THE PATHOGENESIS OF DEFICIENCY DISEASE.

No. X. THE EFFECTS OF SOME FOOD DEFICIENCIES AND EXCESSES ON THE THYROID GLAND.

BY

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I PROPOSE in this report to summarize the observations I have hitherto made with respect to the influence of imperfect and ill-balanced foods on the thyroid apparatus. In it are included certain experiments dealing with the effects of overfeeding.

The dietaries employed in these researches group themselves, with respect to their influence on the thyroid gland, into two categories: (1) those inducing a diminution in its size and weight, and (2) those inducing an increase in its size and weight.

Inanition leads to marked atrophy of the thyroid gland in pigeons. The average weight of both thyroids per kilo of original body-weight was 59 mgs., as compared with 85 mgs. in healthy controls. Histologically the vesicles may be shrunken into various shapes and partially emptied of colloid, their size reduced and the intervesicular tissue relatively increased in amount.

A.—DIETARIES INDUCING A DIMINUTION IN SIZE OF THE THYROID.

1. *An exclusive diet of autoclaved milled rice.*—This diet is deficient in all classes of vitamines, in suitable protein, in fats and in salts, while it is excessively rich in starch. It is possible also that the high temperature of the autoclave destroys other food elements requisite for perfect nutrition. There is in such a dietary a shortage of roughage.

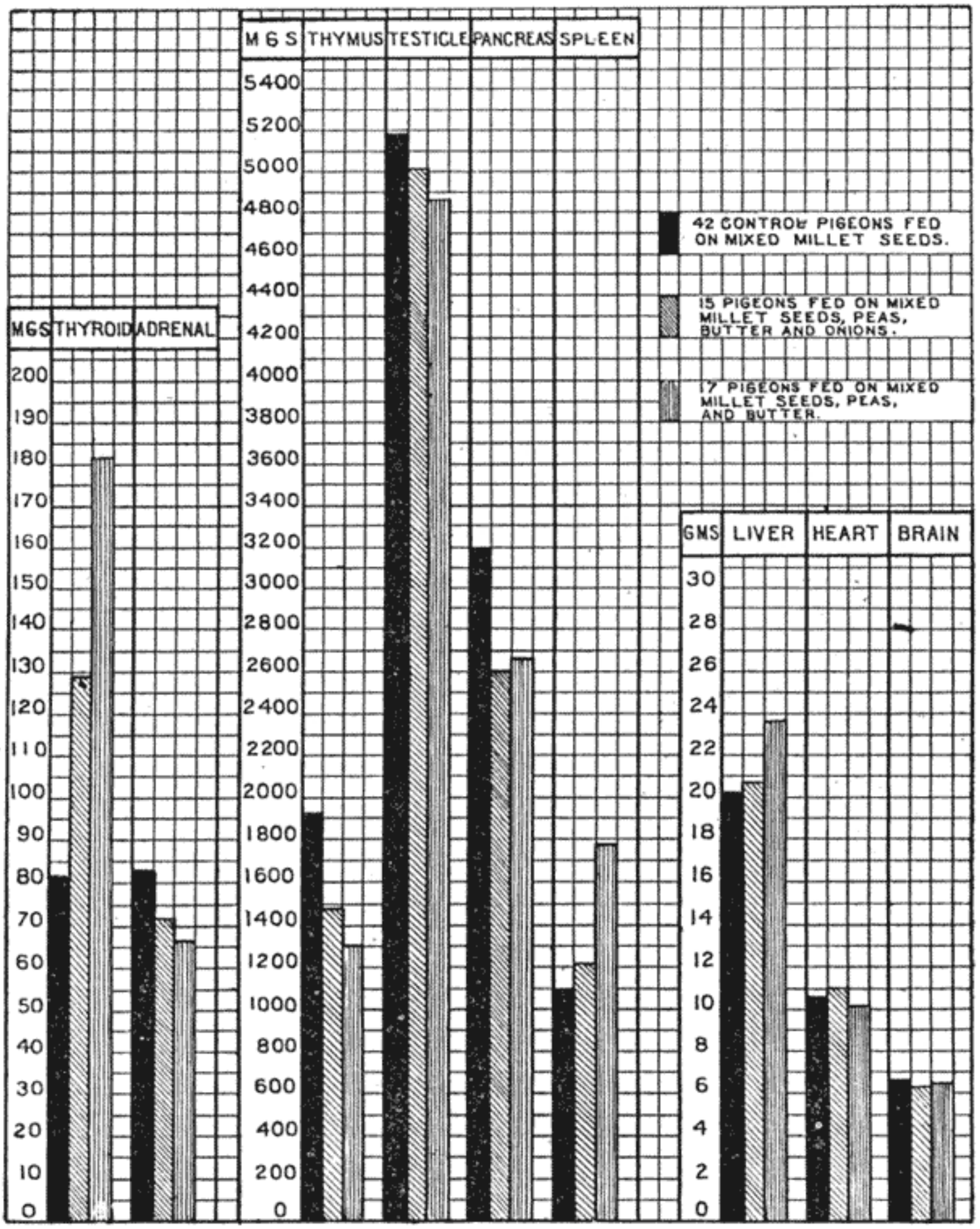

Fig. 1.—Chart showing average weight of organs per kilo of body-weight in control pigeons and in over-fed pigeons. Note the effect of onions in controlling the enlargement of the thyroid, spleen and liver. The smaller size of the adrenals and possibly also the smaller size of the pancreas in butter-fed pigeons is related to the excess of fats in the food. The variations in size of the thymus and testicles in over-fed birds is too small to admit of any conclusions. In view of the causation of "goitre-heart" it is to be noted that no enlargement of the heart is associated with the thyroid hyperplasia in these experiments. The pituitary (not included in the Chart) tends to be reduced in weight in over-fed birds.

Its effects on the thyroid gland were studied in thirty-three pigeons and in twelve monkeys (*macacus sinicus*). It gives rise in both species to a moderate degree of atrophy. In one experiment in pigeons the average weight of both thyroids per kilo of original body-weight was 75·9 mgs. as compared with 85·1 mgs. in healthy controls. In monkeys the diminution in weight of the organ is not so marked, owing no doubt to the short time these animals survive an exclusive dietary of autoclaved rice. The thyroid glands in both species presented the same varying

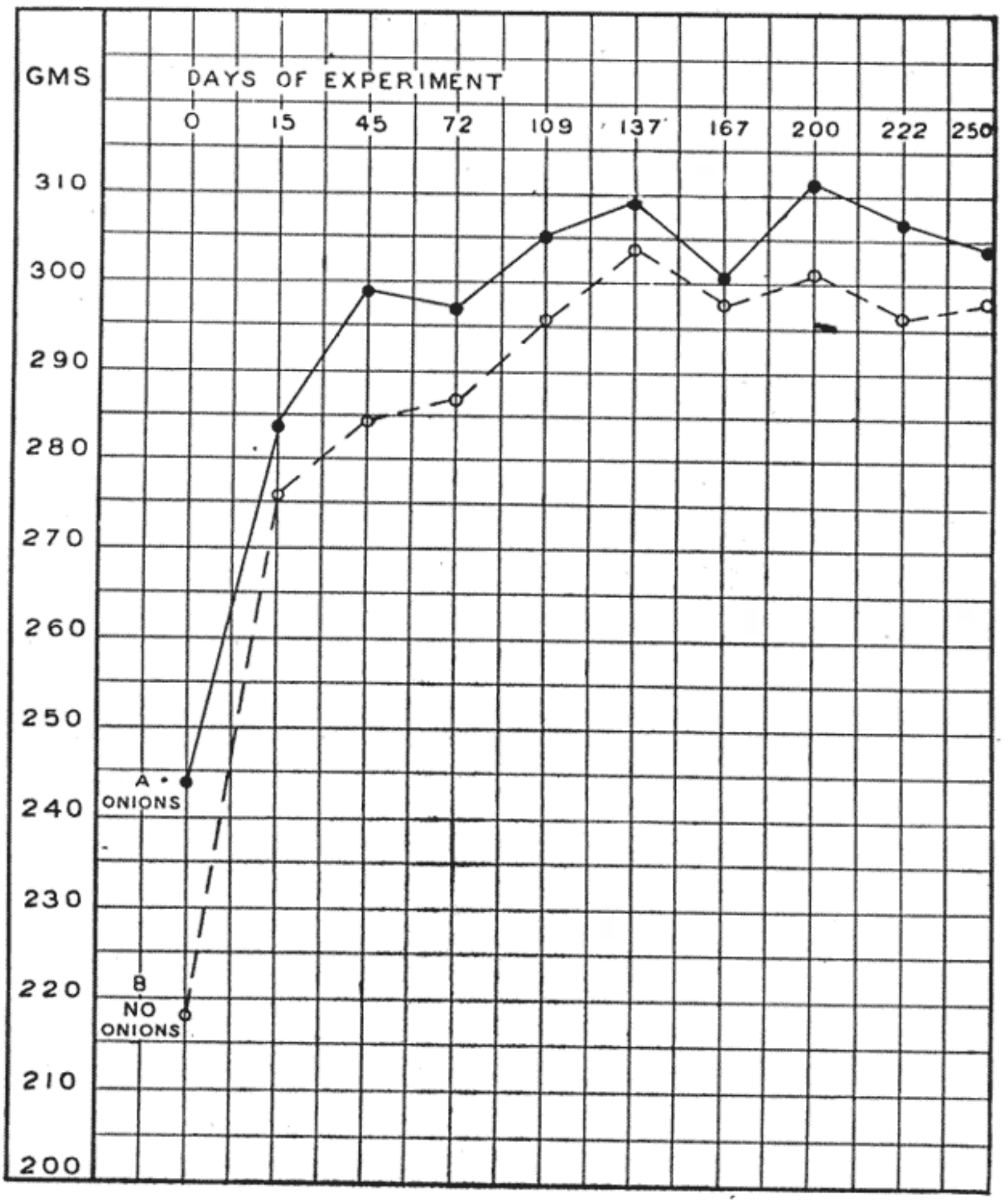

Fig. 2.—Chart showing monthly average weights of two series of pigeons—
(A) Fed on mixed grains with butter and onions.
(B) On the same diet, but without onions.

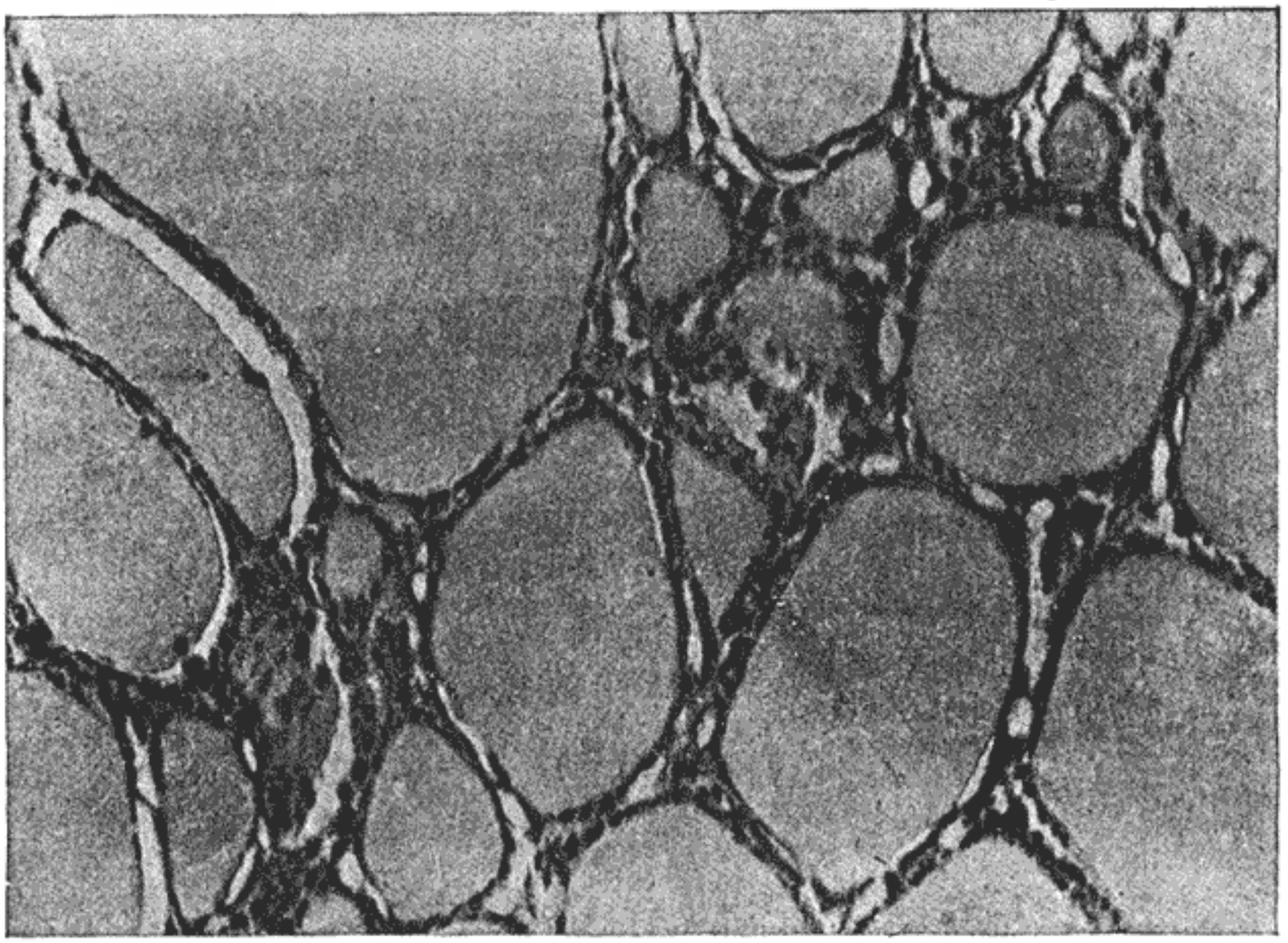

Fig. 3.—Colloid gland, not enlarged, from monkey fed on autoclaved rice. A similar histological picture was seen in 35% of controls. × 265.

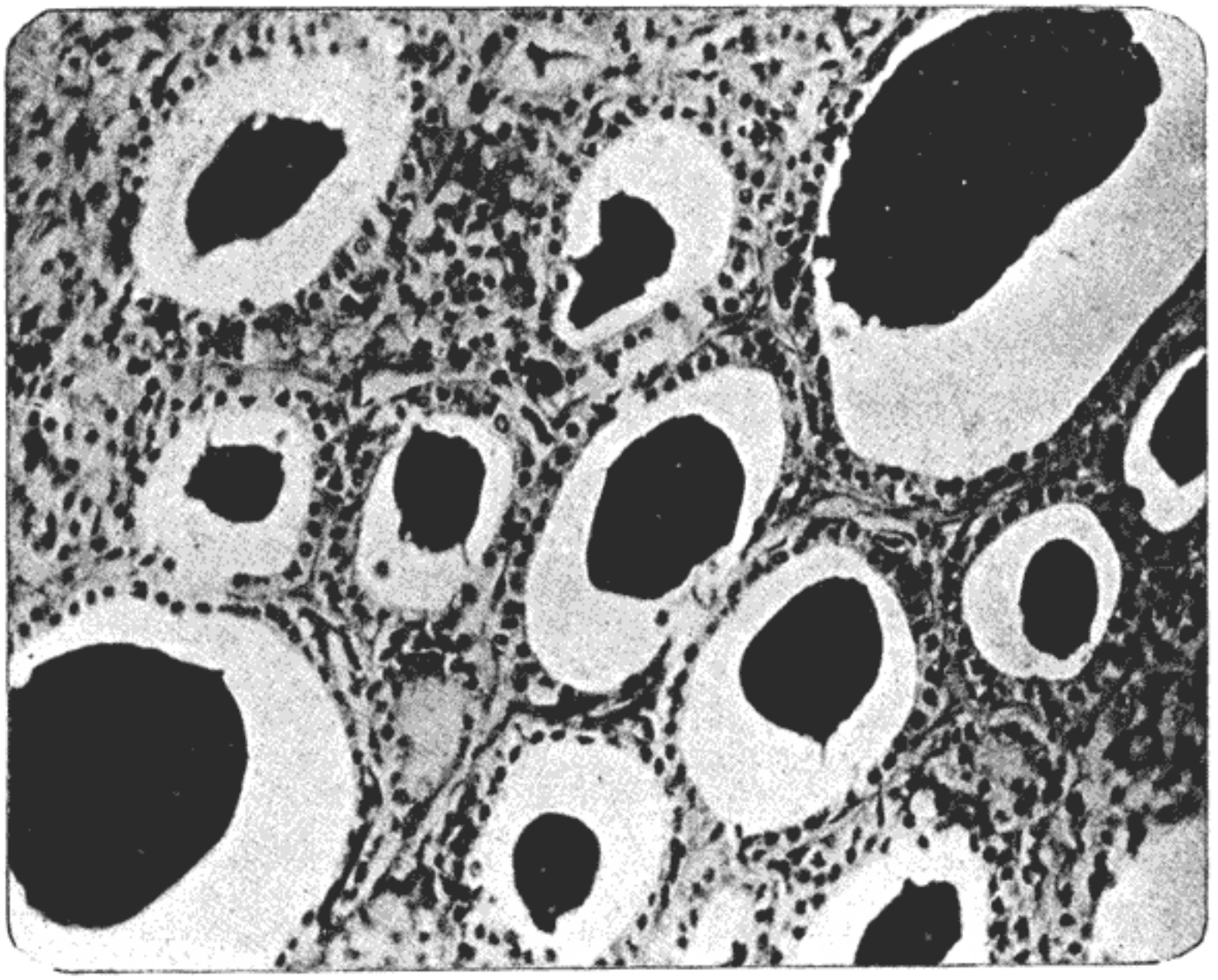

Fig. 4.—Thyroid gland, not enlarged, from monkey fed on autoclaved food, butter and onions. Note proportion of intervesicular tissue to acini. × 265. A similar histological picture was seen in several control animals.

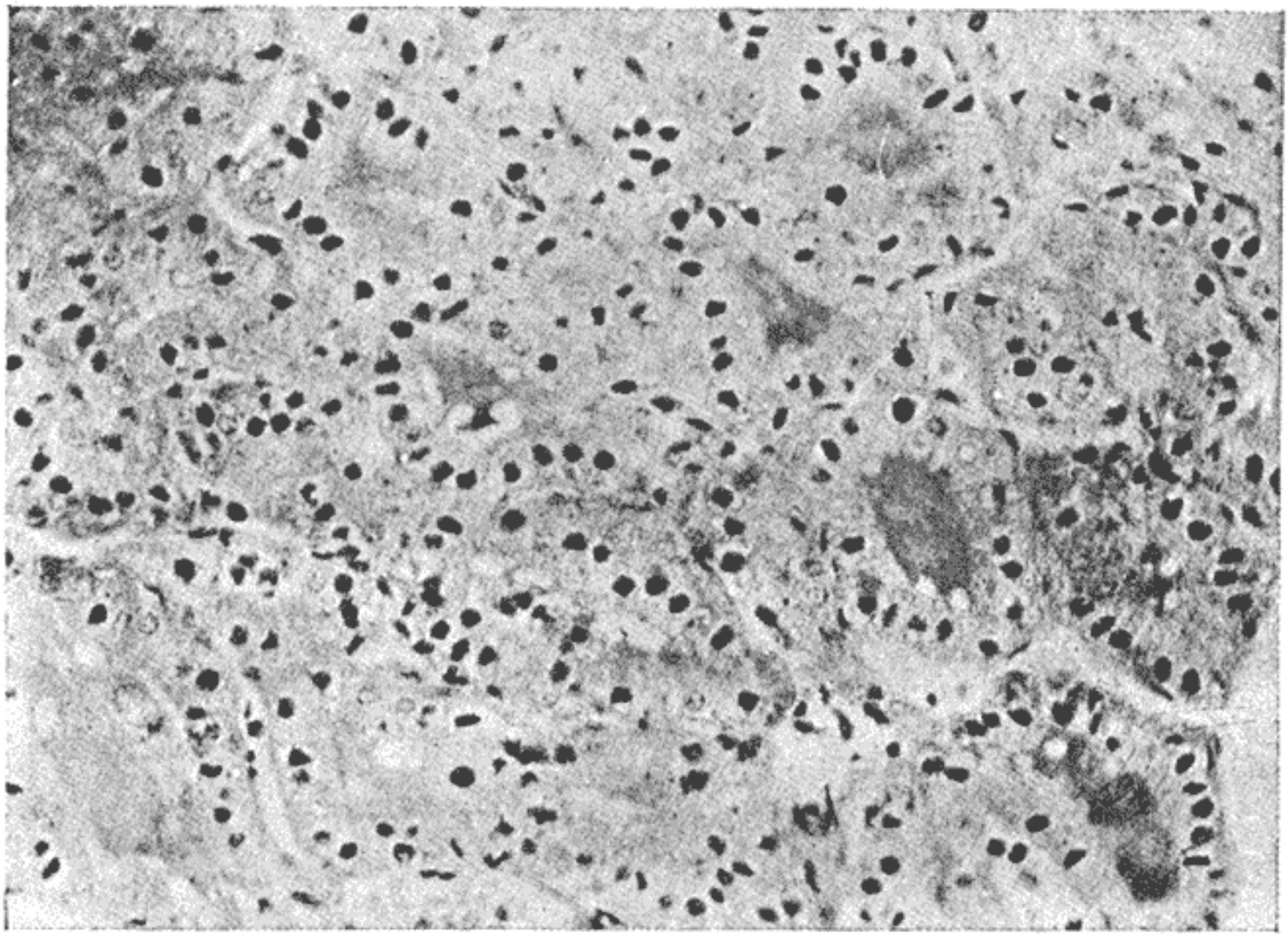

Fig. 5.—Normal actively secreting thyroid from a control monkey. Note increase in height of acinar cells, vacuolation and absorption of colloid. × 265.

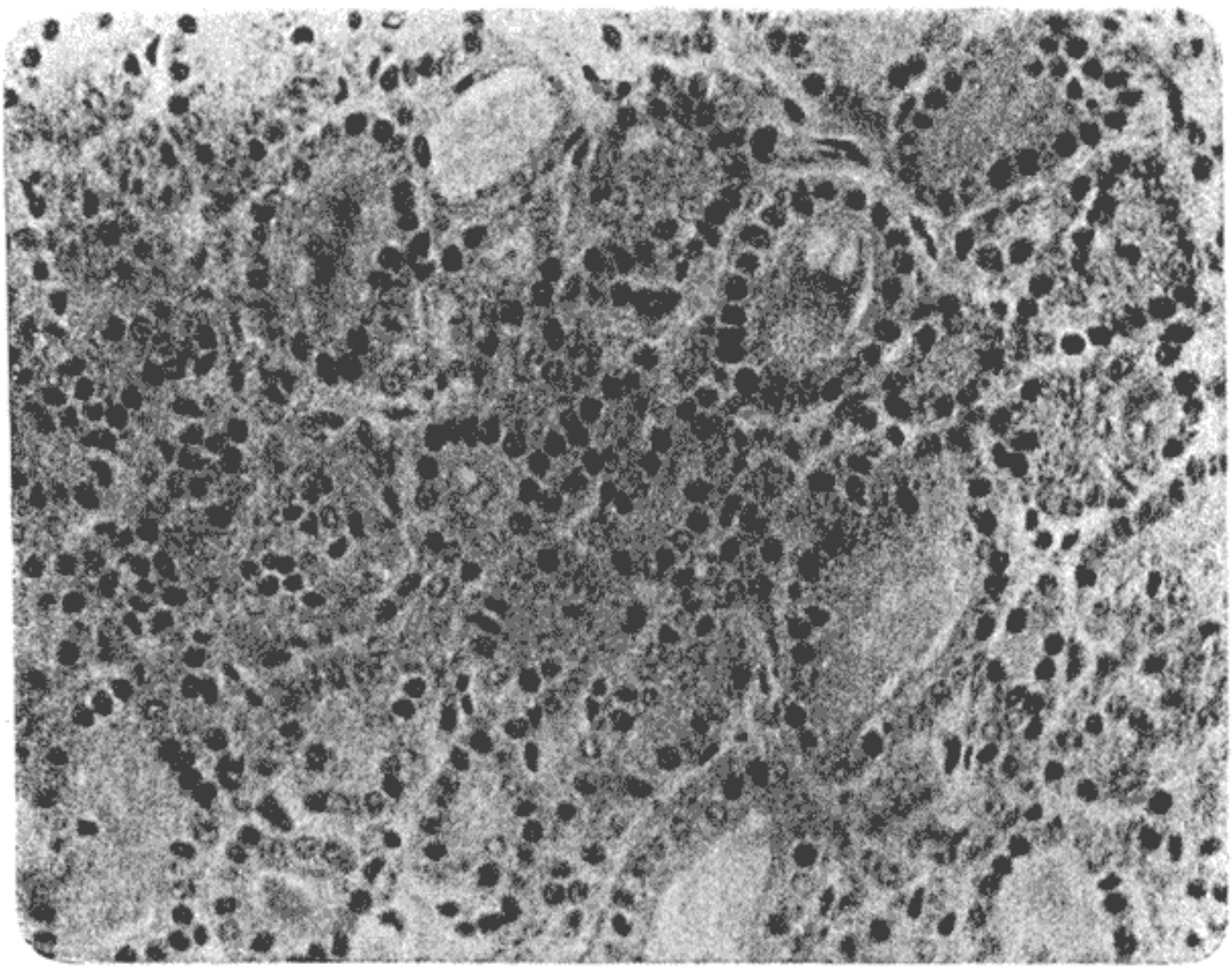

Fig. 6.—Non-enlarged thyroid from a monkey fed on autoclaved food and onion. Note increase in height of acinar cells, increased number of nuclei (Compare fig. 5), vacuolation of colloid and small size of many vesicles. × 265.

histological pictures seen in health (Figs. 3 & 4), colloid glands ([1]) preponderating. The evidences of pathological change were comparatively slight and limited to congestion (Fig. 9) and to a greater proportion of cells showing evidence of necrobiosis. Congestion was not present in all cases; the number so affected in monkeys was five out of twelve. The most notable pathological appearance was found in animals presenting hæmic infections, a not infrequent consequence of this dietary. Then the organ showed marked congestion, desquamation of acinar epithelium, varying degrees of necrosis of parenchyma cells, and complete or partial disappearance of colloid.

2. *A diet of autoclaved rice and butter.*—This diet is deficient in vitamines of the 'B' and 'C' classes and in roughage; it is also excessively rich in starch and in fat. Its effects were studied in four monkeys. The degree of atrophy was considerable having regard to the rapidity with which the animals died (fifteen days) ([2]). The average weight of the organ was 73 mgs. per kilo of original body-weight, as compared with 83 mgs. in healthy controls. It may here be noted that the amount of thyroid tissue as estimated by weight is the same in healthy pigeons and in healthy monkeys (*macacus sinicus*). In all four cases in this category the glands were of the colloid type (Figs. 3 & 4), or of a type showing a tendency to reversion from the colloid state (Fig. 10) ([1]). The vesicle walls consisted of a single layer of cuboidal epithelial cells; the acini contained a pale pink staining colloid in which a few vacuoles, indicating absorption of colloid, were present. In all cases, the periacinar capillaries were much distended (Fig. 9), each acinus being sharply outlined, in part of its circumference, by a capillary envelope of pink-staining blood corpuscles. The intervesicular parenchyma was very scanty, and necrobiosis of parenchyma cells was slight. The parathyroids in three cases, in which they were found in sections, were intensely congested (Fig. 10), and in one hæmorrhagic infiltration had caused disruption of the compact masses of polygonal cells composing the gland, and death of many of them. Similar changes in these organs have been encountered on one other occasion only in my experimental experience: in the parathyroids of new-born rats whose mothers were fed daily throughout pregnancy on anærobic cultures of fæcal bacteria ([3]). The cause of the hæmorrhagic infiltration of the parathyroids was probably the same in both instances. In the one, the micro-organisms, or their products, operated through the medium of the maternal blood, in the other, the deficient dietary caused such changes in the intestinal mucosa

as subjected the parathyroids to the noxious effects of micro-organisms or of their products, derived from the intestinal tract. It is remarkable that only in this category were the parathyroids found to be notably altered by morbid change. A point of considerable interest in this connexion is that the adrenal medulla of pigeons fed on this dietary was almost invariably intensely engorged and the adrenalin content subnormal.

3. *A diet of autoclaved rice, butter and onions.*—This diet is deficient in 'B' vitamine and excessively rich in fats and in starch. Its effects were studied in twenty-four pigeons. The atrophy of the thyroids was considerable, their average weight amounting to 69 mgs. per kilo of original body-weight, as compared with 88 mgs. in butter-fed controls. Histologically the glands presented appearances similar to those seen in the case of birds fed exclusively on autoclaved rice; congestive and infective changes were, however, less frequently present. It may here be noted that the addition of onions to the dietary did not prevent the onset of avian polyneuritis.(4)

4. *A diet of autoclaved food and onion.*—This diet is deficient in vitamines of the 'A' and 'B' classes. Its effects were studied in six monkeys. The atrophy of the thyroid was considerable, its average weight per kilo of original body-weight amounted to 69 mgs., as compared with 83 mgs. in healthy controls. Histologically the thyroid presented more definite evidences of departure from normal than in other categories. Whereas in the control animals the number of thyroids of the colloid type (Figs. 3 & 4) (1) exceeded those of the actively secreting type (Fig. 5) (1), in monkeys fed on autoclaved food and onion the histological appearances were in all six animals of the latter type.

In addition to this preponderance of glands of the actively secreting type there was present area for area a greater number of nuclei. Thus the nuclear count in the normal actively secreting gland (Fig. 5) was 175 to a given field, whereas it was 275, 195, 250 and 238, respectively, in four animals fed on autoclaved food and onion. This piling up of nuclei might be regarded as indicative of hyperplasia, but in no case did I detect evidences of nuclear division. A section of the thyroid from one such case is shown in Fig. 6. While, therefore, there is in animals of this category an appreciable loss of weight of the thyroid gland, there is no histological evidence of atrophy of its parenchyma cells; the tendency is rather to hyperplasia of these cells. No notable changes were observed in the parathyroids.

5. *A diet of autoclaved food, butter and onion.*—This diet is deficient in 'B' vitamine. Its effects were studied in five monkeys. The diminution in weight of the organ was considerable, the average being 70 mgs. per kilo of original body-weight, as compared with 83 mgs. in healthy controls. The histological pictures did not differ appreciably from the normal (Figs. 3 & 4). There was a tendency for glands of the actively secreting type (Fig. 5) to predominate. No notable changes were observed in the parathyroids.

There is one factor which is common to these five dietaries—deficiency in vitamines—as there is one result which is common to their use—diminution in size and weight of the gland.' It seems reasonable to believe that deficiency of these substances is the cause of the reduction in size of the organ. A further effect of these deficient dietaries is that they expose the thyroid cells to the noxious action of bacteria, and their products, derived from the intestine.

B.—Dietaries inducing enlargement of the thyroid.

1. *A scorbutic diet of crushed oats and autoclaved milk.*—This diet is deficient in 'C' vitamine. It is also deficient in essential salts and roughage. Its effects were studied in five guinea-pigs. The average weight of the thyroid per kilo of body-weight in five controls was 95 mgs. The average weight of the organ in five guinea-pigs fed on the scorbutic diet was 218 mgs. per kilo of original body-weight, and 295 mgs. per kilo of final body-weight, or from two to three times the weight of the healthy organ. This increase in weight was found on histological examination to be due in the main to hæmorrhagic infiltration of the organ. It would be of considerable interest to observe whether the thyroid gland undergoes enlargement in infantile scurvy. I have myself no data in this regard.

2. *A diet of mixed varieties of millet seeds without sand or grit.*—The effects of this dietary were studied in forty-two pigeons. No great departure from normal was observed either by gravimetric or histological methods of examination. The birds appeared to derive from the mixture of millet seeds all the vitamines (including antiscorbutic substances and salts) requisite for the maintenance of normal nutrition. It is true that a few cases (three in number) presented evidences of moderate degrees of hyperplasia—the glands weighing in these cases 45, 42 and 34 mgs. respectively, as compared with an average weight of 24 mgs. But such examples of thyroid hyperplasia are inseparable from

confinement of animals within narrow bounds. These forty-two pigeons, a number of which were under experiment for 250 days, served as controls to the two remaining observations.

3. *A diet of mixed varieties of millet seeds, peas, butter and onions without sand or grit.*—The effects of this dietary were studied in pigeons:—

(*a*) Eighteen young birds, age not exceeding six months, were confined in a single, large, netted-wire bottomed cage ($\frac{1}{2}$-inch mesh) of the following dimensions: 5 ft. × 3 ft. × 2 ft. Their daily ration consisted of white millet seeds (*cholam*) 12 oz., small dry millet seeds (*ragi*) 8 oz., small green peas of the variety known in India as *mung dal* 8 oz., fresh butter 3 oz., chopped onions $6\frac{1}{2}$ oz. No sand or grit was provided. The onion was a small local variety, grown in the Madras Presidency, of very pungent odour. The birds were allowed to eat as much of this mixture as they wished. Fresh water was supplied daily in large shallow troughs suspended above the bottom of the cage. The water became very dirty from the birds' droppings and from their habit of bathing in the troughs. The experiment commenced on the 14th April, 1919, and terminated 248–250 days later on the 18th–20th December, 1919. During its course three birds died in consequence of maltreatment by their fellows. The pigeons were weighed weekly, their live weight was taken just before they were killed for examination. Fig. 2 shows the composite monthly average weights of these birds. It will be noted that after a sharp rise up to the fifteenth day, the average weight showed a steady increase up to the end of the experiment.

(*b*) Eighteen young pigeons, age not exceeding six months, were confined in a cage precisely similar in every respect to the preceding. They received the same food as the birds in the previous experiment but *without onions*. In all other respects the two experiments were identical, both commencing on the 14th April, 1919, and terminating on the 18th–20th December, 1919. The sole difference was the absence of onions from the dietary in the present instance. During the course of the experiment one bird was killed by its fellows. The pigeons were weighed weekly; their live weight was taken just before they were killed. Fig. 2 shows their composite monthly average weights. It will be noted that the weight curve runs parallel with that of birds receiving onions.

The dietary employed in these two experiments was excessively rich in protein and in fats. In the case of the birds receiving onions all classes of vitamines were present in abundance. In the case of the birds receiving no onions, 'C' vitamine was more scanty, but appears

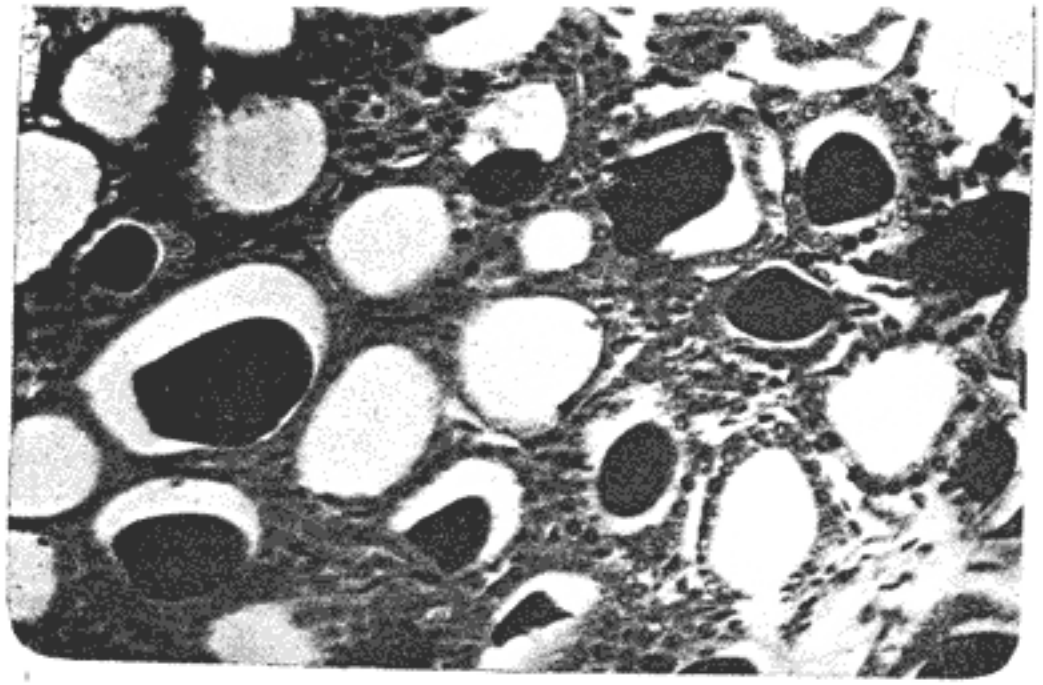

Fig. 7.—Thyroid from healthy control pigeon. × 210. Note regular shape and size of vesicles, low columnar acinar epithelium and proportion of intervesicular tissue to acini. The masses of colloid have dropped out of most of the vesicles in the process of staining.

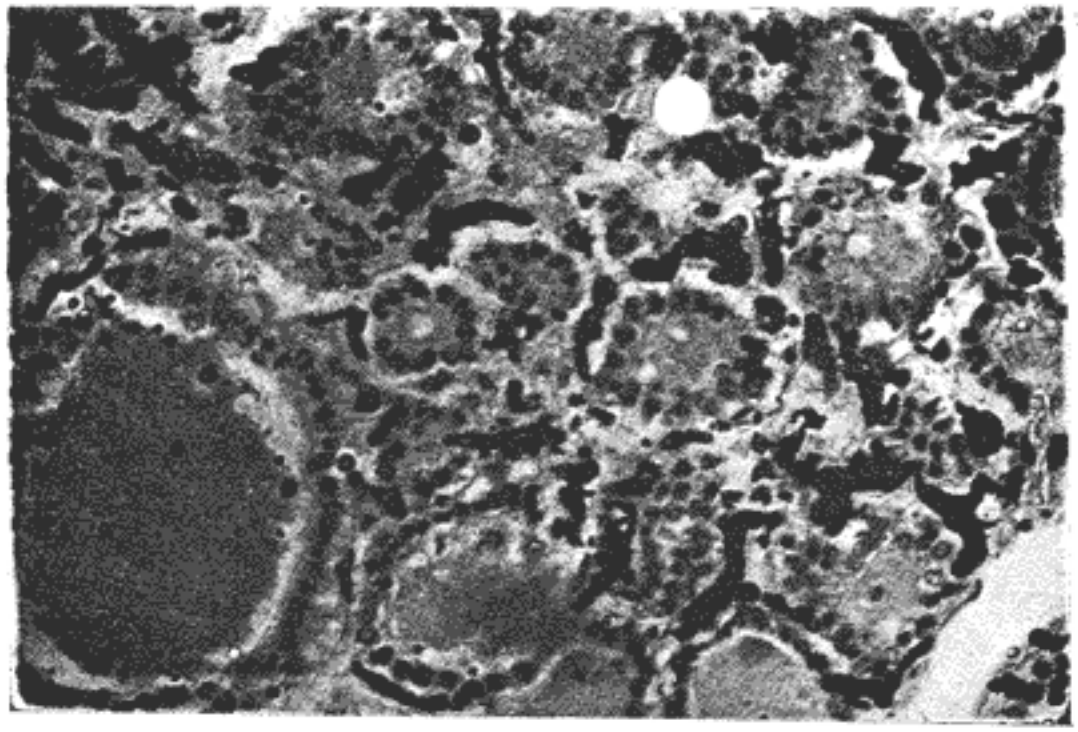

Fig. 9.—Thyroid from monkey fed on autoclaved rice and butter. Note great engorgement of peri-acinar capillaries. The darker staining cells are blood corpuscles. × 210.

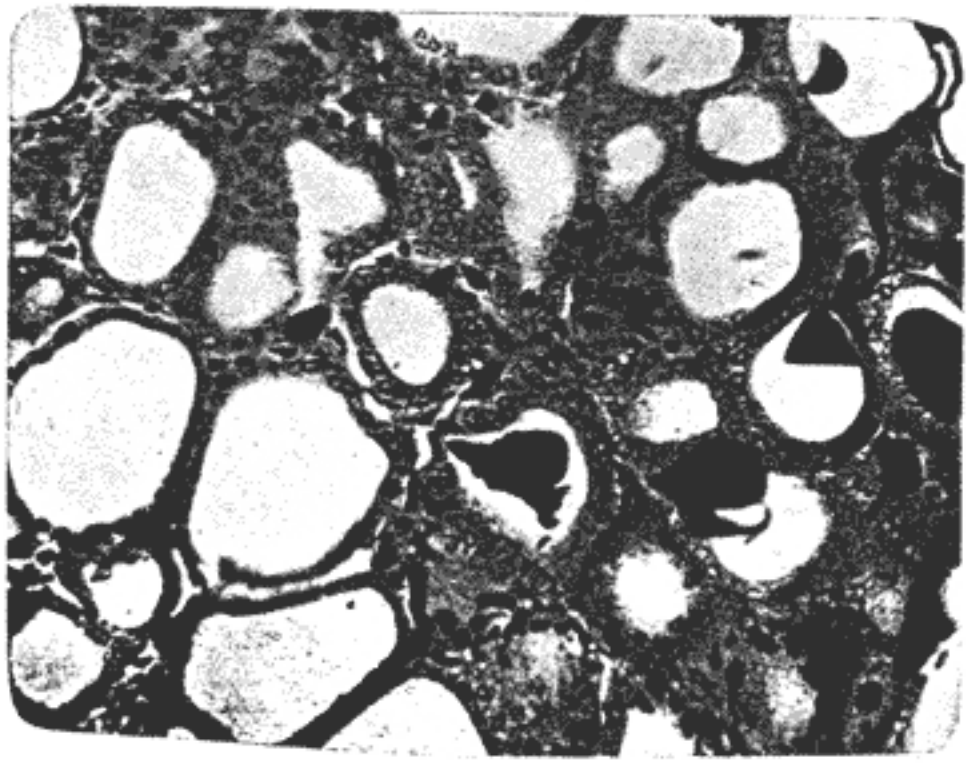

Fig. 8.—Thyroid from control pigeon kept in confinement for 250 days. × 210. Note slight departure from normal, increased proportion of intervesicular parenchyma.

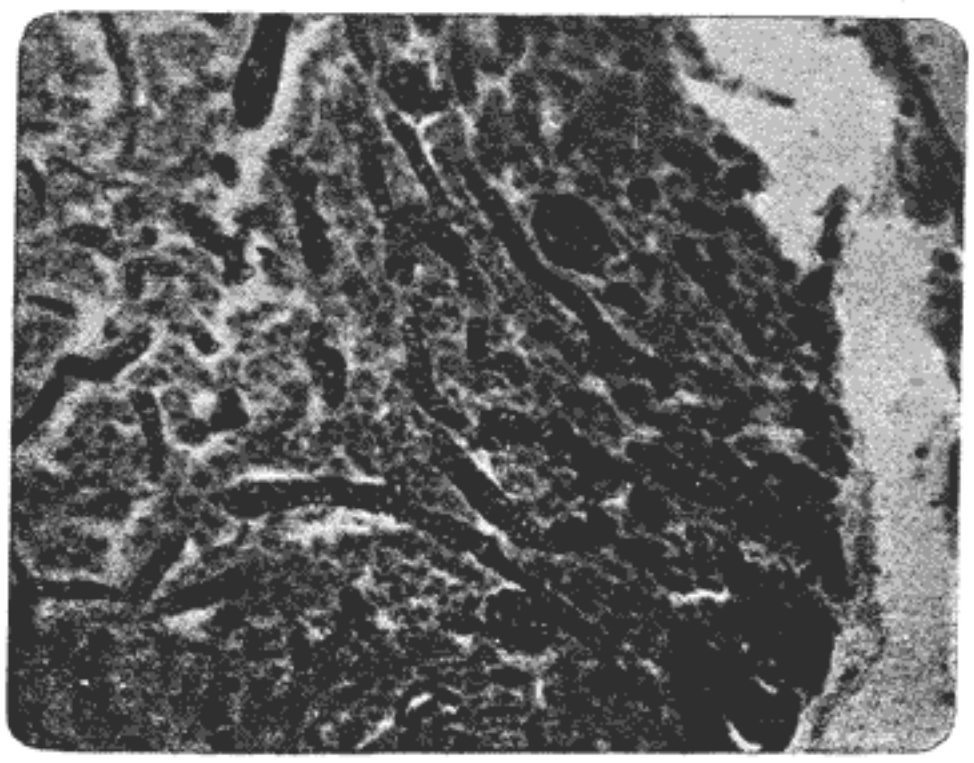

Fig. 10.—Parathyroid from monkey fed on autoclaved rice and butter. Note great engorgement of capillaries. × 210.

to have been present in quantity sufficient for their needs since the forty-two controls on mixed milled seeds exhibited no evidence of scurvy. There was in the dietary of both categories, as well as in that of the forty-two controls, a deficiency of grit, and of mineral substances which the birds pick up in the natural state. In those receiving onions, deficiency of salt and cellulose was largely made good by the onions. The two dietaries presented a further difference: that which did not include onions was made up mainly of acid and neutral foods (the seeds and butter); that which included onions contained a much higher proportion of alkaline foods (onions). It may here be mentioned that endemic goitre is unknown in this locality (Coonoor, the Nilgiris, Madras Presidency, 6,000 feet).

The pigeons in these two experiments were killed on the 248th, 249th and 250th days of the experiment, and their organs removed and weighed. The following table, and the chart (Fig.1) which illustrates it, show the average weight of the organs per kilo of final body-weights as compared with forty-two control pigeons fed on mixed millet seeds.

TABLE.

Showing average weights of organs per kilo of body-weight in control pigeons and in over-fed pigeons. Duration of experiment—250 days.

	42 control pigeons fed on mixed millet seeds.	15 pigeons fed on mixed millet seeds, *mung dal*, butter and onions.	17 pigeons fed on mixed millet seeds, butter and *mung dal*.
Thymus	1·862 gms.	1·485 gms.	1·306 gms.
Thyroids	82 mgs.	128 mgs.	183 mgs.
Liver	20·286 gms.	20·720 gms.	23·610 gms.
Spleen	1·081 gms.	1·203 gms.	1·775 gms.
Adrenals	83 mgs.	72 mgs.	66 mgs.
Testicles	5·186 gms.	5·068 gms.	4·875 gms.
Pancreas	3·180 gms.	2·613 gms.	2·671 gms.
Heart	10·675 gms.	11·026 gms.	10·135 gms.
Brain	6·62 gms.	6·32 gms.	6·52 gms.

In control pigeons the weight of the thyroids varied between 15 and 42 mgs. with an average weight of 24 mgs., or 82 mgs. per kilo of body-weight.

In pigeons fed on mixed millet, *mung dal* and butter *with onions*, the weight of the thyroid ranged between 15 and 87 mgs. with an average weight of 39 mgs., or 128 mgs. per kilo of body-weight.

In pigeons fed on mixed millet, *mung dal* and butter but *without onions*, the weight of the thyroid ranged between 16 and 130 mgs. with an average weight of 54 mgs., or 183 mgs. per kilo of body-weight.

Naked eye evidences of thyroid enlargement were rarely met with in pigeons fed on mixed millet seeds, and when present were never excessive. Some degree of thyroid hyperplasia is undoubtedly attributable to the factor of confinement alone. It is difficult, however, to determine the precise value of this goitrigenous factor apart from food influences. The average weight of 82 mgs. per kilo of body-weight in controls is inclusive of any increase in weight of this organ which may be attributable to confinement, and to the absence of gritty mineral particles from the dietary. It follows, therefore, that in pigeons overfed on mixed grains and butter whether with or without onions, any enlargement of the thyroid over 82 mgs. per kilo of body-weight is attributable to the excessive richness of the food in proteins and fats. In those fed on mixed grains and butter with onions the thyroid enlarged considerably, whereas the enlargement was much greater when onions were withheld from the dietary. In the former category the weight of the organ exceeded the highest limit found in controls in five out of fifteen cases, in the latter this limit was exceeded in eleven out of seventeen cases. Thus the incidence of goitre as well as the average weight of the thyroid was greater in animals recieving no onions. In both categories the larger glands presented to the naked eye appearances of hyperplastic organs : they were increased in size, dark in colour, firm in consistency, and appeared to hold little or no colloid. The right was almost invariably the larger of the two, thus conforming to the rule in the human subject. The thyroids were examined histologically in eight cases fed on mixed grains and butter *with onions*, and in ten cases fed on mixed grains and butter *without onions*. Amongst the eighteen thyroids there were five types of histological picture :—

Type A.—Glands of normal structure or differing from normal only in a slight or moderate increase of the intervesicular parenchyma, vesicles regular in outline, lined

by regular cuboidal cells and containing eosinopl le colloid (Figs. 7 & 8). Glands of this type were met with in two cases amongst the ten from pigeons fed on mixed grains and butter but without onions ; they were not enlarged.

Type B.—Enlarged glands showing slight or moderate congestion with the formation of many new acini. Acini small in size and irregular in shape, lined by a single layer of cuboidal cells of no greater height than that seen in health, and showing no, or but a slight, tendency to the formation of intra-acinar buds or plications. Colloid scanty or absent and either basophile staining or unstained. Intervesicular tissue was very scanty, having all been utilized for the formation of new vesicles. The multiplication of vesicles is the essential feature of this type (Figs. 11, 12, 13). Glands of this type were met with in five out of eight cases from pigeons fed on mixed grains, butter and onions : no thyroids of this type were found in pigeons receiving no onions.

Type C.—Glands, not always enlarged, similar to those of type B, but showing pronounced desquamation of acinar cells. Colloid absent or very scanty and basophile staining. Glands of this type (Fig. 14) were encountered in three cases out of eight fed on mixed grains, butter a d onions, and in one case (Fig. 18) which received no onions. The histological picture in this type resembles closely that seen in animals suffering from hæmic infections, or in those which had received experimental inoculations of the toxic products of bacteria.

Type D.—Enlarged glands showing slight or moderate degrees of congestion, the formation of many new acini and an almost complete absence of stainable colloid. The acini are very small, and lined by a single or multiple layer of cells which are usually *high* cuboidal in type, or low columnar. There is a marked piling up of nuclei in the acinar wall—the evidence of commencing budding. The small acinar cavity is often

distorted in shape and slit-like (Fig. 15). The organ presents an almost solid appearance in section, colloid being very scanty, and such as is present either retaining the basic stain or failing to stain. Glands presenting this histological picture throughout sections were met with in only one case amongst pigeons receiving no onions. This type represents an earlier stage of Type E.

Type E.—Enlarged glands showing the typical histological picture of the thyroid in Graves' Disease. Vesicles small, irregular in shape, and lined by high cuboida or low columnar epithelium, the vesicle walls being often several cells thick and showing a very pronounced tendency to the formation of intra-acinar buds or plications (Figs. 16 & 17). Stainable colloid absent, or but scanty and unstained or faintly basophile. Glands of this type were found in six cases out of ten fed on mixed grains and butter but without onions.

It is thus seen that the great majority of enlarged thyroids from pigeons, fed on mixed grains, butter and onions, are included in Type B—organs exhibiting abnormal multiplication of acini with cuboidal acinar cells and a *slight* tendency to intra-acinar budding—while the great majority of enlarged thyroids from pigeons fed on mixed grains and butter but without onions are included in Type E—organs exhibiting abnormal multiplication of acini with high cuboidal or columnar acinar cells and with a very *marked* tendency to intra-acinar budding. It is to be noted that the tendency to budding was present in both categories, but that this tendency was much less pronounced when onions formed part of the dietary. The conclusion is thus forced upon one that the onions restrain the tendency to hyperplasia of the Graves' Disease type. It seems probable that *succus alii* might be used with advantage for this purpose in Graves' Disease. In none of the numerous experiments which I have carried out in connexion with the experimental production of goitre have I found this tendency to the production of a Graves Disease type of goitre so predominant as in the case of pigeons fed on a diet excessively rich in proteins and fats and deficient in roughage and vegetable salts.

It will be noted also that in this experiment the chemical reactions of the colloid are altered. The secretion lost its eosinophile staining

Fig. 18.—Thyroid from pigeon over-fed on mixed grains and butter but *without onions*. Note similar appearances to those seen in Fig. 14, but desquamation associated with budding. × 210.

Fig. 16.—Thyroid from pigeon over-fed on mixed grains and butter but *without onions*. Note practical disappearance of colloid, great irregularity in shape of vesicles and marked budding. × 210.

character and remained either unstained or retained the basic element of the stains employed.

Here then is a result in marked contrast to that found in the case of dietaries deficient in vitamines. Foods deficient in vitamines cause the thyroid to diminish in size whereas those containing abundance of vitamines, but excessively rich in proteins and fats, cause in pigeons, confined within narrowed limits, an enlargement of the thyroid amounting, in over 50% of cases, to actual goitre. In these circumstances the goitrigenous changes in the thyroid are attributable to confinement, lack of exercise, overfeeding with food excessively rich in proteins and fats, the absence of mineral particles from the food, and it may be of appropriate vegetable salts or other unknown substances which in the natural state pigeons may require for the maintenance of perfect health. It is extremely difficult to narrow the goitrigenous factors in these cases down to a single influence. For my own part I believe that the goitres were due to the combination of a number of unhygienic and nutritional causes. Thus an excessive proteid diet alone, all other hygienic conditions being perfect, will not, as Forsyth[6] has shown, cause thyroid hypertrophy. In the present experiments, overfeeding was the main causal agent in the production of the goitres, since pigeons fed only on millet seeds, similarly confined and deprived of mineral gritty matter, did not exhibit thyroid hyperplasia to any great degree. This is not to be taken to indicate that overfeeding *per se* is a cause of goitre, but rather that imperfect balance of the food and its over-richness in certain directions *when associated with unhygienic conditions of life* is a potent factor in the production of goitre.

The factor of duration of exposure to the goitrigenous influence is of considerable importance in determining the size of the thyroid enlargement. In an experiment where twenty-four pigeons were fed for forty-three days on a dietary of mixed grains, butter and onions, the average weight of the thyroid per kilo of body-weight was 88 mgs., whereas in pigeons fed on the same dietary for 250 days it reached 128 mgs. The degree of thyroid hyperplasia is thus in some measure proportionate to the duration of exposure to the goitrigenous influence which, in this instance, was overfeeding.[5]

We come now to consider the most remarkable and, I think, the most important result of this experiment, *viz.*, the effect of the onions in restraining the tendency to the thyroid hyperplasia, as well as the tendency to the pronounced acinar budding

characteristic of goitre in Graves' Disease. This effect may have been due—

(1) to enrichment of the dietary in iodine which onions may have afforded ;

(2) to the action of the antiseptic juice contained in the onions ; and

(3) to the increased richness of the food in vegetable salts and cellulose when onions formed part of the dietary.

With regard to the first of these possibilities I have no chemical evidence to offer either for or against it. But the experiments themselves provide evidence which appears to indicate that the thyroid hyperplasia was not the result of deficiency of iodine in the food. For, when pigeons were fed on *autoclaved rice*, butter and onions, no thyroid hyperplasia occurred. Whereas when pigeons were fed on *mixed grains*, butter and onions, hyperplasia resulted. Any deficiency in iodine would, it may be presumed, be more marked in the former case. Further, when monkeys were fed on autoclaved food, butter and onions, no enlargement of the thyroid resulted. It may be assumed that the autoclaved food contained less available iodine than the unautoclaved grains fed to pigeons in the present experiment. Although the factor of time is not the same in these cases, it may, I think, be concluded that the goitre was not the result of lack of iodine in the food : the determining factor in its production would appear to have been the overfeeding with mixed grains and fat. With regard to the second possibility, the action of oil of garlic as a stimulant, stomachic and antiseptic, and its value in tubercle, pneumonia and chronic bronchitis, are well recognized. Amongst native hakims in India onions are credited with a curative and prophylactic action in cholera. It is reasonable then to suppose that the onions used exerted a considerable influence on the character of the bacterial flora of the intestinal tract. In the present experiment this influence may have been due in part to the pungent juice in the onions ; it was probably also connected with the maintenance of a more normal H-ion concentration of the bowel contents, by virtue of the alakaline salts they contributed to the food. The grains themselves being rich in protein and belonging to the class of foods yielding an acid ash are likely to promote the preponderance in the bowel of a bacterial flora of putrefactive (anærobic) types, and especially so when confinement and unhygienic conditions of life favour the entry of such bacteria into the intestinal tract ; whereas the addition of onions to the dietary of mixed

grains and butter provides the requisite alkaline elements of a properly constituted food. Thus the harmful effects of the high protein-content of the grains may have been corrected in considerable measure, and the tendency to the preponderance of noxious types of putrefactive flora correspondingly restrained. It seems probable also that the more generous provision of salts in the case of onion-fed pigeons served to maintain a more normal metabolism and a more normal state of health and of permeability of the intestinal mucosa. Whatever be the mode of action of onions, whether by virtue of their salt or antiseptic content or both, one of their effects is to render the conditions in the gastro-intestinal tract less favourable to the absorption from it of bacterial toxins, or of poisonous products of proteid cleavage. For, amongst the most important of the functions of a well-balanced food, are (1) the maintenance of healthy functional activity of all elements of the gastro-intestinal tract, and (2) the maintenance of a normal intestinal flora. The effects of food deficiencies and excesses on the body tissues cannot be adjudged apart from these fundamental facts.

The chart (Fig. 1) showing the comparative weights of the organs in the two classes provides additional evidence of the noxious effects of the products of intestinal bacteria on the body tissues and of the influence of onions in restraining them. It will be noted that in birds receiving no onions, not only was the thyroid greatly enlarged but the liver and the spleen also, a circumstance which may, I think, be attributed to the greater toxicity of substances absorbed from the intestinal tract. This experience provides further evidence of the very important part played by intestinal influences in the genesis of goitre and of its congenital manifestations and of the inter-dependence of nutritional and bacterial factors in their production—a truth which I have amply demonstrated by previous epidemiological, therapeutic and experimental methods of study.[1] *

Conclusions.

1. Dietaries deficient in vitamines lead to a reduction in size and weight of the thyroid gland.

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* The attention of the reader is especially directed to my papers "On the experimental production of Congenital Goitre" Proc. Roy. Soc., London, 1916, B. LXXXIX, pp. 322–327, 1 pl. and *Ind. Journ. Med. Research*, 1916, IV, No. 1, pp. 183–189, also "Experimental Researches on the Etiology of Endemic Cretinism, Congenital Goitre and Congenital Parathyroid Disease," *Ind. Jour. Med. Research*, 1914, I, No. 3, pp. 505–522.—R. McC.

2. Dietaries deficient in vitamines render the thyroid gland susceptible to the noxious action of intestinal bacteria, or of their products, with resultant atrophic and necrotic changes.

3. A scorbutic diet of crushed oats and autoclaved milk may cause in guinea-pigs considerable enlargement of the thyroid gland. The enlargement is, in the main, the result of congestion and hæmorrhagic infiltration of its tissues.

4. Dietaries containing adequate provision of vitamines, but excessively rich in proteins and fats, induce in the thyroid gland of pigeons in confinement marked degrees of hyperplasia, the extent of the hyperplasia being largely dependent on the duration of the organs' exposure to the goitrigenous influences induced by the excessive protein and fat content of the food.

5. The addition of onions to a dietary excessively rich in protein and fats, while containing at the same time an abundance of vitamines, markedly retards the development of thyroid hyperplasia, and the tendency to acinar 'budding' in pigeons living in confinement. The beneficial influence of the onions is held to be due in part at least to their action in restraining the growth of putrefactive types of bacteria in the gastro-intestinal tract and in retarding the absorption of their products. It is suggested that *succus alii* might prove of benefit in restraining the thyroid hyperplasia of Graves' Disease.

6. The changes in the parathyroids induced by a diet deficient in vitamines and excessively rich in starch and fat appear to be related in their origin to intestinal anærobes, the noxious action of which is greatly favoured by the defective diet.

REFERENCES.

1. McCarrison, R. The Thyroid Gland in Health and Disease, London, 1917.
2. *Id.* The Pathogenesis of Deficiency Disease, VII, *Ind. Jour. Med. Research*, Vol. VII, No. 2, October 1919, pp. 283–307.
3. *Id.* "Experimental Researches on the Etiology of Endemic Cretinism, Congenital Goitre, and Congenital Parathyroid Disease," *Ind. Jour. Med. Research*, 1914, I, No. 3, pp. 505–522.
4. *Id.* The Pathogenesis of Deficiency Disease II, *Ind. Jour. Med. Research*, 1919, VI, No. 4, pp. 550–556.
5. *Id.* "An Inquiry into the Causation of Goitre at the Lawrence Military Asylum, Sanawar," *Ind. Jour. Med. Research*, 1914, I, No. 3, pp. 536–588.
6. Forsyth, D. "Experiments on Prolonged Proteid Feeding with special reference to the Thyroid Gland and the Osseous System," *Lancet*, 1907, July, 20.

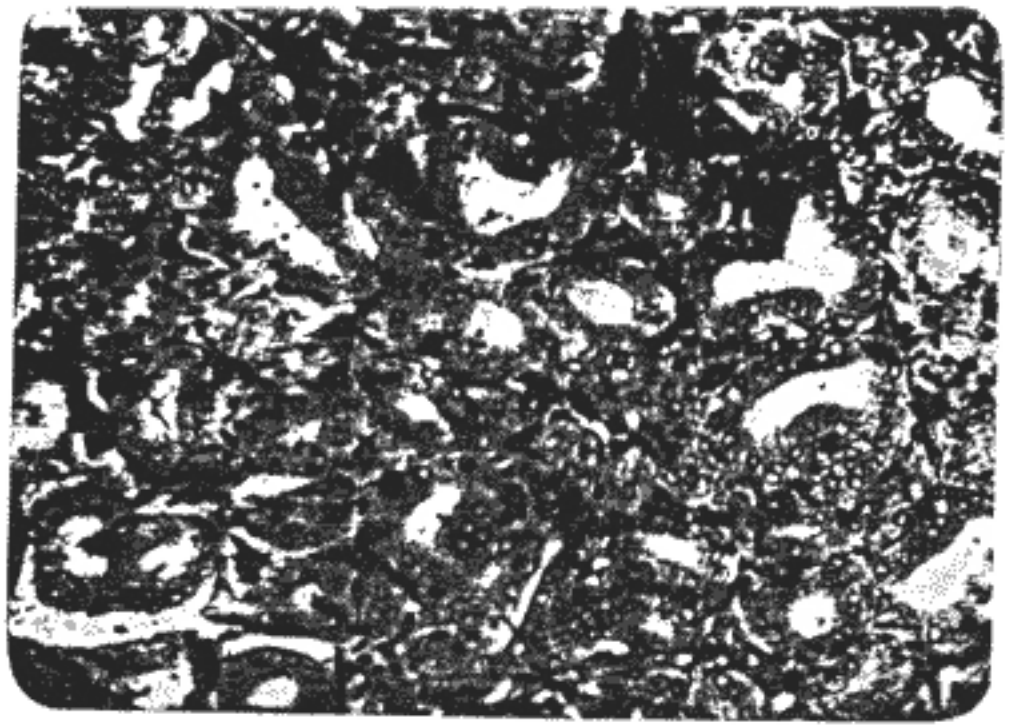

Fig. 15.—Thyroid from pigeon over-fed on mixed grains and butter but *without onions*. Note very small size of acini, disappearance of colloid, increase in height of acinar cells and in thickness of acinar walls, irregular shape of acini and commencing protrusion of acinar walls into acini. × 210.

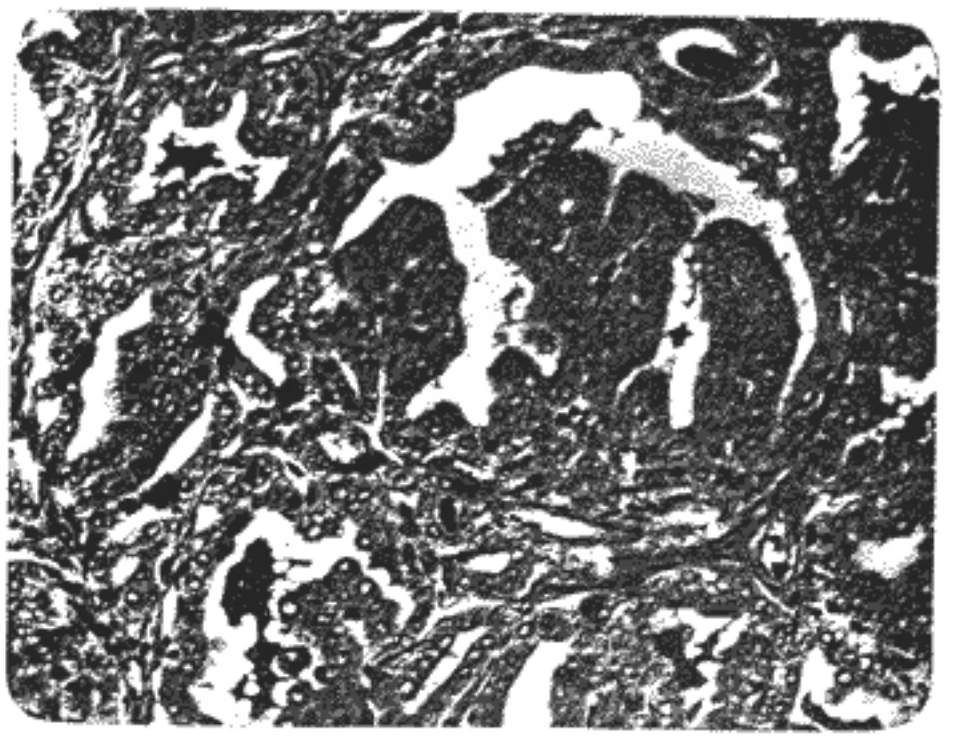

Fig. 17.—Thyroid from pigeon over-fed on mixed grains and butter but *without onions*. Note similar appearances to those seen in Figs. 15 and 17, but more intense budding. Appearances identical with those of Graves' Disease. × 210.

Fig. 16.—Thyroid from pigeon over-fed on mixed grains and butter but *without onions*. Note practical disappearance of colloid, great irregularity in shape of vesicles and marked budding. × 210.

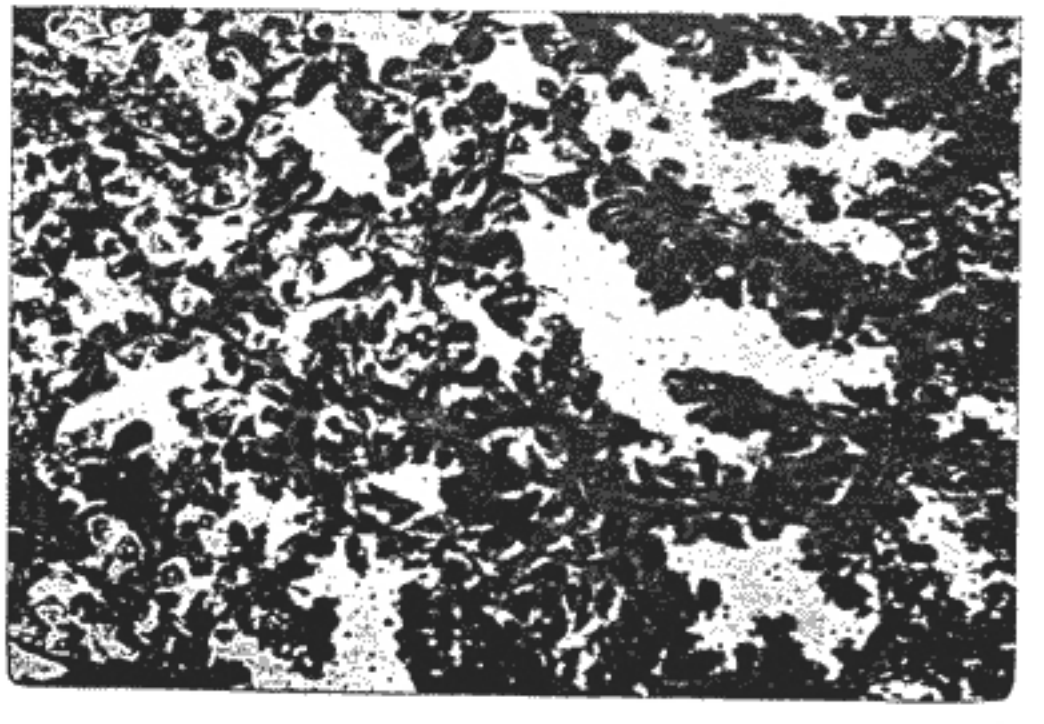

Fig. 18.—Thyroid from pigeon over-fed on mixed grains and butter but *without onions*. Note similar appearances to those seen in Fig. 14, but desquamation associated with budding. × 210.

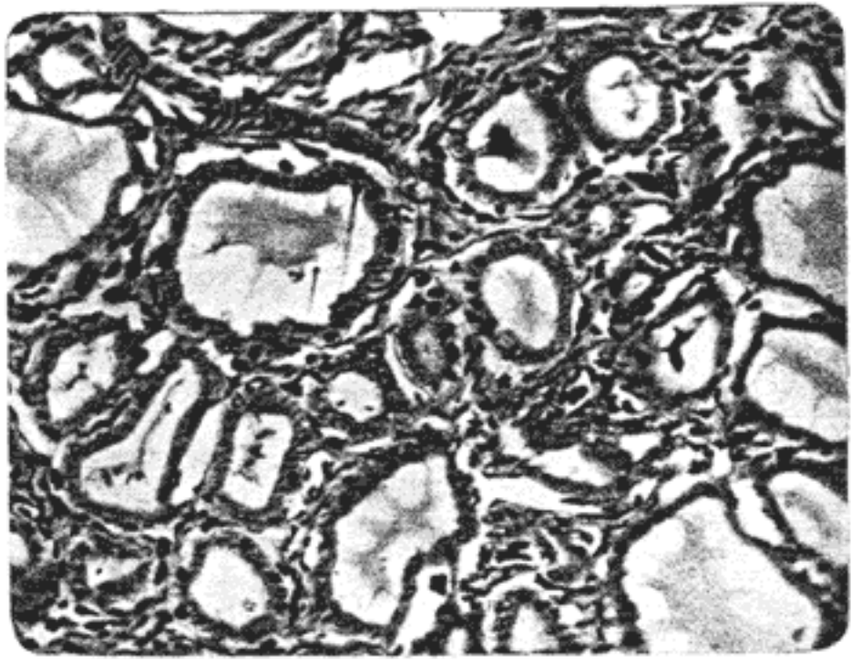

Fig. 11.—Thyroid from pigeon over-fed on mixed grains, butter and onions. Note commencing irregularity in shape of vesicles, and their increased number per field. Colloid basophile. No acinar budding. × 210.

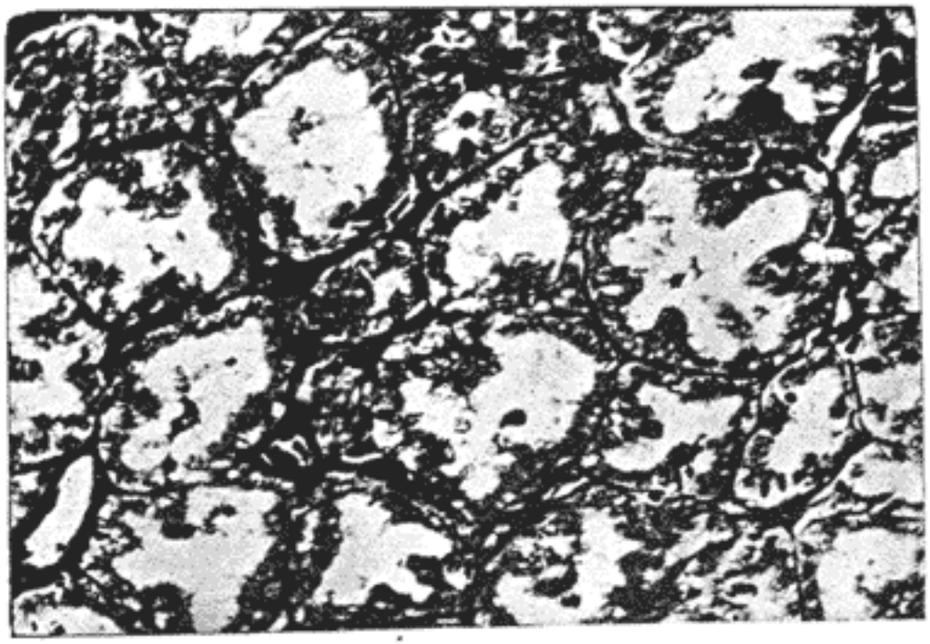

Fig. 13.—Thyroid from pigeon over-fed on mixed grains, butter and onions. Note disappearance of colloid, ragged and desquamating acinar cells and tendency to acinar 'budding.' × 210.

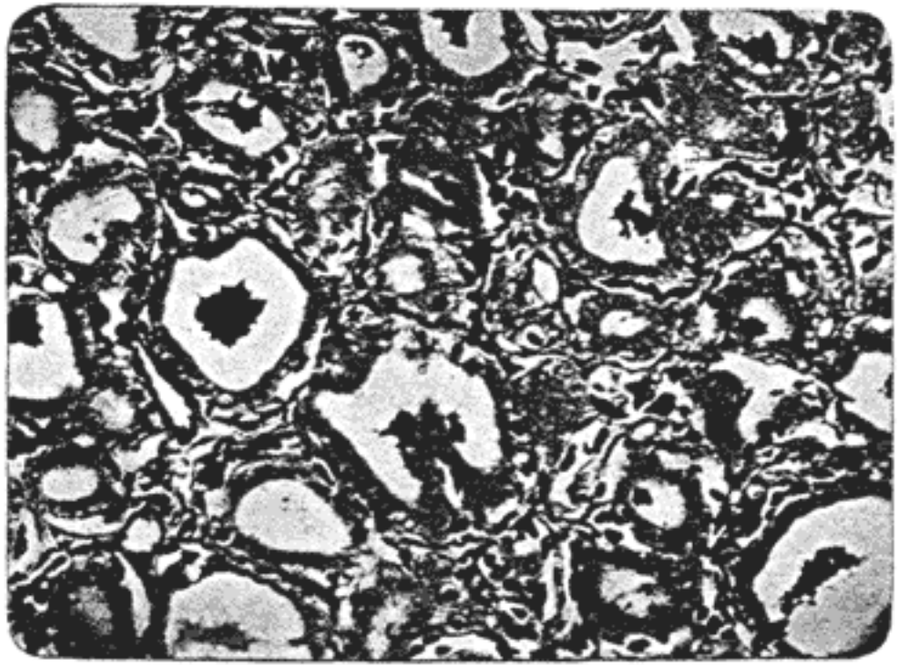

Fig. 12.—Thyroid from pigeon over-fed on mixed grains, butter and onions. Note similar appearances to those seen in Fig. 11, greater number of newly formed vesicles, also intra-acinar 'bud.' × 210.

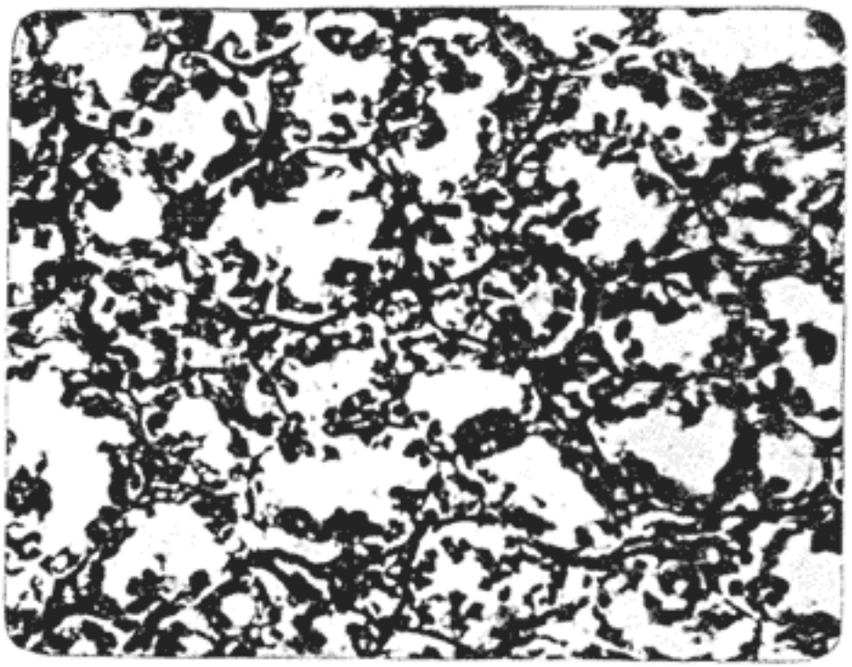

Fig. 14.—Thyroid from pigeon over-fed on mixed grains, butter and onions. Note disappearance of colloid and intense desquamation of acinar cells. × 210.