosine to produce organic I. In all other sites, it remains as iodide. Iodinated tyrosine within thyroglobulin combines to form the thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4). At any

one time, thyroglobulin contains mono-iodothyronine, diiodothyronine, T_3 and T_4 , and iodination and de-iodination processes occur continually, with I shifting between tyrosine and thyronine at random (Rosenberg *et al.* 1964). However, the tyrosine has to be converted into iodinated thyronine before it can be released into the blood stream. Although the principal function of T_4 is the control of cellular oxidation, significant roles are also played in the pituitary gland and gonads. For example, T_4 in some way facilitates the dissipation of juvenile, and the initiation of adult, photorefractoriness in turkeys, and possibly in broiler breeders (Proudman & Siopes, 2002). The removal of T_4 production, either pharmacologically (Siopes, 1997) or by thyroidectomy (Lien & Siopes, 1989, 1991), has a major influence on the inhibition or extension of reproductive function.

In the event of I deficiency, and the consequential reduction in T_3 and T_4 production, the pituitary gland releases thyroid stimulating hormone, which stimulates a compensatory enlargement of the thyroid gland (goitre). Breeding-hens fed an I-deficient diet will lay eggs with reduced I content, and suffer decreased hatchability,

Abbreviations: AFE, age-at-first-egg; T_3 , triiodothyronine; T_4 , thyroxine; WL, White Leghorn.

* **Corresponding author:** Dr Peter Lewis, present address, Northcot, Cowdown Lane, Goodworth Clatford, Andover SP11 7HG, Hants., UK, fax +44 1264 350556, email peter.lewis@dsl.pipex.com

extended hatching time and delayed yolk-sac absorption. In the extreme, a lack of thyroid hormone synthesis will cause laying hens to stop egg production and to become obese (Scott *et al.* 1982). Although an excess of I (at least in comparison with the usual 1–2 mg/kg concentration) might occur accidentally from time to time, there has been interest in the deliberate provision of high-I diets to commercial laying hens with the aim of enriching the I content of their eggs. Elevating the I content of eggs is an ingenious, but little used, way of preventing I deficiency in man; in addition, the consumption of such eggs is also claimed to prevent and cure hypercholesterolaemia (Ishikawa & Kamimae, 1980). However, toxic doses of I, whilst benefiting the consumer of the I-enriched egg, might cause undesirable physiological changes in the bird and thus have consequences for bird welfare and performance. The present paper reviews the literature and includes unpublished results from the experiments reported by Perry *et al.* (1989, 1990) to describe the effects that excess dietary I have on domestic fowl.

Reproductive traits

Sexual maturation

The effect of excess dietary I on sexual development in pullets depends on its concentration, and on the timings of its introduction and withdrawal. Wilson *et al.* (1968) observed that when White Leghorn (WL) hybrids were photostimulated and given diets containing 2500 or 5000 mg I/kg from 17–24 weeks old, mean ages-at-first-egg (AFE) were 23 and 30 d respectively after the return to normal diets. However, because AFE for normally fed controls was 24 weeks, it is likely that none of the birds had started rapid gonadal development when the high-I diets were introduced. Ovarian and oviducal weights between 18 and 24 weeks confirmed this to be the case. When the same two diets were fed from 19 or 20 to 24 weeks, AFE was only delayed by about 1 week, and when the 5000 mg I/kg diet was fed from 20 to 24, 28 or 32 weeks, egg production commenced 6–12 d after changing to a normal diet. These intervals between withdrawal of the experimental diets and sexual maturity are much shorter than the 15–20 d required for a pullet to complete the final stages of gonadal development, and suggest that most birds had already commenced final ovarian and oviducal maturation before the introduction of the high-I diets. Egg-laying in the birds that were given the high-I diet at these later ages was most probably prevented by an inhibition of ovulation, as happens in mature laying hens, and not by a retardation of gonadal development. Indeed, the authors reported that four pullets receiving 2500 mg I/kg diet from 20 weeks laid some eggs before going out of lay soon after the diet was introduced. It is probable, therefore, that it is not age at introduction *per se*, but the amount of time before the mean AFE of normally fed controls that is the influencing factor. Sexual maturity in modern hybrids has advanced markedly since the publication of this work in 1968; it is likely that a high-I diet would now need to be given from 13 or 14 weeks to truly delay sexual development, rather than just inhibiting ovulations in birds that are already gonadally

mature. If high-I diets, at least with concentrations ≥ 2500 mg/kg, are introduced after the majority of pullets within a flock have commenced rapid gonadal development, the onset of egg-production will be exclusively controlled by the age at which the high-I diet is withdrawn. If the high-I diet is introduced when some of the birds in a flock have started the final stages of sexual maturation and others have not, there is likely to be a widened range of individual AFE: some birds will still have to develop their reproductive organs, undergo follicular maturation and initiate ovulation, whilst others will only have to ovulate. Conversely, higher concentrations of I given at younger ages will result in the least amount of variation in sexual maturity in a flock, as observed by Wilson *et al.* (1968) in the group given 5000 mg I/kg diet from 17 weeks, because all pullets will be at the same stage of gonadal development.

The two I concentrations studied by Wilson *et al.* (1968) were close to those that have been shown to uniformly stop egg-laying in mature hens (Fig. 1), and when fed from 17 weeks resulted in a 7 d further delay in maturity for the 5000 mg I/kg treatment; therefore, it is likely that dietary I concentrations of < 2000 mg/kg will neither totally prevent gonadal maturation, nor suppress ovulation and egg-laying in all members of a flock. The threshold concentration of I at which sexual maturation is inhibited has yet to be determined, and will probably vary with genotype. When excess I is given close to first egg, the threshold is probably similar to that for the inhibition of ovulation in laying hens. A regression of the three influencing factors, I concentration, introduction age and withdrawal age (both expressed relative to mean AFE for normally fed controls) can be used to predict the delay in AFE, at least for dietary I concentrations between 2500 and 5000 mg/kg. The multiple regression is described by the equation:

$$y = W - 12.1 + 0.00144I + 0.645RS + 0.126RW \\ + k(r^2 0.990, \text{SD } 2.80, P < 0.0001),$$

where y is the mean AFE (d), W is the withdrawal age (d), I is the dietary I concentration (mg/kg), RS is the starting age

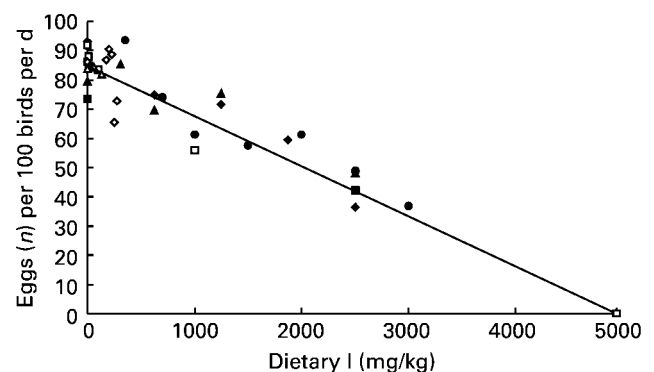


Fig. 1. Effect of dietary iodine concentration on mean rate of lay during the third week following introduction of the diet. (From Perdomo *et al.* 1966 (■, trial 1; ▲, trial 2), Arrington *et al.* 1967 (◆), Roland *et al.* 1977 (○), Perry *et al.* 1989 (□) and 1990 (●), Yue & Kang, 1995 (Δ) and Kan *et al.* 1995 (◇), adjusted by least squares for differences between a trial mean and the mean values of Perry *et al.* (1990).)

of I-containing diet relative to mean AFE for normally fed controls (d), RW is the withdrawal age of I-containing diet relative to mean AFE for normally fed controls (d) and k is an adjustment for environmental and genetic variation. A test for goodness of fit yielded an r^2 value of 0.990, SE 0.036 and $P < 0.0001$ for a regression of actual mean AFE *v.* predicted AFE (d).

Within 2 weeks of the resumption of a conventional diet, egg numbers and egg weight are normal (Wilson *et al.* 1968), at least for birds introduced to high-I diets at 19 or 20 weeks. This might appear surprising, especially for birds that did not commence egg-laying until 34 weeks; however, it is further indication that sexual maturation *per se* was unaffected by the excess I, and that the correlation of egg weight is not strictly with body weight at first egg, as reported by Lewis *et al.* (1994), but with body weight at gonadal maturation even if ovipositing does not occur because of a failure of the ova to ovulate. Wilson *et al.* (1968) did not report egg weight data for the birds given excess I from 17 weeks, but egg weight might have been increased in these birds because final gonadal development would have taken place at a later age and, presumably, at a heavier body weight. This hypothesis is worth testing, because the use of high-I diets from an early age and the consequential retardation of sexual maturation might prove to be a useful management tool for eliminating small eggs at the beginning of the laying cycle, especially if there are no detrimental effects on subsequent rate of lay. It would then be an economic consideration, because supplementing diets with I at grossly high-I concentrations is expensive.

In two trials conducted by Wilson & Harms (1972), the effects of feeding 5000 mg I/kg diet to photostimulated WL male fowl between 17 and 24 weeks old were equivocal; in one, the mean age at which spermatozoa was first collected was delayed by 10 d compared with normally fed controls, whereas in the other, there was no significant difference. Although the birds for the two trials were hatched at slightly different times of the year and reared to 17 weeks on natural daylight, this does not provide an explanation for the divergent findings, because there was only 1 d difference in mean age at spermatozoa production for normally fed controls between the two trials. When 2500 or 5000 mg I/kg was fed from 20 to 24 weeks old, however, age at first spermatozoa was not significantly different from the 18-week maturity of the normally fed controls. This is in agreement with the findings for feeding high-I diets to pullets, where gonadal development was unaffected by feeding excess I from 20 weeks old, despite an overt delay in sexual maturation because of an inhibition of ovulation (Wilson *et al.* 1968). It appears that it is the chronological relationship between the high-I feeding and expected timing of sexual development, and not the age when excess I is introduced *per se*, that is important in both sexes.

Although neither the timing of sexual development nor the hatchability of fertile eggs was affected by a high-I diet fed from 20 weeks, there were adverse effects on bird health, sperm motility and the number of dead sperm. Within 4 d of feeding a high-I diet, irrespective of its concentration or age at introduction, cockerels showed

altered reflexes, vertigo and diarrhoea, conditions similar to those observed by Wilson & Rowland (1970) when high-I diets were given to mature males. However, as observed for egg production, all semen characteristics were normalised and the signs of I toxicity disappeared within 1 week of the resumption of a normal diet (Wilson *et al.* 1968).

Rate of lay

Excess dietary I generally results in a progressive reduction in egg production in WL hens and modern brown-egg hybrids, with the rate of decline and the minimum rate of lay primarily dependant upon the concentration of I (Perdomo *et al.* 1966; Arrington *et al.* 1967; Roland *et al.* 1977; Perry *et al.* 1989, 1990; Kan *et al.* 1995; Yue & Kang, 1995). The response also appears to vary with age of bird, with older birds being more adversely affected than younger birds (Arrington *et al.* 1967). Indeed, Wilson *et al.* (1967) achieved a cessation of egg production and initiated a moult by feeding 5000 mg I/kg diet to hens that had been in lay for 11 months. Contrary to these detrimental influences on egg production, Ishikawa & Kamimae (1980) claimed that if birds are given 230 mg $\text{Ca}(\text{IO}_3)_2$ (150 mg I)/kg rather than supplementing with KI, rate of lay increases (no results were provided). Other reports support these general findings (Asmundson *et al.* 1936; Wilson *et al.* 1968; Cao *et al.* 1999; Yang *et al.* 2001). Whereas unpublished results from the study of Perry *et al.* (1990) (GC Perry, PD Lewis and MJ Hannagan, unpublished results) in Fig. 2 illustrate the typical dual influence of exposure time and dietary I concentration ≤ 3000 mg/kg, virtually all birds are reported to have stopped egg-laying within 7 to 14 d when given 5000 mg I/kg (Arrington *et al.* 1967; Marcilese *et al.* 1968; Roland *et al.* 1977). Fig. 3 suggests that the reason for the dose-effect of I on the mean rate of lay is a progressive increase in the number of birds that stop laying, and not a reduced rate of egg production for all birds. A regression of rate-of-lay data from Perdomo *et al.* (1966), Arrington *et al.* (1967), Roland *et al.* (1977), Perry *et al.* (1989, 1990),

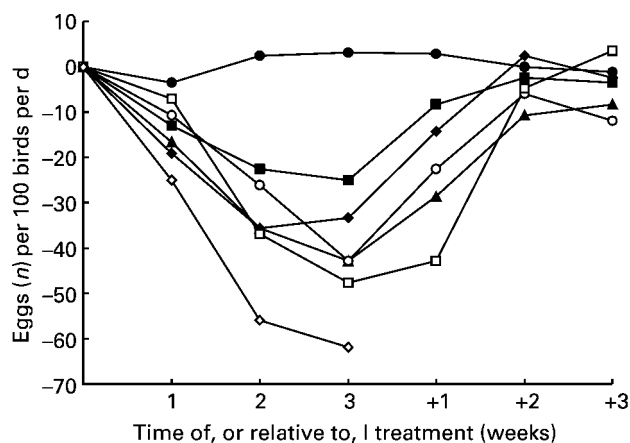


Fig. 2. Change in mean weekly rate of lay during 3 weeks of 350 (●), 700 (■), 1000 (▲), 1500 (◆), 2000 (○), 2500 (□) or 3000 (◇) mg iodine/kg diet, and during 3 weeks of a normal diet immediately following the high-iodine treatment period. (From Perry *et al.* 1990.)

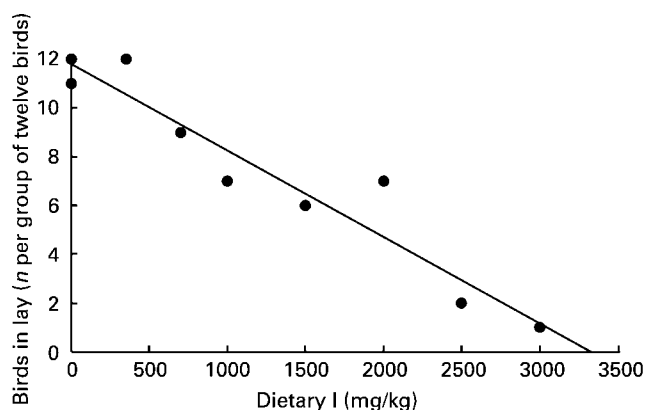


Fig. 3. Hens in-lay at the end of a 3-week period on diets containing progressively higher concentrations of iodine. (From Perry *et al.* 1990.)

Yue & Kang (1995) and Kan *et al.* (1995), adjusted by least squares for differences between trial means and the data of Perry *et al.* (1990), indicates that mean rate of lay for the third week of I treatment decreases by almost two eggs per 100 birds per d for each 100 mg increase in dietary I/kg (Fig. 1). The regression is described by the equation:

$$y = 84.7 - 0.017I$$

$$(r^2 0.910, \text{slope SE } 8.84^{-04}, P < 0.0001),$$

where y is the mean rate of lay for the third week of excess I and I is the dietary I concentration (mg/kg). However, the reduction in egg production for dietary I concentrations of <100 mg/kg is minimal, especially, it is claimed, if $\text{Ca}(\text{IO}_3)_2$ is used as the supplement rather than KI (Ishikawa & Kamimae 1980). Notwithstanding that data from Perry *et al.* (1989), who also used $\text{Ca}(\text{IO}_3)_2$, support the statement, it is difficult to substantiate it, because no detailed data were included in the US Patent application by Ishikawa & Kamimae (1980) and none of the experiments that used KI included such moderate excesses of I. These findings concur with a report of feeding high-I diets to turkeys, where egg production was unaffected

with supplements of <35 mg I/kg, but was significantly reduced at 350 mg I/kg (Christensen & Ort, 1991).

With the one exception of the report by Wilson *et al.* (1967), who fed 5000 mg I/kg diet to older hens for 6 weeks and observed a moult, all other reports state that egg production returns to normal within 2–3 weeks of returning birds to a normal diet (about 1 mg I/kg); Wilson *et al.* (1968) noted that when high-I diets were fed to peri-pubertal pullets, egg production commenced within 4–12 d of transfer to a normal diet. This indicates that, unlike the response to excesses of other minerals, such as Zn (e.g. Praharaj *et al.* 1994), excesses of I do not result in gonadal regression.

Arrington *et al.* (1967) and Marcilese *et al.* (1968) observed that vitellogenesis was still occurring, but that atresia of ova was also taking place, in birds that had stopped egg production whilst on a 5000 mg I/kg diet or when given the equivalent of a 5000 mg I/kg dose by oesophageal administration of a NaI solution. Fig. 4 illustrates this confused ovarian state in a bird killed after 3 weeks on 3000 mg I/kg diet (GC Perry, PD Lewis and MJ Hannagan, unpublished results). In addition, Perry *et al.* (1990) and Marcilese *et al.* (1968) reported similar hierarchical numbers for controls and for birds given either 3000 mg I/kg diet or the equivalent of 5000 mg I/kg into the oesophagus. The observation by Arrington *et al.* (1967) that the physical condition and appearance of younger and older hens was such that they would have been judged to have been in-lay is further evidence that the physiological processes leading up to, but not including, ovulation are almost normal in these non-laying birds. Collectively, these findings indicate that the cessation of egg-laying in birds on excessively high-I diets is caused by an inhibition of ovulation, and not by regression of the reproductive system, as occurs in forced-moulted or photorefractory birds.

Egg weight

Egg weight is abruptly reduced within 7 d of being transferred from normal-I to >350 mg I/kg diets, and Fig. 5 shows that it continues to decrease until about the third

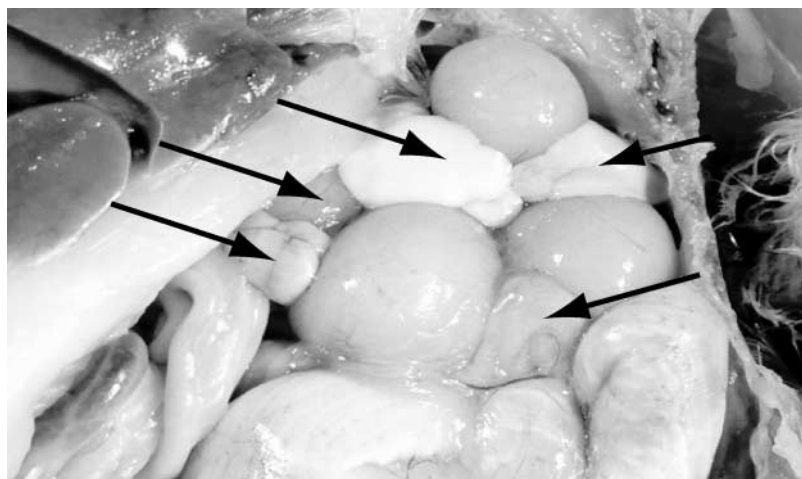


Fig. 4. The ovary of a hen 21 d after consuming 3000 mg iodine/kg diet. This illustrates the continued follicular development that occurs simultaneously with follicular atresia in a bird that has stopped egg-laying whilst consuming a high-iodine diet. →, Atretic follicles. (From GC Perry, PD Lewis and MJ Hanagan, unpublished results from the experiment reported by Perry *et al.* 1990.)

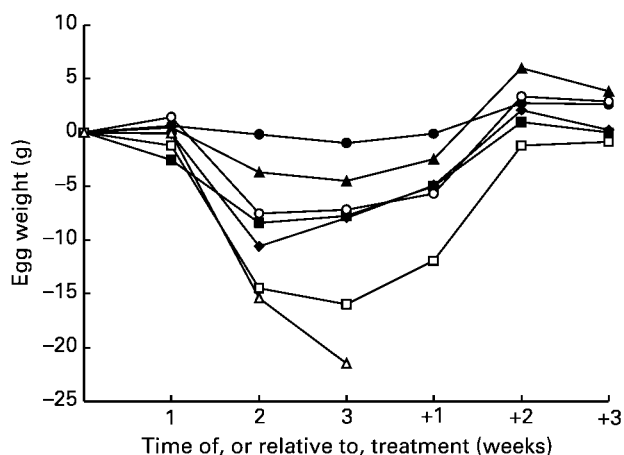


Fig. 5. Change in mean egg weight (g) during 3 weeks at 350 (●), 700 (■), 1000 (▲), 1500 (◆), 2000 (○), 2500 (□) or 3000 (◇) mg iodine/kg diet to laying hens and during 3 weeks of normal feed immediately following the treatment period. (From Perry *et al.* 1990.)

week (Perry *et al.* 1989, 1990) of excess I. Similar reductions in egg weight were observed by Arrington *et al.* (1967), and reduced ovarian weights were recorded by Marcilese *et al.* (1968), Roland *et al.* (1977) and Perry *et al.* (1990). The mean total weight of the five largest ovarian follicles in WL hens that had ceased laying, following daily administration for 14 d of NaI solution equivalent to a 5000 mg I/kg diet, was only 30% of that for hens that were still in-lay (Marcilese *et al.* 1968). A regression of data from Perry *et al.* (1989, 1990) shows that egg weight during the third week is reduced by about 0.6 g for each 100 mg increase in dietary I concentration/kg. The correlation is described by the equation:

$$y = 0.0061I (r^2 0.756, \text{ slope SE } 7.30^{-04}, P < 0.0001),$$

where y is the mean egg weight (g) in week 3 of high-I diet treatment compared with initial mean egg weight and I is the dietary I concentration (mg/kg).

Similar responses of reduced egg weight by birds consuming excess I have been reported by Yue & Kang (1995) and Yang *et al.* (2001). In contrast, Fig. 5 shows that within 14 d of a return to normal feed, egg weight rises significantly to exceed the egg weight before the provision of excess I (Arrington *et al.* 1967; Perry *et al.* 1989, 1990). However, this is a transient surge in egg weight, and pre-I-treatment egg weights prevail from the third week of normal feed onwards (Arrington *et al.* 1967; Perry *et al.* 1989, 1990). Subsequent egg weight for birds that were given normal laying diets, but which had been sexually retarded by high-I diets in rearing, were not significantly different from normally fed controls (Wilson *et al.* 1968). Similar reductions in egg weight were reported for turkey hens fed a diet supplemented with 35 or 350 mg/kg I, but with no adverse effects at 2.1 or 3.5 mg supplemented I/kg (Christensen & Ort, 1991).

Egg quality

Shell weight and percentage shell weight appears to be unaffected by dietary I concentrations of ≤ 100 mg/kg;

however, at concentrations of ≥ 1000 mg/kg, shell weight is reduced simultaneously with the decrease in egg weight that occurs at these excesses of I intake, but only to an extent to maintain percentage shell weight (Perry *et al.* 1989, 1990). This is in contrast to a significant reduction in shell weight and shell thickness, and a significant thickening of the shell membrane for turkey hens given 2.1 mg supplemental dietary I/kg (Christensen & Ort, 1990). The structure of the turkey eggs was also modified by the elevated I concentration, with significant reductions in the length, area and number (especially around the equator) of pores in the shell. Christensen & Ort (1991) noted that egg-shell conductance was progressively reduced by the addition of 3.5, 35.0 and 350.0 mg I/kg to a basal diet containing 0.7 mg I/kg. This may indicate that the toxicity threshold for shell formation is higher for domestic fowl than for turkeys.

There is a dearth of information regarding the effect of excess I on the internal quality of eggs, with just one report (Arrington *et al.* 1967) that 10 weeks after WL hens had been withdrawn from being given 2500 mg I/kg diet for 42 d, their internal quality was higher than normally fed controls (70.4 *v.* 62.5 Haugh units).

Fertility and hatchability

The fertility of eggs laid by hens consuming excess I, but inseminated with semen from normally fed males, does not appear to be compromised. In contrast, early embryonic mortality, the incidence of dead-in-shell and hatchability of fertile eggs are adversely affected, and incubation time is significantly extended (Perdomo *et al.* 1966; Arrington *et al.* 1967). Meta-analyses of data from Perdomo *et al.* (1966) and Arrington *et al.* (1967) were conducted, removing differences among data sets by least squares. Hatchability of fertile eggs decreased according to the \log^{10} value of dietary I (Fig. 6), with the regression described by the equation:

$$y = 82.1 - 14.54I$$

$$(r^2 0.827, \text{ slope SE } 2.08, P < 0.0001),$$

where y is the hatchability of fertile eggs (%) and I is the dietary I concentration (\log^{10} mg/kg).

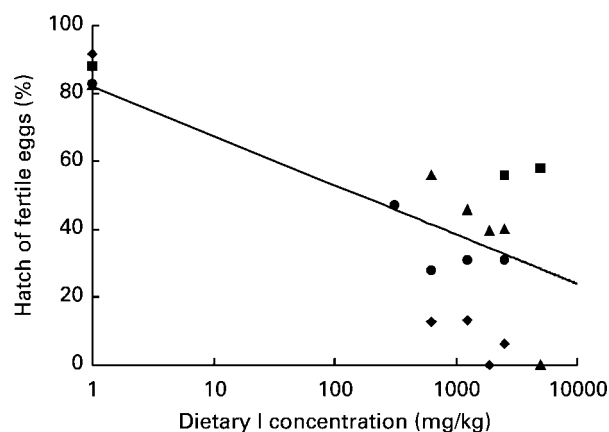


Fig. 6. Effect of dietary iodine concentration on hatchability of fertile eggs. (From unadjusted data of Perdomo *et al.* 1966 (■, ●) and Arrington *et al.* 1967 (▲, ◆).)

The causes of the markedly reduced hatchability were increases in the proportion of early dead embryos ($P=0.0007$) and dead-in-shell ($P=0.0014$). In addition, excess I resulted in about 2% more chicks having their hatch time extended by at least 24 h for each 100 mg increase in dietary I/kg ($P=0.0016$). The effects of excess I also appear to be more adverse with the prolonged feeding of high-I diets; for example, hatch of fertile eggs was reduced to 40.0% compared with 82.5% for controls after 12 d of feeding 2500 mg I/kg diet. However, after 45 d hatchability was down to zero (Arrington *et al.* 1967). All hatchability variables were normalised soon after the high-I diets were withdrawn. These findings concur with a significant reduction in hatchability and increased embryonic mortality in turkey hens fed 350 mg I/kg diet (Christensen & Ort, 1991), and with extended gestation periods, a lack of lactation, fewer young and reduced survival rates, but with no effect on corpora lutea, in rats fed dietary I concentrations of between 500 and 2500 mg/kg (Ammerman *et al.* 1964). In addition, extended parturition times, fewer young and reduced survival rates have also been observed in rabbits, despite apparently normal lactation, when diets containing between 250 and 1000 mg I/kg were fed (Arrington *et al.* 1965). In both of these mammalian experiments, normal reproduction and the ability to lactate (in rats) also returned after transfer to a normal diet.

In contrast to the findings for breeder hens, the feeding of a 5000 mg I/kg diet to WL males significantly reduced fertility through a 10-fold increase in the incidence of dead spermatozoa in the semen, but semen volume and the hatchability of fertile eggs (presumably from normally fed female fowls) were unaffected (Wilson & Rowland, 1970). In addition, signs of I toxicity were exhibited within 7–14 d of transfer to the diet, with birds having altered reflexes, vertigo and diarrhoea, but disappeared within 7 d of a return to a normal diet. Whereas this contrasts with the observations in female fowl, it is in agreement with the findings for immature cockerels.

Mechanism for effects on reproductive system

Similar numbers of ova within the ovarian hierarchy for in-lay and out-of-lay hens (Marcilese *et al.* 1968; Perry *et al.* 1990) indicate that the effect of excess I works downstream of hierarchal recruitment. One possibility is that I toxicity causes the ova to have a reduced uptake of yolk material (initially resulting in a reduction in egg weight), and that subsequently changes in the vitelline surface prevent progesterone production by the largest follicle, thus blocking the cue for the pre-ovulatory surge in luteinising hormone release (and so egg production ceases). Marcilese *et al.* (1968) suggested that follicular maturation ceases because the I uptake by the smaller and less well developed ova of high-I-fed birds reaches some threshold, probably about 7 mg per follicle, and atresia begins. Thyroid hormones can exert marked stimulatory and retardational influences on testicular and ovarian function (e.g. Dawson *et al.* 2001), and because of the major accumulation of I in the thyroid gland and its indispensable role in T_3 and T_4 synthesis, it is highly probable that the effects of excess I are primarily a consequence of changes in

thyroid hormone release (Wilson *et al.* 1968; Travnicek *et al.* 1999). The resumption of normal reproductivity when abnormal plasma thyroid hormone concentrations are rectified by a return to a conventional diet is consistent with this view. Contrary to this suggestion, Wilson & Rowland (1970) postulated that excess I, at least in male fowl, might act directly on gonadal cells. Whilst accepting the possibility of some disruption to progesterone production, these workers considered that the mechanism did not involve gonadotrophins.

Following the return to normal levels of I intake, the steady, but reduced, vitellogenesis that continued during the period of excess I ingestion and ovulatory inhibition temporarily results in larger than normal follicles being ovulated, and, as a consequence, a transient increase in egg size. When yolk synthesis is normalised, egg weight returns to normal (Fig. 5).

Body weight and feed intake

High concentrations of dietary I suppress body-weight gain in young meat-type chickens. Leach & Nesheim (1963) reported that concentrations of 537 and 1074 mg I/kg suppressed 14 d body weight by 21 and 42% respectively; May & Vardaman (1978) observed that body-weight gain was reduced by 3% in three of four comparisons when 500 mg I/kg diet was fed to male broilers between 22 and 57 d; female weight-gain was unaffected. In this latter experiment high dietary I had no effect on feed conversion efficiency in either sex. May (1976) also noted reduced body-weight gains when 5000 mg I/kg diet was given to broilers between 28 and 39 d of age. It is probable that reductions in body-weight gain are indirect consequences of suppression of thyroid hormone activity by excess dietary I and the consequential reduction in cellular oxidation. Diets supplemented with 200 mg KI (153 mg I)/kg reduced the production of T_4 in chickens (Wheeler & Hoffman, 1950), the addition of T_3 to broiler diets at 1 mg/kg was observed to reduce serum concentrations of T_4 to 0.4 of controls and to suppress growth (May, 1980), and body-weight gain was severely reduced in 3-month-old fowl following radiothyroidectomy at 7 d (Mellen & Wentworth, 1962).

At concentrations of ≤ 100 mg/kg, dietary I had no effect on body weight in laying hens (Perry *et al.* 1989; Yang *et al.* 2001), but 8 mg I/kg from desiccated thyroid and 160 mg I from NaI/kg caused a significant loss in body weight in laying hens (Asmundson *et al.* 1936). In contrast, when laying hens were given diets with ≥ 700 mg I/kg, body weight increased to become greater than in normally fed birds (Perry *et al.* 1990), but within 21 d of withdrawal of the high-I diet, body weight was similar to that of controls.

Diets with ≤ 100 mg I/kg have no effect upon feed intake (Perry *et al.* 1989; Yue & Kang 1995), but with diets containing >350 mg I/kg, excess I is associated with a reduction in consumption (Perry *et al.* 1990). However, within 21 d of a return to normal feed, feed intake returns to pre-I levels (Fig. 7). The effect on feed intake appears to be an indirect result of the effects of excess I on rate of lay and egg weight, because a regression of feed intake

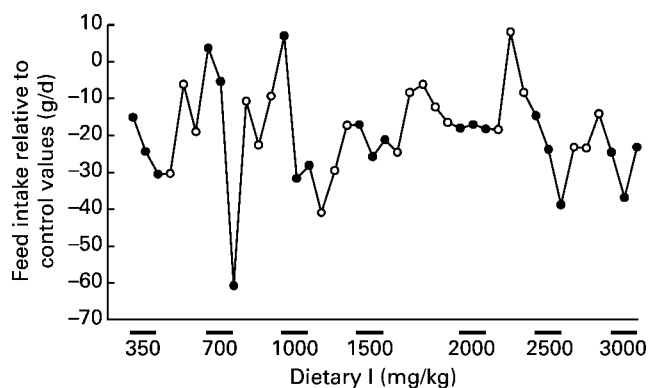


Fig. 7. Differences in mean daily feed intake, relative to normally fed controls, for hens given diets for 21 d periods with an iodine concentration of between 350 and 3000 mg/kg, and alternating with 21 d periods on normal feed. ●, Mean daily feed intake differences for 7 d periods whilst being given high-iodine diets; ○, difference when the experimental birds were given normal feed. (From GC Perry, PD Lewis and MJ Hanagan, unpublished results from the experiment reported by Perry *et al.* 1990.)

data for a brown-egg hybrid from Perry *et al.* (1989, 1990) on egg mass output (r^2 0.861, slope SE $7.4^{-0.2}$, $P < 0.0001$) showed that feed intake changes by 0.8 g/d for each 1 g change in egg output (Fig. 8). The abrupt decrease in egg production, through an inhibition of ovulation in individual birds, and increases in body weight despite a decrease in feed intake, clearly indicate that egg output is influencing feed intake and not *vice versa*.

Physiological and biochemical changes

Yolk iodine

Although the majority of ingested I accumulates in the thyroid gland, up to 15% may also be deposited in the ovary (Pena *et al.* 1967); this phenomenon has been identified as a useful method to enhance the I content of eggs for consumer benefit (Ishikawa & Kamimae, 1980; Kaufmann *et al.* 1998). Accumulated quantities have been reported to vary with dietary concentrations of I, period of excess-I provision, source of I and genotype. The rate of deposition and peak values also seem to be dependant upon dietary I concentration (Marcilese *et al.* 1968). In contrast to the

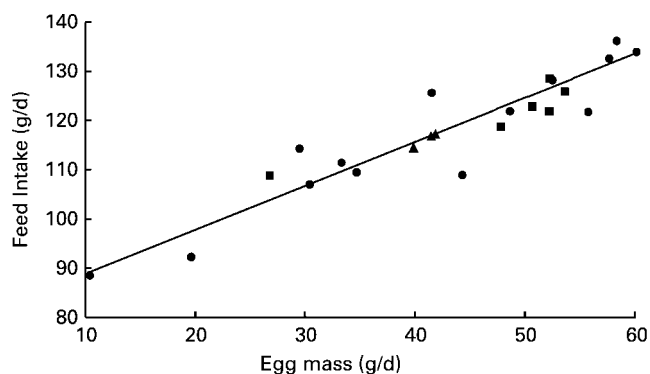


Fig. 8. Regression of mean daily feed intake (g) on mean daily egg mass output (g) for hens fed various concentrations of dietary iodine. (From Perry *et al.* 1989 (■) and 1990 (●), and Yue & Kang, 1995 (▲), adjusted by least squares for differences between a trial mean and the mean value of Perry *et al.* (1990).)

effects of excess I on egg production, body weight and feed intake, Table 1 shows that significant depositions in the yolk can occur at relatively moderate excesses of dietary I (Wilder *et al.* 1933; Asmundson *et al.* 1936; Kan *et al.* 1995; Yue & Kang, 1995; Rys *et al.* 1997; Kaufmann *et al.* 1998; Kroupova *et al.* 1998, 1999; Cao *et al.* 1999; Travnicek *et al.* 1999; Yang *et al.* 2001). The optimum dietary I concentration required to produce an I-enriched egg will obviously depend on the definition of, and the reason for, I enhancement. Ishikawa & Kamimae (1980) considered that a concentration of 7 mg iodinated amino acids/kg egg (about 0.4 mg I per egg) was the minimum for the cure and prevention of hypercholesterolaemia in a human subject eating one egg per d. Kroupova *et al.* (1999) considered that the provision of 3.5 mg I/kg diet was optimal for the production of I-enriched eggs. Ishikawa & Kamimae (1980), however, suggested that the minimum dietary $\text{Ca}(\text{IO}_3)_2$ inclusion necessary for the hen to produce the desired egg was about 230 mg (150 mg I)/kg, and that only $\text{Ca}(\text{IO}_3)_2$ should be used as the I source. At substantially higher concentrations of dietary I than these, Marcilese *et al.* (1968) observed a linear rise in yolk-I content, from initially negligible quantities to about 3 mg within 10 d of administering the equivalent of a 1000 mg I/kg diet by daily intra-oesophageal intubation of NaI solution, and a rise to 7 mg after 8 d of administering the equivalent of a 5000 mg I/kg diet. It is evident that 7 mg must be about the maximum possible egg-I content, because ovulatory inhibition occurs soon after a 5000 mg I/kg diet is introduced, and egg production ceases. Indeed, Marcilese *et al.* (1968) suggested that this concentration (about 110 mg I/kg) might be the threshold of follicular I content beyond which development stops and atresia begins. However, the amount of egg-I declines equally rapidly when birds are returned to normal feed (Wilder *et al.* 1933; Marcilese *et al.* 1968). When excess-I diets are fed for extended periods (>10 weeks), but at levels that do not inhibit ovulation, the yolk content peaks at about 3 mg before progressively declining, but to a level that is still greater than that of eggs laid by normally fed birds; the decline, Travnicek *et al.* (2000) suggested, was probably due to some homeorhetic mechanism, such as decreased absorption.

Plasma or serum iodine

Not surprisingly, the consumption of high-I diets elevates blood-I concentration. May (1976) and May & Vardaman (1978), using various I concentrations between 0.3 and 5000.0 mg/kg, recorded significant increases in serum I concentration in male and female broilers. Cao *et al.* (1999) fed diets containing 50 and 100 mg I/kg to laying hens for 56 d, and observed plasma I rise by factors of 1.35 and 2.01 respectively; Travnicek *et al.* (2000) fed diets containing 3.5 and 11.0 mg I/kg for 74 d and recorded peaks of 4.9 and 6.5 mg/l.

Yolk cholesterol

Ishikawa & Kamimae (1980) stated that feeding diets supplemented with 230 mg $\text{Ca}(\text{IO}_3)_2$ (150 mg I)/kg would

Table 1. Effect of various iodine sources, fed at various concentrations and for various periods, on the iodine content of the yolk

Reference	Source	Dietary I concentration (mg/kg)	Period of treatment (d)	Yolk I content (mg per egg)
Wilder <i>et al.</i> (1933)	Natural sources	–	28	0.006
	Kelp*	20	28	0.454
	Iodised linseed*	20	28	0.441
	KI*	20	28	0.527
	Iodised linseed*	50	+28	0.857
	KI*	50	+28	1.010
Asmundson <i>et al.</i> (1936)	Natural sources	0.5	42	≤0.003
	Oyster shell	2.5	42	0.042
	Desiccated thyroid†	8	42	0.126
	Iodosalicylic acid	8	42	0.125
	Nal	80	42	1.300
	Iodosalicylic acid	8	140	0.010
	Nal	8	140	0.095
	Natural sources	0.5	42	0.010
	KI	14	42	0.125
	KIO ₃	14	42	0.130
	Iodosalicylic acid	14	42	0.030
	Diiodotyrosine	14	42	0.030
	Iodised olive oil	14	42	0.025
	Desiccated thyroid	14	42	0.030
	Marcilese <i>et al.</i> (1968)	Nal solution	1000	10
Nal solution		5000	8	7
Ishikawa & Kamimae (1980)	Ca(IO ₃) ₂	> 150	10	0.6‡
Yue & Kang (1995)	Unknown	> 65	Unknown	SR
Kan <i>et al.</i> (1995)	Unknown	> 225	42	> 0.3
Rys <i>et al.</i> (1997)	Cal	2.7 and 7.2	Unknown	SR
	Kelp	2.0 and 4.4	Unknown	SR
Kaufmann <i>et al.</i> (1998)	KIO ₃	0.5 and 5.0	14	SR
	Seaweed	2.5 and 4.9	14	SR
Kroupova <i>et al.</i> (1998)	Unknown	0.3	74	0.14§
	Unknown	7 then 15	0–34, 34–74	1.41§
Cao <i>et al.</i> (1999)	Unknown	50	56	× 14 increase
	Unknown	100	56	× 18 increase
Kroupova <i>et al.</i> (1999)	KI	0.3	Within 21	0.17
	KI	0.3–0.7	Within 21	SR
	KI	15	Within 21	2.58
Travnicek <i>et al.</i> (1999)	KI	0.3	74	0.14§
	KI	3.5	74	0.29§
	KI	10	74	0.64§
	KI	15	74	1.77§
Yang <i>et al.</i> (2001)	Unknown	35	30	× 9 increase
	Unknown	70	30	× 12 increase

SR, significant rise from initial values.

* Dietary concentration calculated assuming a feed intake of 100 g/d.

† 1.74 g I/kg.

‡ Iodinated amino acids.

§ 'mg/kg' data calculated assuming a mean egg weight of 60 g, so 16.7 eggs weigh 1 kg.

enhance the iodinated amino acid content of eggs, and that the consumption of one of these eggs per d would both prevent and cure hypercholesterolaemia. Although the cholesterol content of the egg was unaffected, it was claimed the egg would have an iodinated amino acid (monoiodohistidine, diiodohistidine, monoiodotyrosine, diiodotyrosine, triiodothyronine and tetraiodothyronine) concentration of at least 7.0 mg I/kg, yielding about 0.6 mg I per egg after 10 d of feeding the special diet. Brown (1988) reported that a feed additive based on kelp, a seaweed high in I, and containing added vitamins and minerals would achieve the aims described earlier at an inclusion rate of 20 g/kg in a layer diet. Perry *et al.* (1989, 1990) confirmed that egg cholesterol concentrations were generally not significantly affected by feeding high-I diets of between 100 and 3000 mg/kg, but that absolute quantities of cholesterol were related to egg weight. However, a multiple regression of egg weight and yolk-cholesterol content data from the

experiment reported by Perry *et al.* (1990) showed that cholesterol content was not only related to egg weight, but that it was also influenced by dietary I supplementation *per se* (regression slopes for normal and I-supplemented diets were not significantly different ($P=0.904$), but their elevations were ($P=0.0033$; GC Perry, PD Lewis and MJ Hanagan, unpublished results). Egg-cholesterol content increased by 3 mg per egg for each 1 g increase in egg weight, irrespective of dietary treatment (r^2 0.357, slope SE 0.63, $P<0.0001$), and for a given egg weight, birds fed a high-I diet had a 10 mg lower cholesterol content than normally fed controls (Fig. 9). Further analysis of the unpublished results from Perry *et al.* (1990) (GC Perry, PD Lewis and MJ Hanagan, unpublished results) showed that the differential in yolk-cholesterol deposition between normally fed controls and birds given high-I diets persisted even when the experimental birds were temporarily transferred back to normal feed for 21 d between

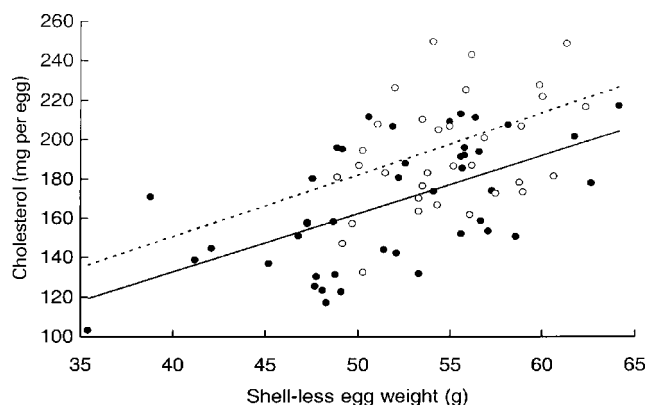


Fig. 9. Regression of egg cholesterol content v. egg weight for birds given diets with an added-iodine concentration ranging from 0 to 3000 mg/kg (●, —) and for controls maintained on normal feed (○, - - -). (From GC Perry, PD Lewis and MJ Hanagan, unpublished results from the experiment reported by Perry *et al.* 1990.)

dietary I treatments. A regression of egg-cholesterol concentration on egg weight, for normally fed controls and hens fed high-I diets, confirmed that the two factors were not significantly related.

Plasma cholesterol

Plasma cholesterol is elevated in laying hens when they are given high-I diets (Perry *et al.* 1989, 1990; Kroupova *et al.* 1998). A regression of data from Perry *et al.* (1989, 1990) showed that cholesterol concentration in the plasma increases by 0.3 mmol/l for each 100 mg/kg increment in dietary I concentration (Fig. 10). The equation for the regression was:

$$y = 3.74 + 0.00308I$$

$$(r^2 0.893, \text{ slope SE } 2.84 \cdot 10^{-4}, P < 0.0001),$$

where y is the plasma cholesterol concentration (mmol/l) and I is the dietary I concentration (mg/kg). The elevated plasma cholesterol concentrations may have been caused by changes in metabolism and intestinal cholesterol absorption. High dietary I modifies thyroid activity (Travnicek *et al.* 1999) and changes in plasma thyroid

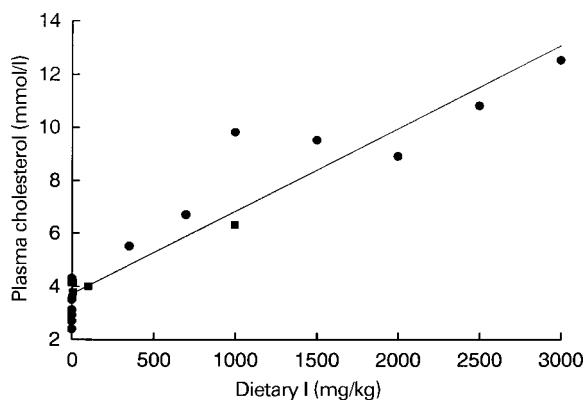


Fig. 10. Effect of dietary iodine concentration on plasma cholesterol concentration in hens after 21 d (Perry *et al.* 1990; ●) or 28 d (Perry *et al.* 1989; ■) of a high-iodine diet.

hormone concentrations have been reported to affect cholesterol biosynthesis in the rat through this mechanism (Mathe & Chevallier, 1976).

Plasma calcium

The provision of 5000 mg I/kg diet to WL pullets, but in combination with a grossly inadequate dietary Ca concentration of 0.5 g/kg, resulted in a virtual cessation of egg laying and an increase in serum Ca that within 14 d was 1.4 times that of a diet containing 30 g Ca/kg, and 2.3 times that of birds given a 0.5 g Ca/kg ration without added I (Roland *et al.* 1977). This occurred despite a 40% reduction in daily feed intake for the experimental group. The markedly depressed intake of a minimal dietary Ca concentration diet suggests that, at very high concentrations of I, Ca is still being mobilised from the skeleton for shell formation, and this despite the absence of an egg in the uterus because of the ovulatory inhibition. The non-use of Ca for shelling presumably leads to the elevated concentrations of Ca in plasma.

Enzymes

The reduction in yolk synthesis by the liver occurring at high intakes of I is accompanied by an elevation in hepatic levels of alanine aminotransferase and aspartate aminotransferase (Yue & Kang, 1995). The effects on plasma concentrations of superoxide dismutase are unclear, with Yue & Kang (1995) recording a significant increase at dietary I levels of 65 and 130 mg/kg, but Yang *et al.* (2001) observing no change following 30 d feeding of 35 and 70 mg I/kg diets. It is not known how long the high-I diets were fed by Yue & Kang (1995), so it is possible that the contradiction in these two findings is due to a difference in treatment period. There was no effect on plasma concentrations of glutamic-pyruvic transaminase or glutamic-oxaloacetic transaminase after 30 d of high-I feeding (Yang *et al.* 2001), but there were indications that increased I concentration elevates alkaline phosphatase (Yue & Kang, 1995; Yang *et al.* 2001).

Blood cells

Moderate excesses of dietary I (3.5–15.0 mg/kg) were reported to significantly decrease phagocytic heterophil activity and the phagocytic index, but only when plasma I concentration exceeded 4.8 mg/l, suggesting that the excess I concentration directly inhibits leucocyte activity (Travnicek *et al.* 2000). The relative increase in heterophilic, compared with lymphocytic, activity was thought to be due to an infiltration of lymphocytes into the thyroid gland, a process similar to that occurring with spontaneous autoimmune thyroiditis. An autoimmune response, concurrent with feeding 15 mg I/kg diet, was also considered to be the cause of an increase in the γ -globulin concentration from 6.4 to 13.2 g/l. Increases in γ -globulin were also recorded by Kroupova *et al.* (1998) at dietary I concentrations of >7 mg/kg, but haemoglobin content decreased after feeding diets >15 mg/kg for 40 d subsequent to a 34 d period on a 7 mg/kg diet.

Anti-microbial properties

I is an efficient disinfectant of water at concentrations as low as 0.1 µg/l (Gershenfeld & Witlin, 1950). A concentration of 15 µg/l in drinking water over a 34-week period was shown to improve egg production in laying hens by 1.06, whilst the performance of hens provided with filtered water was no different from control birds given plain water (Babu *et al.* 1994). In contrast, the addition of 500 mg I/kg to a broiler finisher diet between 22 and 57 d neither prevented the suppression of body gain following an artificial infection of *Mycoplasma synoviae*, nor reduced the incidence of carcass downgrades (May & Vardaman, 1978). Unexpectedly, the incidence of mortality tended to be higher for birds given the high-I diet than for normally fed controls.

Source of iodine

The evidence that the source of I is important seems to be equivocal. Data for comparisons of seaweed with dietary Ca(IO₃)₂ (Perry *et al.* 1989) and KIO₃ (Kaufmann *et al.* 1998) suggest that the responses of laying hens to these three sources are similar. In addition, Wilder *et al.* (1933) did not believe that there were any differences among kelp, iodinated linseed and KI in their efficiency of I transfer into the yolk. Ishikawa & Kamimae (1980), however, claimed that when diets containing >230 mg Ca(IO₃)₂ (150 mg I)/kg were given, there was an increase, rather than a decrease, in rate of lay when KI was used as the supplement. Several papers have reported adverse reproductive responses to KI supplementation (Perdomo *et al.* 1966; Arrington *et al.* 1967; Wilson *et al.* 1968; Wilson & Rowland, 1970; Wilson & Harms, 1972), but inclusion levels in these trials were markedly higher (usually ≥2500 mg I/kg) than those used by Ishikawa & Kamimae (1980). Asmundson *et al.* (1936) concluded that whereas egg production, body weight and feed intake were not significantly affected by I sourced from diiodotyrosine, iodised olive oil, iodosalicylic acid, kelp, oyster shell, KIO₃, KI and NaI (concentrations in Table 1), the provision of NaI at 160 mg/kg diet and the administration of desiccated thyroid at 0.8 mg/d would elicit a drop in feed intake, a loss in body weight and cessation of egg-laying. Presumably, the effects of the desiccated thyroid were a consequence of its T₃ and T₄ contents as well as its I content; the loss in body weight was in agreement with the findings of Hutt (1930) and Asmundson (1931). Asmundson *et al.* (1936) also concluded that the deposition of I into the yolk depended on both the source and the concentration of I. Rys *et al.* (1997) reported that I sourced from kelp (2.0 and 4.4 mg I/kg) was transferred into the egg more efficiently than from CaI₂ (2.7 and 7.2 mg I/kg).

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