HEREDITARY HYPOTHYROIDISM IN THE DOMESTIC FOWL

R. K. COLE

Department of Poultry Husbandry, Cornell University Agricultural Experiment Station, Ithaca, New York

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POPULATIONS of fully pedigreed chickens often contain individuals which deviate considerably in one or more respects from the average for the flock. When pedigrees reveal close genetic relationship among those similarly affected, further studies are warranted. Such was the case for the trait now recognized as hypothyroidism. Affected 5½-month old White Leghorn pullets, which were somewhat smaller in skeletal size than normal, possessed long silky feathers, and were rather obese, began to lay before there was a development in size and redness of the comb. Reported egg production by two such birds had to be witnessed in person by the author before he would believe!

The fact that the few such individuals all came from one of three strains and that they often were half- or full-sisters prompted a study to determine the role of heredity in the development of this trait.

Individuals with similar phenotype have now been observed in several other unrelated stocks. It is apparent that the trait may be more common than at first believed but, because of the associated defects in normal physiology, affected individuals rarely survive to reach the age of maturity.

Review of pertinent literature: As far as the author knows, no similar trait has been described in chickens or other species, save possibly man. The most obvious deviation from normal phenotype is the obesity which is especially pronounced during the period of from 8 to 16 weeks of age. Obesity of hereditary origin has been described in mice, rats, and dogs, and is obvious in man. Obese (*ob ob*) (INGALLS, DICKIE and SNELL 1950) and adipose (*ad ad*) (FALCONER and ISAACSON 1959) are simple Mendelian recessive traits but nonallelic, while the inheritance of the New Zealand obese mice (BIELSCHOWSKY and BIELSCHOWSKY 1956) is not a simple Mendelian type. The *ob ob* and New Zealand obese traits are associated with hyperglycemia and hyperinsulinism but differ in some respects, including reproduction and general activity. The famous yellow mouse of CUÉNOT (1905), a heterozygote, A^YA, is also characterized by obesity (DANFORTH 1927); the homozygote, A^YA^Y, being the first known genetic lethal. The fatty mutation in rats, *fa fa* (ZUCKER and ZUCKER 1961), is associated with abnormal lipid metabolism, while obesity in MAYER's Shetland Sheepdogs (1954) may be associated with disturbed hypothalamic functioning. In all these cases the obese individuals are heavier than the normals and in most cases, if not all, the thyroid gland is essentially normal. (The obese chicken, on the other hand, is definitely smaller in size than its normal siblings if measured in terms of body weight, and even more so if skeletal size rather than body weight is considered.)

A hereditary type of dwarfism in the fowl was described by LANDAUER (1929) with genetic evidence for its inheritance as a simple Mendelian recessive provided by UPP (1934) who included some of WARREN's data. Rhode Island Red dwarfs, possibly of similar origin, were also studied by PAYNE (1944). In LANDAUER's case the thyroids were enlarged, while in PAYNE's birds they were small, and in both instances with little or no colloid. In these cases no special mention

was made of obesity, while the earlier recognition of the dwarfing and the effects on the skeleton were stressed. In the absence of detailed studies of the thyroid gland, and at different periods during the chick's growth, it is not possible to say definitely whether this dwarfism is the same as our hypothyroidism, but they are probably not, although abnormal thyroid activity is present in both conditions.

FRASER (1964) has reviewed the genetical aspects of thyroid disease in humans. In addition to infantile hypothyroidism associated with congenital absence of the thyroid gland, there are at least five types of sporadic goiterous cretinism. These are associated with errors of thyroxine synthesis and are believed to be inherited as recessive Mendelian traits. Nongoiterous sporadic cretinism may be associated with aplasia of the thyroid gland or with its failure to descend from the embryonic lingual region. Damage to the thyroid, caused by auto-immunity (HASHIMOTO's disease), shows definite familial incidence. In fact, HALL, OWEN and SMART (1960) suggest, from their data on the presence of circulating thyroid antibodies in relatives of individuals affected with thyroid disease, that the development of antithyroid antibodies is a simple dominant trait.

Description of the Trait

Phenotypic expression: The typical hypothyroid-obese chicken, as first recognized at 6 to 10 weeks of age, is slightly smaller than normal and shows a rather silky plumage, which is especially obvious at that time on the face and head region. The birds are plump and soft and have a very pliable skin. They appear normal, save for the accumulation of fat, supported by a skeleton that is rather light in structure. They have a quiet disposition and are sensitive to low temperature after the syndrome has become well established. These traits are also observed following thyroidectomy.

In most birds, the trait (hereafter called obesity) can be definitely recognized at 6 to 8 weeks of age. Within 2 to 4 weeks of the initial recognition, the expression of the syndrome, as indicated by the accumulation of fat and changes in structure of the developing feathers, will increase in most cases and, thereafter, often remain static during the entire growing period. In some cases only a mild degree of obesity is observed and this may subsequently disappear.

The structure of the chick feathers of the first coat is normal, as expected, for thyroid tissue and hence thyroxine production is normal, or nearly so, during the period these feathers are developing. With the first juvenile molt, starting at 8 ± weeks and being completed by the 13th week, feather structure indicates a deficiency of thyroxine. On the basis of histopathology of the thyroid glands at the age these feathers are developing, one would expect the changes, as observed. At maturity, the syndrome is less marked in some birds. This is especially true for feather structure. Perhaps improved thyroxine secretion, although still abnormal, is adequate to support normal feather development at that age. Frequently the plumage which develops at the first annual molt is essentially normal or nearly so.

All feathers are affected but the remiges and rectrices considerably less so than other contour feathers. Not only are the feathers abnormal in structure, but they continue to grow in length. Consequently those from the body and ventral portion of the femoral pterylae often touch the ground. In the male, the saddle and sickle feathers are extremely long. (Figures 1 and 2).

The mature female will lay before there is obvious growth of comb or redness of the comb and facial region. In the case of the male, comb development and coloration, though somewhat delayed, are approximately normal.

Males are clearly less severely affected than females. They show a lower incidence and those affected are more apt to recover. However, selection intensified the syndrome as well as the indicidence in both sexes. Even some that are severely affected at 10 weeks of age become nearly normal in appearance at 20 to 24 weeks of age, although perhaps a little small in body size.

Even after several generations of selection there is considerable variation in phenotypic ex-

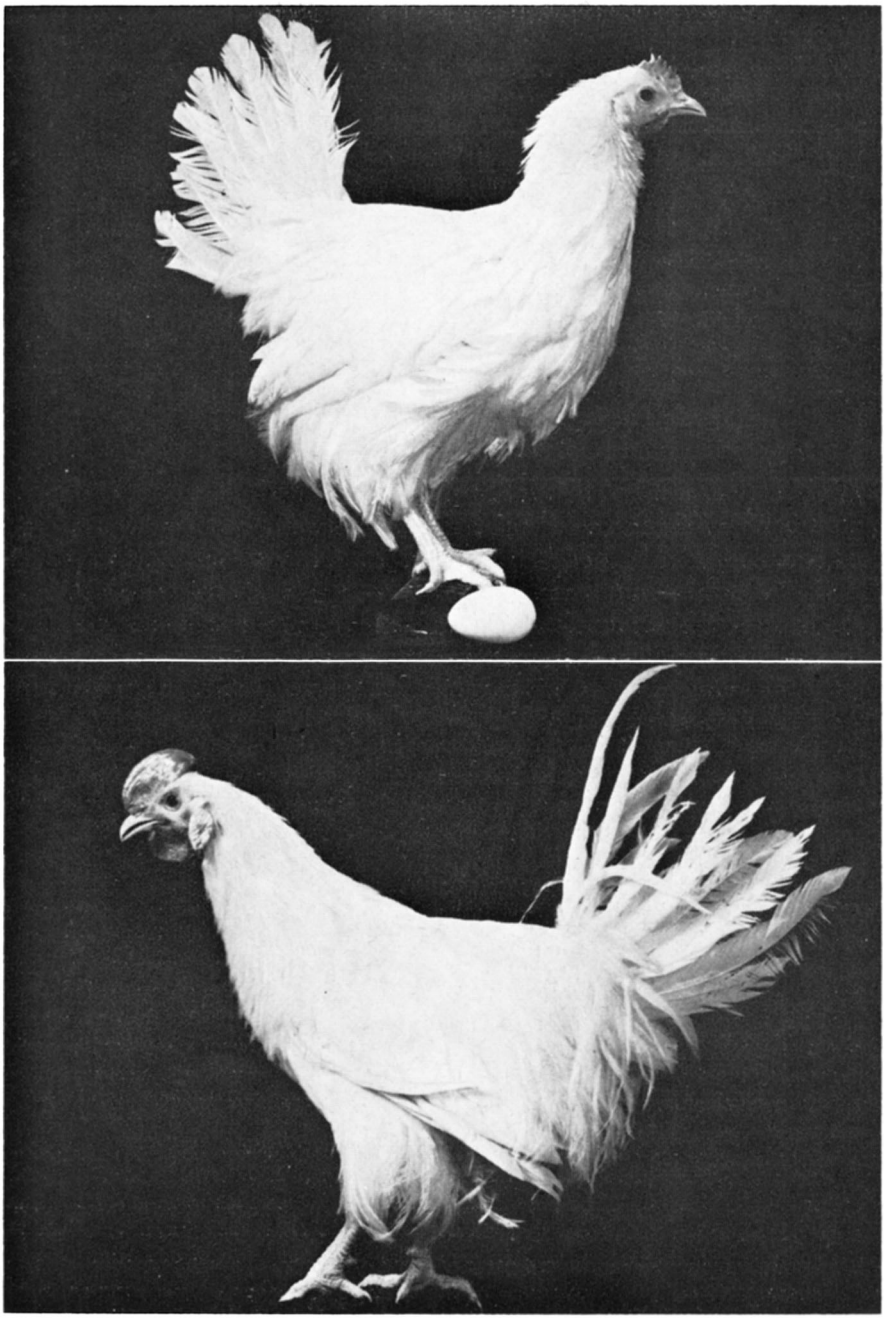

FIGURE 1.—Hypothyroid-obese pullet, 6 months of age and laying. The contour feathers, especially those from the femoral and crural pterylae, are long and silky. The comb and wattles are very small (and lacking in red color) for a laying female of the S.C. White Leghorn breed. FIGURE 2.—Hypothyroid-obese cockerel, 6 months of age, comb and wattles partially removed earlier. The contour feathers, especially those from the saddle region, are excessively long and silky. The remiges are much elongated, extending well behind the body.

pression of the trait. Although some birds appear normal, their thyroids are abnormal. It is obvious, however, that in such birds an adequate amount of thyroxine is being produced in spite of defects in the thyroid glands.

Post-mortem findings: Aside from the reduction in body size, light-weight skeleton, and accumulation of subcutaneous and abdominal fat, the most striking defect is found in the thyroid glands. These are much smaller than normal and, if present, tend to be flat and elongated or spindle-shaped. In some cases only one or no gland can be found. In a great majority of the cases the rudimentary remains of the thyroids are to be found in their normal location, suggesting that the apparent lack of one or both glands represents extremes rather than the possibility that they have failed to descend from the lingual region of the developing embryo. Birds which recover well enough to lay have enlarged and elongated thyroids containing follicles large enough to be seen with the naked eye. They appear to be filled with amber-colored fluid.

Regardless of age at time of autopsy, birds showing more pronounced symptoms will usually have thyroids that are smaller and that show greater deviations from normal microscopic structure. The milder symptoms in the males are associated with a more normal size, appearance, and structure of their thyroids.

The thyroid glands: The thyroids are normal in size when the chick hatches. Limited data suggest that at two weeks of age, or even before, the thyroids are larger than those from normal chicks. Although quite variable, the average size at 6 to 8 weeks of age is less than for glands from normal chicks. However, thyroid weight *per se* is very misleading because varying proportions of the glands are not thyroid follicles but invading tissues. In some cases, especially of the smaller "glands," thyroid follicles are quite rare.

At hatching the thyroids are also essentially normal in microscopic structure. The time of onset and the extent of the pathological changes that soon appear in the thyroid vary from bird to bird, but to a very much lesser extent between the two glands within the same individual. A description of these changes has been presented previously (VAN TIENHOVEN and COLE 1962).

Basically, two types of changes appear to be under way at the same time. One is an invasion by lymphoid-type cells which are often so numerous as to dominate the microscopic structure of the gland. Secondly, there is evidence of some proliferation of thyroid epithelium. Within established follicles the epithelium may be thrown up in folds. Elsewhere, cell-cords of epithelial-like cells appear and may even displace existing follicles. This situation is similar to that in man known as lymphadenoid goiter or Hashimoto's disease. The proliferation of epithelial-like cells may be a response to an increased production of TSH by the thyrotrophs of the pituitary gland. Histological changes in the pituitary of obese birds support such an interpretation (VAN TIENHOVEN and COLE 1962).

In older birds that survive and lay, the thyroids may actually be enlarged. They consist of a relatively few very large colloid-containing follicles. The epithelium is low, as if stretched out by the expanding content of the follicle. Small conglomerations of small-sized follicles, but containing no colloid, lie between the large follicles. They are similar to the masses of epithelial-cell cords seen in younger birds but are better organized to resemble gland structures. Occasionally there are areas of lymphoid-type cells in the interfollicular spaces. However, these do not present a picture of intense activity as seen in the younger birds.

Normal-appearing individuals from the obese stock often show similar, but less severe, alteration in thyroid structure. Thus the frequency of the syndrome, as measured by the phenotypic appearance of the living bird, is obviously a minimum estimate.

Selection for Hypothyroidism or Obesity

Starting with a few (20) obese females, including several pairs of full sisters,

that segregated out of the populations of the Cornell C strain, hatched in 1955, 1956, and 1957, matings were initially made to sires known to have produced affected offspring. Less than half of these obese females reproduced. Subsequently sons and daughters of obese dams were used as breeders and eventually, as the number of obese individuals increased, matings were limited to those showing well developed symptoms of hypothyroidism. The data for these matings and the results are shown in Table 1.

The method of selecting breeders gradually evolved as the population increased in size, eventually (1960) permitting selection based upon the incidence of the syndrome within full-sib families in addition to selection within families for the

TABLE 1

Phenotype and bases for selection of breeders and matings employed to develop the obese-hypothyroid stock, with incidence of obesity among offspring

	Sires			Dams			Incidence of obesity among offspring			
							Male		Female	
Year	No.	Phenotype	Selection	No.	Phenotype	Selection	No.*	%	No.*	%
1955–57	.	(C-strain matings, no selection for obesity)					450	0	3200	0.6
1956	2	Normal	Sire of an obese pullet	2	Obese (from C strain)		9	0	14	21
1957	1	Normal	Sire of an obese pullet	2	Obese	Phenotype	5	0	11	9
1957	(1)	Normal	Sire of an obese pullet	3	Normal	Daughter of obese dam	9	0	9	11
1957–58	6	Normal	Son of an obese dam	10	Obese (from C strain)		52	4	56	11
1957–58	(4)	Normal	Son of an obese dam	4	Obese	Phenotype	13	0	12	17
1957–58	(6)	Normal	Son of an obese dam	21	Normal	Daughter of obese dam	141	1	157	8
1959	2	Obese	Phenotype	25	Obese†	Phenotype	121	18	127	72
1959	(1)	Obese	Phenotype	4	Normal	Daughter of obese dam	29	17	28	64
1959	1	Normal	Son of an obese dam	9	Obese†	Phenotype	94	9	118	41
1960	(1)	Obese	Progeny test	10	Obese	Family‡	75	32	99	80
1960	1	Obese	Family‡	9	Obese	Progeny test	46	19	35	86
1960	3	Obese	Family‡	24	Obese	Family‡	213	24	221	61
1961	5	Obese	Family‡	60	Obese	Family‡	313	50	357	81
1962	4	Obese	Family‡	50	Obese	Family‡	376	67	328	88
1963	5	Obese	Family‡	67	Obese	Family‡	493	76	498	83
Outcross										
1962	(4)	Obese	Family‡	7	Normal	Unrelated to Strain C	68	6	65	6
Backcross										
1963	(5)	Obese	Family‡	10	Normal	F_1	83	23	79	42

* Number of birds classified.
† Includes a few obese females from the C strain.
‡ Individual phenotype *but only* from sibships showing high incidence.
( ) Males used in other matings, of the same or previous year.

degree of expression of the trait. In one year (1960) the use of progeny-tested breeders resulted in a marked increase in incidence of the obesity.

The incidence of obesity was raised from less than 1% to over 80% in females and from 0 to over 75% in males (Figure 3). Along with the increase in incidence, there was also an increase in the average degree of expression of the trait as well as an earlier appearance. Matings of obese × obese (possible for the first time in 1959) yielded a higher incidence than did those of obese × normal segregates. Progress was further enhanced when affected breeders were selected on a basis of family rather than solely on individual phenotype.

The fact that the trait also appeared in a low percentage of an outcross generation showed that the genes involved are not completely recessive. Backcross of the normal F_1 females to obese males resulted in a significant increase in incidence in both sexes. The levels in the backcross generation are not different from those of essentially similar type matings in 1959—(one parent obese and the other a normal offspring from an affected parent)—when the levels were 45 and 11% for females and males, respectively.

Nothing would be gained by attempting to assign a genetic basis for the syndrome. The trait is obviously hereditary and polygenic. It is expressed somewhat

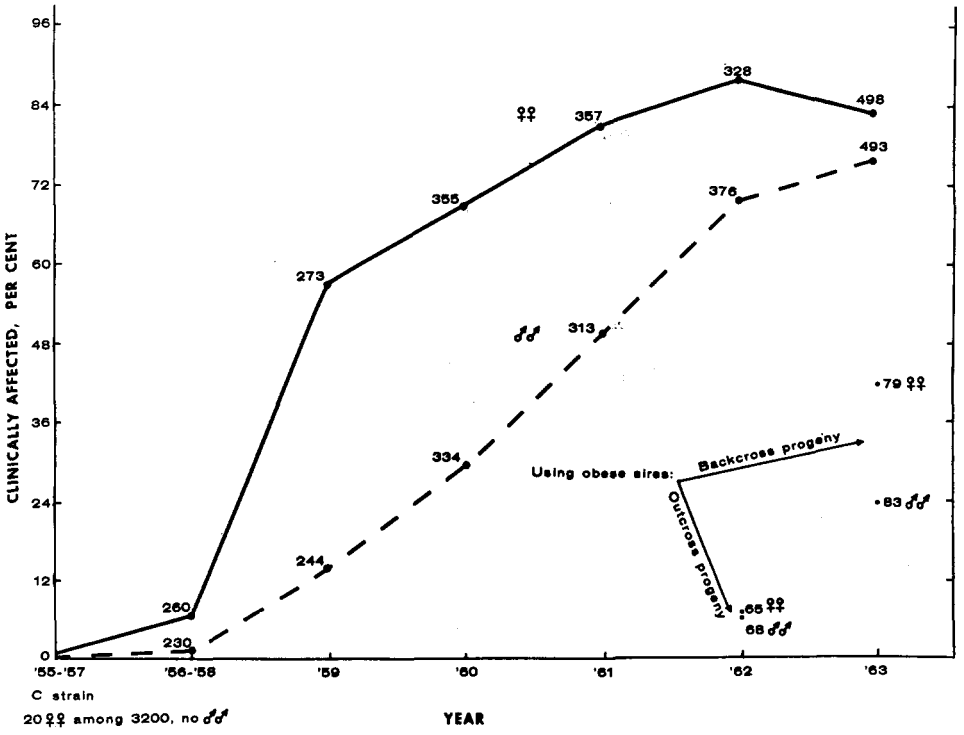

FIGURE 3.—The effect of selection on the frequency of obesity within the C strain of White Leghorns. The difference between the sexes has become less after several generations of selection. The outcross and backcross progenies are discussed in the text. The numeral indicates the number of individuals classified to determine the specific point on the graph.

more frequently and to a more pronounced degree in females than in males. Considerable variation in individual and family expression still exists after several generations of selection.

Other Effects of Hypothyroidism

Body size: Body weights of more than 200 chicks were taken at weekly intervals from the 2nd through the 8th week and at the 10th week. Individuals subsequently classified for the syndrome as severely (++), moderately (+), or nonaffected (−) showed only minor differences in average body weight at five weeks of age (Table 2). Thereafter the relative rate of growth declined for those birds which subsequently developed a severe degree of obesity (Figure 4).

Although the moderately affected individuals grew at a slightly slower rate than did those not affected, data for both groups, within sex, are combined in Figure 4.

Body weights for 484 females at 26 weeks of age are given in Table 3. Females severely affected, and especially so at an early age, made poorer growth. A greater proportion of them did not lay by six months of age. Affected pullets that did lay weighed approximately 300 grams more than did non-layers which had shown the same degree of obesity. The difference was due in part to physiological changes associated with egg production. Within the groups, classified as "not laying" or as "laying," there was a consistent increase in body weight as the degree of obesity became less. Those few birds which showed little or no evidence of the syndrome had reasonably good body weight at 6 months of age.

TABLE 2

Body weights at 5 weeks of age for chicks showing different degrees of obesity when classified at 14 weeks

	Females		Males	
Degree affected	No.	Weight	No.	Weight
++	98	279 g	35	308 g
+	17	302 g	24	315 g
—	5	290 g	33	320 g

TABLE 3

Body weights, in grams, with standard errors, of obese females at 6 to 6½ months of age, in relation to degree of obesity and sexual maturity

Classification for obesity at		Not laying		Laying	
10 wks	14–16 wks	No.	Weight	No.	Weight
++	++	215	904±166	88	1286±170
— or +	++	30	1000±184	42	1302±140
— or +	+	31	1175±176	41	1415±175
— or +	—*	8	1585±194	29	1648±155

* Pullets free of symptoms at 16 weeks were discarded in 1961.
Data are from populations hatched in 1961 and 1962.

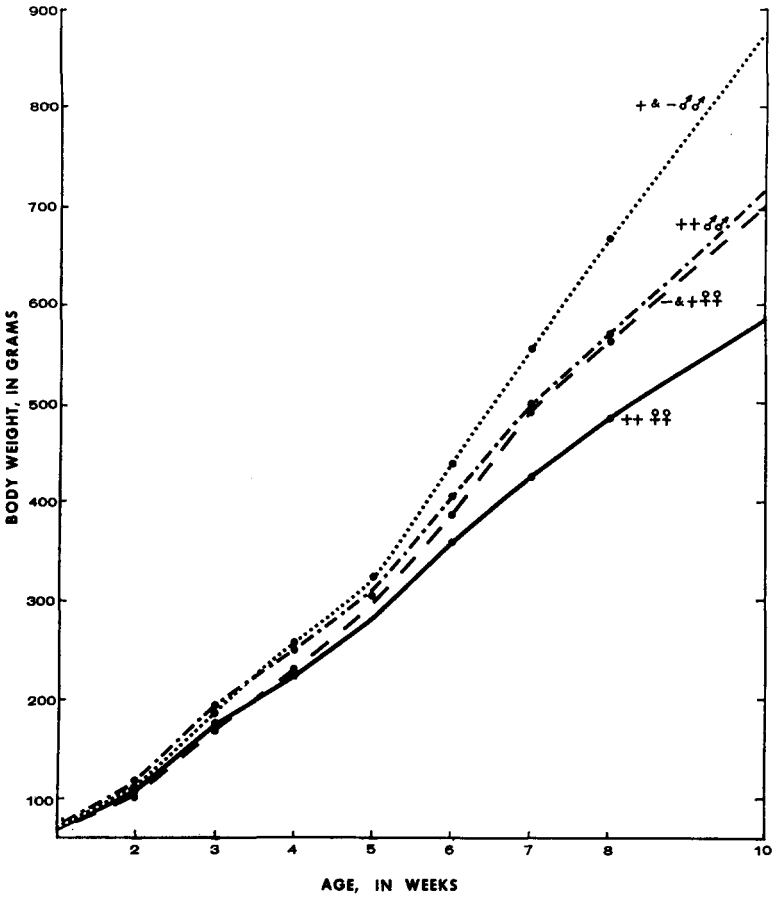

FIGURE 4.—The effect of the hypothyroid-obese syndrome on growth is not obvious until after 5 weeks of age. Thereafter growth is less rapid for birds subsequently classified (14 weeks) as severely affected (++). See Table 1 and the text.

Differences in body weight do not reflect true differences in body size. Females severely affected (++) possess many grams of fat in the abdomen, subcutaneous areas, and elsewhere. During the first few months of egg production there is usually a loss or at least no change in body weight rather than the expected gain of 10 to 12%. Data for normal controls (of Strain C) for a 4-year period, 1950 through 1953, show a body weight at first egg of 1758 g and a gain of 206 g during the first 3 months of production.

During the development of the obese stock the size of the bird, as well as the degree of obesity, might have led to selection for small size, apart from other manifestations of the syndrome. The small size of the birds of the obese stock could, therefore, be a consequence of an unintentional bias in the selection procedure. The fact that this did not occur is shown by the following comparisons of the weights of a few obese segregates, from matings of Strain C in 1962, with the average weight of their normal laying-sisters.

Sex	Weight, g	Normal full-sisters* 150–170 days of age	
		No.	Average weight, g
F	960	6	1581
F	1150	3	1770
F*	1170	2	1765
M	1250	5	1498

* Laying.

The weights of the normal sisters are typical for White Leghorns at the age given.

Sexual maturity: A majority of the obese pullets are delayed in maturity and some will not commence laying without supplementary thyroxine (supplied as iodinated casein, known as Protamone). Among 196 pullets classified at 10 weeks in 1961, the proportion of the normal and only moderately affected birds (78) that subsequently laid eggs by 7½ months was 65%, but the corresponding figure for the 118 pullets showing extreme obesity was only 37%.

Egg production: (a) 1959 population:—Among the obese females, varying from 260 to 380 days of age, remaining in early January, 1960, there were 16 that had not laid. They had been housed in heated pens, but not provided with extra light. When transferred to heated and lighted quarters, half of them were fed Protamone (0.22 g per kilogram of an all-mash breeder diet). Each of the eight on Protamone laid within 21 days, while only five of those on the non-supplemented diet did so. Obviously, the lack of previous egg production was caused in part by inadequate length of day (light). Egg production by most birds not given Protamone was, however, poor and sporadic during the 115 days on test. The seven pullets that survived laid an average of only 18 eggs. In sharp contrast, the eight pullets on Protamone ranged from 37 to 74 eggs, and averaged 54.9.

(b) 1961 population:—Seventy-two nonlaying obese pullets, 230 to 240 days old, were selected to provide, insofar as possible, pairs of full sisters of similar body weights, and transferred December 19th to cages (2 per cage) and given 14 hours of light per day. One of each pair (total 36 pullets), was fed on all-mash laying diet containing Protamone at the rate of 0.22 g per kilogram of diet. The others served as controls. As in 1960, some in both groups began to lay promptly, even within 7 days for one bird in each group. In less than four weeks, 32 of the 35 on Protamone (one of the original 36 had died from an accident) began to lay, and the other three did so within 14 weeks. Among the 36 controls, only 14 laid within four weeks while 14 others had not laid by June 14th, and two others had died in March without laying. Because the birds were housed two per cage, individual records of egg production are not available; but the rate of laying during the 165-day period, January 1st to mid-June, was 47% for birds on Protamone, while only 17% for their controls. All birds on Protamone were laying sometime during the first half of June. Fewer than one half (14) of the surviving controls (33) laid during this period.

On June 15, the controls still in good health were further divided and half were

TABLE 4

Effect of supplementary thyroxine on egg production by obese hens during a 45-day test period

Previous status*	On thyroxine			Controls		
	No. of hens	Eggs, number		No. of hens	Eggs, number	
		Average	Range		Average	Range
Never laid	7	19.4	10–34	6	0	–
Poor layers	2	18.5	17–20	3	1	0–3
Better layers	7	32.1	28–35	7	25.4	10–38

* Period of 165 days, as explained in text.

given supplementary thyroxine, as Protamone, for the first time. The subsequent performance by these birds during a 45-day test is shown in Table 4.

These data clearly indicate that some of the obese females can lay eggs only when thyroxine-like substances are provided. It is obvious also that some "hypothyroid-obese" birds can produce sufficient thyroxine to permit fair egg production, but that this can, in many cases, be improved with supplemental hormone of thyroxine type. The natural production of thyroxine is apparently adequate for maximum egg production by some obese-stock hens, although during the growing period they showed clinical evidence of severe hypothyroidism (obesity and feather structure).

Egg size: The reduction in egg size does not approach that in body weight. The obese females lay eggs that are of quite good size and shell texture. This tendency may be enhanced, in part, by the relatively poor rate of lay by most obese hens, even those on Protamone.

Egg size was determined for obese birds on Protamone and for their controls (obese birds not fed Protamone) over a 9-day period in mid-April, 1962, when they were approximately one year of age (Table 5). The nonobese controls of Strain C were hatched the same year while body and egg weights were recorded 3 to 4 weeks earlier, but at approximately the same age. The 64 obese hens used in 1963 were the breeders used to reproduce the stock in that year.

Body size of the obese hens was reduced by approximately 36% but egg size

TABLE 5

Weight of eggs laid by obese females, approximately 12 months of age

	No. of hens	Egg weight, g		(Egg wt./body wt.) × 100
		Average	Range	
1962				
Obese, on Protamone*	32	53.5	48.0–59.2	4.85
Obese, no Protamone	11	54.0	49.8–58.2	4.38
Controls, of Strain C	679	58.8	48.0–69.0	3.21
1963				
Obese, on Protamone†	64	55.8	49.0–65.6	4.33

* 0.22 g per kg of diet.
† 0.11 g per kg of diet.

was reduced by only 7 to 8%, when compared to comparable hens of Strain C from which the obese stock had been derived. The higher level of Protamone (0.22 g) caused the laying obese hens to lose much of their accumulated fat, but had no effect on egg size, and this is reflected by the higher egg weight : body weight ratio.

Reproduction: The obese stock was derived from a flock (Cornell C-resistant strain) already relatively inbred. Moreover, the five sires and 43 dams used in 1960 included male GG 5016, his three sons, and 30 daughters. In 1961, all five sires were grandsons of GG 5016, and of the 60 dams 15 were his daughters and 28 were his granddaughters. In spite of all this inbreeding, fertility and hatchability have both been very good.

During four breeding seasons, 1960 to 1963, 18 young sires were tested by natural matings with pullets approximately 11 months of age. During the last three seasons all the breeding birds received Protamone.

Year	No. of sires	Fertility	Hatchability
1960	3	85.1%	77.4%
1961	5	90.0%	81.4%
1962	4(+1)	92.9%	88.3%
1963	5	91.0%	85.7%

With the exception of one young sire, which was completely infertile in 1962, all have shown good fertility (60 to 98%) and good hatchability (73 to 95% of fertile eggs). The effect of the hypothyroidism on reproduction, if any exists, is thus overcome by the use of Protamone, while the restriction of the size of the breeding population, with the resulting inbreeding, has not led to low hatchability.

Effects of the Thyroid-Stimulating Hormone

The reduced size of the thyroids in most individuals of the obese stock, as recorded during the period of 6 to 12 weeks of age, suggested that the physiological defect might lie in a low level of available thyrotrophin (TSH).

Matings of three sires and 36 dams, selected on the basis of previous progeny tests for obesity, were used to provide obese pullet chicks for the test of supplemental TSH. Armour's Thytropar was injected intramuscularly, daily, for a period of 8 weeks at the rate of approximately 0.4 international units of TSH per kilogram of body weight. Samples of five pullets each were sacrificed at hatching, and at 1, 2, 4, 6 and 8 weeks of age. Control chicks from stock believed to be free of the syndrome were injected with normal saline solution.

The data on thyroid weights (Table 6) show that the TSH was able to stimulate the thyroids of at least some of the obese chicks, with gland weights as large as 261 mg at 4 weeks. Three of the ten chicks sampled at 6 or 8 weeks had thyroid glands weighing 163 to 192 mg. By 8 weeks, and in spite of the TSH, three of the five treated chicks had thyroids that weighed only 6.2 to 14.9 mg. Clearly, in some cases, if not all, the thyroids can initially be stimulated by TSH, and just as clearly the presence of TSH cannot prevent the thyroids in other pullets from undergoing the changes that result in the hypothyroid-obese syndrome.

TABLE 6

Effect of TSH on the weights of thyroids from obese pullets, five birds per group

Age	Obese stock		Controls
	TSH	Saline	Saline
1 day	5.9 ± 1.3 mg		4.8 ± 0.8 mg
1 week	11.2 ± 1.4	10.6 ± 2.5	8.3 ± 2.6
2 weeks	24.8 ± 5.4	25.0 ± 1.5	12.4 ± 1.3
4 weeks	82.7 ± 100.1	38.9 ± 7.4	30.2 ± 6.0
6 weeks	113.4 ± 71.6	32.2 ± 23.3	40.7 ± 9.1
8 weeks	44.6 ± 66.4	62.8 ± 53.4	75.9 ± 21.4

At 6 weeks of age only one of the five TSH-injected pullets showed clinical evidence of obesity compared to four of the five that received only saline. By 8 weeks, however, only one from each group of five was free of symptoms and both of these had rather large thyroids.

SUMMARY

The frequency of a hypothyroidism in a strain of White Leghorn fowls was increased by selective breeding to a level exceeding 80% in females and 75% in males. Females, on the average, are more severely affected than are males.—The trait, first recognizable in the living bird at 6 to 8 weeks of age, is characterized by obesity, silky and elongated feathers, a subsequent marked reduction in rate of growth, and often a delayed sexual maturity, or none, in the pullets. Pathological changes in the thyroid glands, consisting of infiltration of lymphoid cells and proliferation of cords of epithelial-like cells, commence as early as the second week of age, are progressive, and result in considerable destruction of the thyroid. Some recovery in gland structure and functioning may occur later, with corresponding changes in phenotypic appearance and physiology of the bird. Supplemental thyroid-stimulating hormone will not maintain the integrity of the thyroid gland. Supplemental thyroxine, administered in the diet as iodinated casein (Protamone), will compensate for the low level or absence of endogenous thyroxine. The obese birds lay eggs of good size and reproduce well when iodinated casein is supplied in the diet.—The results of six generations of selective breeding, together with outcrosses and backcrosses, indicate that the inheritance of the hypothyroidism is polygenic and that some of the causative genes must be dominant. Even after six generations of selection, considerable variation was still found in the expression of the syndrome. It ranged from those so severely affected that iodinated casein (or thyroxine) is required for egg production to those with normal phenotype. Many of the latter, however, do show pathological changes in their thyroids.

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