SUMMARY.

I. Our Examinations Related to the Hypertrophy oft he Suprarenal Gland and the Function of the Hypertrophied Cortex.

1. General considerations on the Hypertrophy of the Suprarenal Cortex.

The methods through which, according to the data of literature, hypertrophy of the suprarenal gland could be produced are briefly discussed. Administration of the thyroid gland per os, injection of thyroxin or the thyreotropic and corticotropic hormone of the anterior pituitary lobe, high dose of insulin, ingestion of cholesterol or lanolin, ricin intoxication, chronic lead or nicotin poisoning, intoxication with thallium or formalin, exercise, B avitaminosis, likewise give rise to the hypertrophy of the adrenal gland. In the experiments reported below the author has demonstrated that the shift of the acid-base balance to acidity produces, like the corticotropic hormone, hypertrophy of the adrenal gland.

2. Production of Hypertrophy of the Suprarenal Gland by Ammonium Hydroxyde.

1. The author treated rabbits with ammonium hydroxyde for a longer time. 50 to 80 ml of a 0.5 to 1 per cent solution were administered every day or every other day. The weight of the two adrenals varied from 40 to 142 ctg. i. e. 78.22 ctg. ± 2.98 medium error on an average. The weight limits of the adrenals of 41 control rabbits of similar age and weight were 20 and 56 ctg. i. e. 40 ctg. ± 1.34 medium error on an average. On the basis of probability calculations the difference to be expected between the weight of the treated and untreated animals respectively is 11.62 (k) i. e. the difference is undoubtedly significant.

2. Thus it may be stated that the average weight of the adrenals of rabbits treated with ammonium hydroxyde is nearly 100 per cent higher than in the control animals.

3. The increase of the adrenal weight is associated with the increase of their volume due to the considerable thickening of the cortex. The medulla is rarely, if at all, enlarged; sometimes it is atrophic.

4. Histologic examinations performed in normal and polarised light have shown a considerable increase of cholesterol and neutral fats in all layers of the cortex especially the zona fasciculata. Further, the numerical increase of the cortical cells by direct division could be demonstrated.

5. In rabbits treated for several months the cortical cells underwent degeneration and necrosis. The confluation of necrotic cell groups gave rise to the formation of foci storing neutral fats.

6. The destroyed cells of the cortex are partly replaced by the direct division of the neighbour cells. Extensive destruction is, however, followed by the proliferation of cicatrising connective tissue.

3. Fat and Cholesterol Content of Normal and Hypertróphic Adrenal Glands.

1. The weight increase of the adrenals of rabbits treated with ammonia is due to the fact that both dry substances and water content are increased. However, the increase of the solid substances is comparatively greater than that of the fuid content. The plus in solid substances is made up mainly of fat and cholesterol. Hypertrophic adrenal glands contain about 4.5-times as much fat and 6.5-times as much cholesterol as normal ones.

2. Thus the results of normal histologic examinations and such as accomplished in polarised light have been ascertained by chemical analysis. It could be stated by both that ammonia treatment results in a considerable increase of the fat and cholesterol content in the adrenal cortex of rabbits treated with the substance.

4. Blood Pressure of Rabbits in Hypertrophy of the Suprarenal Glands.

1. The administration of NH_4OH resulted in an initial depression of the blood pressure. First, this phase of depression lasted for 2 to 6 hours and the decrease was about 20 to 30 mm Hg. Later, hte decrease of blood pressure was less and less long-lasting. However, its duration and degree could be increased by raising the dose of NH_4OH After some months of treatment the initial depression of the blood pressure was followed by its lasting increase amounting to 10 to 30 mm Hg above the initial value. In some cases the blood pressure gradually decreased, in the course of the treatment lasting for several months, below the starting level (e. g. to 40 mm Hg). Finally, these animals died after several weeks characterised by low blood pressure.

2. In the adrenals of the rabbits which died under the symptoms of lasting hypotonia there was an extensive necrosis and cicatrisation present. On the other hand, no tissue destruction could be seen in the adrenals of those rabbits having an elevated blood pressure during the whole experiment.

3. In accordance with EDMUNDS, we attribute the initial decrease of the blood pressure to the hyperaemia showing itself in the splanchnic area. The lasting hypertonia occurring later may

derive from the hyperfunction of the adrenals whereas the stable hypotonia preceding the death of the animals may be due to the hypofunction of the glands.

5. Changes in the Body Weight of the Rabbits Having Hypertrophied Suprarenal Glands.

1. The body weight of the rabbits which were treated with NH_4OH for a longer time did, at the onset experiment, diminish to a varying degree for 2 to 3 weeks, then it gradually increased for several months until the initial value was surpassed. The increase of the body weight was in some cases 850 to 1800 Gr. Some animals (13) preserved their weight increase while in others (12) weight loss occurred some weeks before their death. In a few cases the body weight of the animals was, directly before their death, markedly lower than it was prior to the experiment.

2. The adrenals of the rabbits characterised by premortal weight loss displayed extensive tissue destruction manifesting itself in a focal necrosis of the cortex and the proliferation of connective tissue at the site of the necrotic foci. No necrotic foci could be found in the animals which preserved their weight increase. In some of these cases necrosis occurred to a very small extent and was unattended by cicatrisation.

3. The preserved increase of the body weight was ascribed to the hyperfunction of the adrenal cortex. The premortal weight loss was explained by the hypofunction of the same organ.

6. The Cause of Suprarenal Hypertrophy.

Since the longlasting administration of extracts of some endocrine glands and the intake of various poisons result, like the NH_4OH treatment, in acidosis and lipaemia or hypercholesterolaemia the hypertrophy of the adrenal cortex associated with these procedures seems to be due to the sequels of the intoxication i. e. to the acidosis and lipaemia or hypercholesterinaemia rather than to the specific action of the administered hormones or poisons. Probably, the acidosis represents a stimulation to the anterior pituitary lobe also whereby the production of the corticotropic hormone bringing about hypertrophy of the adrenal cortex is enhanced.

7. Demonstration of the Hyperfunction of the Hypertrophied Suprarenal Cortex.

The extracts made of the adrenals of healthy untreated rabbits and of the hypertrophied adrenals of rabbits treated with NH_4OH were prepared with the combined method of SWINGLE and PFIFFNER. The efficacy of the two extracts was compared by BOMSKOV—BAHNSEN's biologic method in infantile white mice weighing 9 to 9.5 Gr. which had been deprived of their suprarenal bodies. Following results have been obtained:

1. The adrenals of 100 healthy untreated rabbits weighed 42.34 Gr. The glands yielded 28.23 ml of an aqueous extract. 1 ml

of the extract contained so much substance as corresponding to 1.5 Gr. of the fresh gland.

2. 50 rabbits of similar weight were given 50 to 70 ml of a 0.5 per cent solution of NH_4OH every other day for 3 months. Their adrenals weighed 36.75 Gr. yielding 24.5 ml of an aqueous extract 1 ml of which corresponded to 1.5 Gr. of the hypertrophied gland.

3. 1 ml of the extract made of the untreated rabbits contained so much effective substance as equaling 5.35 corticodynamic mouse units of corrected effect. The extract made of the adrenals of the rabbits treated with NH_4OH contained 17.88 of the same units in each ml.

4. Thus it could be stated that a weight unit of the adrenals of the treated rabbits contained 3.5 times as much effective cortical substance as the adrenals of the untreated animals. With regard to the degree of hypertrophy (73.59 per cent) this ratio may be stated to be 6:1.

Hereby it has been proved beyond doubt that

5. the function of the adrenal cortex can be considerably enhanced by the application of external, chemical, influences.

6. The adrenal cortex of the rabbits treated with NH_4OH exerts a function exceeding many times, in our cases six times, the degree of hypertrophy as compared with the adrenal cortex function of the untreated animals.

8. Correlation between the Function and the Lipoid Content of the Adrenal Cortex.

In our examinations, two kinds of adrenal hypertrophy could be distinguished.

a) *Hypertrophy associated with hyperfunction;* the lipoid, first of all cholesterol, content of the cortical cells is increased, the cells are enlarged and frequently increased in number. Parallel with the increase of the lipoids, mainly the cholesterol, the quantity of the cortical hormone also increases. In other words, the increase of cortical lipoids, mainly cholesterol, and hyperfunction are parallel phenomena.

b) *Hypertrophy associated with hypofunction;* the adrenal bodies are largen than under normal conditions but it is chiefly the neutral fats that increase in the cortex cells or the intercellular substance whereas cholesterols are rather scanty. Moreover, extensive destruction (degeneration, necrosis, haemorrhages, scar formation) can be found.

9. The Serum Sodium and Potassium of Rabbits Having Hypertrophied Suprarenal Glands.

First the effect of a single dose (60 ml) of the 0.5 per cent NH_4OH solution was examined in 6 animals. Then 22 rabbits were given doses of 50 to 70 ml of the same solution every other day for 10 weeks through a gastric sound until hypertrophy of the adrenal glands occurred. The sodium and potassium content of the serum was examined once a week during and after the treatment.

1. A single dose of the NH_4OH solution resulted in a decrease of the serum sodium after ½ hour. The deep point of the decrease occurred after 2 hours. After 20 hours the starting value was attained and after 48 hours a slight increase could be noted.

2. The serum potassium also decreased ½ hour after a single dose of the NH_4OH solution. The decrease became gradually marked and after 20 hours the deep point of the curve was reached. After 48 hours, either the initial value was obtained or a value slightly below the initial one.

3. The decrease of sodium and potassium in the serum following the administration of ammonia represents, from the viewpoint of the organism, a loss of alkali. This is in full accordance with our earlier statements that the administration of ammonia results in the reduction of the reserve alkali of the serum and in an increase of the hydrogen ion concentration i. e. acidosis.

4. Under the effect of a lasting ammonia treatment the sodium content of the serum gradually increased. Two weeks after the treatment had been interrupted the serum sodium level was still considerably above the normal.

5. Lasting administration of ammonia resulted in a considerable reduction of the serum potassium level. The latter was still markedly lowered as late as two weeks after the experiment had been finished.

6. With regard to the fact that the shift of serum sodium and serum potassium is, in rabbits having hyperfunctioning adrenal glands, a contrast of that observed in suprarenal failure it may be assumed that the increase of the serum sodium level and the diminishing of the serum potassium occurring at the same time are due to the hyperfunction of the adrenal cortex. The fact that the serum sodium did, unlike its behaviour observed under the acute ammonia effect, increase during the protracted ammonia therapy speaks in favour of this assumption.

7. Starting from these observations the simultaneous increase of the serum sodium and decrease of serum potassium is considered a sign of adrenal hyperfunction in the living also.

8. These examinations have furnished new evidences for the hyperfunction of the hypertrophied suprarenal bodies, further, they have supplied a method by which the hyperfunction of the cortex can be demonstrated in living persons also.

10. The Effect of Extracts Made of Hypertrophic and Hyperfunctioning Adrenal Cortex on the Liver and Muscle Glycogen of White Mice Deprived of their Adrenal Glands.

1. The extract of normal and hypertrophic adrenal cortex raises the glycogen content of muscles and liver in white mice deprived of their adrenals. This increase is proportional to the quantity of the extract injected i. e. more hormones produce a greater increase in glycogen formation.

2. Following the injection of extracts prepared of hypertrophied adrenals considerably more glycogen can be found in the liver.

and muscles of the mice than after the injection of normal extracts containing the same number of hormonal units (mouse units).

3. This is a biologic evidence for the presumption that the vital hormone indispensable for life is not identical with the substance promoting glycogen formation. In other words: the adrenal cortex produces, beside the vital hormone, a substance promoting glycogen formation.

4. The hyperfunctioning adrenal cortex produces not only more vital hormone but more glycogen forming hormone also than the adrenal cortex of normal function.

5. The hyperfunctioning adrenal cortex produced by ammonia treatment exhibits an increase in the hormone forming glycogen which exceeds the increase in the vital hormone.

11. Liver and Muscle Glycogen Content in Rabbits Having Hypertrophic (Hyperfunctioning) Suprarenal Glands.

1. The adrenal glands of rabbits treated for 5 months with ammonium sulfate, ammonium carbonate, sodium-ammonium phosphate, ammonium acetate, and calcium chloride, underwent considerable enlargement.

2. In these rabbits the liver glycogen exceeded the normal value by 186 to 319 per cent on an average, the glycogen content of the muscles was 43 to 77 per cent above the normal level.

3. The greater the hypertrophy of the adrenal glands produced by the compound administered the greater the increase in the glycogen content of muscles and liver.

4. The increase of the glycogen content of liver and muscles is to be attributed to the hyperfunction of the adrenal cortex. This is a new evidence of the statement that the cortex of the hypertrophied adrenals developed under the effect of the administered compounds exerts an increased function.

5. The possibility arises that the therapy of diabetes could be ameliorated by enhancing the function of the adrenal cortex or administering the extract of hypertrophic-hyperfunctioning cortices.

12. Evidences for the Fact that the Function of the Adrenal Cortex Can be Influenced by Chemical Compounds and Importance of this Fact.

Several facts have been found to furnish evidence for the hyperfunction of the hypertrophic adrenal cortex. These evidences may be divided in three main groups: I. Histologic phenomena: 1. Hyperaemia of the cortical substance, 2. numerical increase of the cells of the cortex (cell divisions), 3. enlargement of the cells of the cortex, 4. chromatine riches of the nuclei of these cells, 5. microscopic observations on the increase in the quantity of lipoids (of simple and double refraction) in the cells. II. Chemical phenomena: 6. The (4.5-fold) increase of the total lipoids of the suprarenal bodies, 7. the (7.5-fold) increase of the cholesterol content of the suprarenal bodies, 8) the (8-fold) increase of the hormone content of the adrenal cortex, 9) the lasting increase of the serum

sodium level, 10. the constant reduction of the serum potassium level. III. Biologic phenomena: 11. The rise of blood pressure, 12. increase of body weight, 13. the fact that the muscle und liver glycogen of white mice deprived of their adrenal glands are to a greater extent increased by the extract of hypertrophic (hyperfunctioning) cortices than by the extract of a normal cortex containing the same number of hormone units, 14. the marked increase of the liver and muscle glycogen in rabbits having hypertrophied suprarenal bodies.

The hypertrophia associated with the phenomena mentioned of hyperfunction occurred at a time when the therapy applied was not very energetic whereby the shift toward acidity of the organism was moderate.

Excessive treatment (high doses, rapid increase of the dose, frequent injections) results in a greater shift of the acid-base balance to acidity whereby the cells of the adrenal cortex may undergo degeneration and focal necrosis. These changes are attended by a hypofunction of the cortex. In this manner, the hypertrophic and hyperfunctioning cortex may, under the action of excessive treatment (and increasing acidosis), be converted into a hypertrophic cortex the function of which is, despite its enlargement in size, lower than the normal one, owing to the degeneration and destruction of cortical cells. The hypofunction of the cortex shows itself in weight loss, lowered blood pressure, degeneration and necrotic foci in the cortex (if they are extensive), the tissue proliferation and scar formation following the regressive changes, the reduction of lipoids (mainly cholesterol) and the focal accumulation of neutral fats.

It should be emphasised that excessive doses of ammonia (or another substance producing acidosis) i. e. any greater shift of the acid-base balance towards acidity results not in the hyperfunction of the adrenal cortex but in the destruction of the cells of the cortex whereby hypofunction of the cortex arises and may be associated with untoward sequels. For this reason, any therapy aiming at the hyperfunction of the cortex should be introduced with small doses which should be slowly and gradually raised. In the course of this treatment the body weight should be often checked. If weight loss is observed the treatment may be interrupted or continued with reduced doses.

Our statements have furnished a proof that one member of the endocrine apparatus i. e. the suprarenal gland can, through external influence, be induced to hyperfunction (or, through energetic treatment, to hypofunction). This fact having been proved for the adrenals, it may be assumed that other endocrine organs also can be influenced by similar stimuli. Hereby, serious results may be expected from the experiments concerning the function of the endocrine glands and the influences acting upon their function.

It is impossible to see, at first sight, the ways and means of influencing endocrine function. In any case, the possibilities refer to theoretical results, further various practical aspects such as therapy, breeding of animals, racial amelioration, knowledges of

heredity, and economics. One of our results can be economically utilised i. e. that referring to the fattening of animals. Our examinations bearing on this problem have been summarised in the following chapter.

II. Fattening Through Inducing Hyperfunction of the Adrenal Cortex.

Starting from the above observations we studied the correlation of weight increase and function of the adrenal cortex in detail. To this end, 100 rabbits belonging to the same race were treated with ammonium hydroxyde for 8 months. 30 rabbits of the same race were kept on the same diet as untreated controls.

Both the treated and untreated rabbits have been divided by their initial body weight into 3 groups. The 1st group was formed by 40 experimental and 10 control rabbits weighing 2200 to 2500 Gr. 40 experimental rabbits and 10 controls weighing 2550 to 3000 Gr. belonged to the second group. In the 3rd group there were 20 experimental rabbits and 10 controls and their weight was 3050 to 3600 Gr. The ammonium hydroxyde was administered through a gastric sound. The animals received 50 to 70 ml of a 0.5 per cent solution every other day.

The data of observation may be briefly summarised as follows:

In group 1 the weight increase of the untreated animals was on an average (in 8 months) 650 ± 38 Gr., that of the animals treated with ammonium hydroxyde 1460 ± 103 Gr. Thus the weight increase of the treated animals was 810 Gr. i. e. 124 per cent more than that of the controls. The significant difference was 7.36, thus the weight plus was undoubtedly relevant.

In group 2 the average weight increase of the untreated rabbits was 560 ± 51 Gr., that of the treated animals 1445 ± 145 Gr. The plus to be attributed to the ammonia therapy was on an average 885 Gr. i. e. 158 per cent. The significant difference related to group 2 was 5.80 i. e. relevant.

In group 3 the controls had a weight increase of 180 ± 30 Gr., the treated rabbits 1024 ± 69 Gr. The plus was 844 Gr. i. e. 468 per cent, the significant difference, 11.25, a relevant difference.

Thus it has been shown that the weight increase produced by ammonia therapy is markedly higher than that obtained by simple feeding of the animals. The post mortem examination of the rabbits has shown that the weight plus was due to the increase of fat tissue. First of all, mesenterial, perirenal, epicardial, and subcutaneous fat tissue displayed a considerable increase.

The adrenal glands of the rabbits treated with ammonium hydroxyde were invariably hypertrophic and they yielded six times as much extract as the same quantity of adrenals of control rabbits. This is rather an evidence of our earlier presumption that hyperfunction of the adrenal cortex leads to an increased formation of fat tissue and its increased deposition.

Other fattening experiments were performed with numerous organic and inorganic ammonium compounds, further organic and

inorganic compounds containing no ammonium radical. All compounds had been learned to produce, like ammonia, a shift of the acid-base balance towards acidity.

Stress is to be laid on the statement that acidifying compounds should, when applied to fattening, be administered in a dose producing but a mild acidity for a short time. Otherwise the animals will, instead of increasing their weight, become emaciated and die, overdosage leading to necrosis in the cortex resulting in its hypofunction and, finally, its failure.

It has been learned from the examinations of Pohl and Münzer, Porges, Leimdorfer and Markovici, further Haldane that ammonium chloride produces acidosis. In our next experiments 30 rabbits of identical race were given increasing doses (0.05, 0.1, 0.15 Gr. per kilo body weight) of NH_4Cl for 5 months, every other day, with intervals free of treatment. The salt was dissolved in water and administered per os (the animals drank the water). The rabbits treated in this way were divided by their original weight in 3 groups containing 10 animals each. Here are the results of the NH_4Cl experiments:

In group 1 the control rabbits displayed a weight increase of 440 ± 35 Gr. on an average in 5 months. The weight increase of the rabbits treated with NH_4Cl was, during the same period, 930 ± 85 Gr. The average difference between the weight plus of the treated animals and that of the controls was 490 Gr. i. e. 111 per cent over the weight increase of the controls. The significant difference was 6.9 corresponding to a relevant deviation.

In group 2 the average weight increase of the controls was 326 ± 32 Gr. that of the treated rabbits 960 ± 58 Gr. The second figure was 634 Gr. i. e. 194 per cent higher than the first one. The significant difference was 10.05.

In group 3 the weight increase of the untreated controls was 60 ± 24 Gr., that of the animals treated for 5 months with ammonium chloride 820 ± 58 Gr. The plus showing itself to the favour of the second figure was 760 Gr. i. e. 1266 per cent. The significant difference was in this group 9.74.

These date show that ammonium chloride does, like ammonia, produce a weight increase considerably exceeding that obtained by simple feeding. Of course, animals of similar age, body weight, race, and feeding, were compared.

On necropsy it could be stated that the weight increase was mainly due to the proliferation of fat tissue i. e. true fattening took place. The fat tissue of the control animals and that of the treated ones was weighed out and compared There was, on an average, 600 to 1000 Gr. of fat in the rabbits treated with ammonium chloride and 50 to 150 Gr. in the untreated controls. The fat of the treated animals was like the fat of the controls with regard to the percentage of fat, water and connective tissue. In the majority of cases, the weight increase of both groups was greater than the weight of the fat tissue found in the animals. This phenomenon may be due to the fact that the weight of other tissues also increased. The difference between weight plus and

fat weight was greater in the rabbits treated with NH_4Cl than in the untreated ones. It may be inferred from this fact that the weight increase of other tissues was, like the weight increase of the fat tissue, greater in the treated animals than in the untreated ones. In the rabbits the adrenals of which became hypertrophic more glycogen was fonud in liver and muscles than in the control animals; thus liver and muscles of the experimental animals were enriched in foodstuffs. The fact that in the muscles of the treated animals more solid substances and less water were found than in the untreated controls may be evaluated in the same sense.

The adrenal glands of the treated rabbits were considerably — 123 to 186 per cent — enlarged as compared with the controls. The enlargement was in these cases also due to the thickening of the cortex. Otherwise, the hypertrophy due to ammonium chloride was like that produced by ammonia, aside from the fact that no necrotic foci were found in the adrenals of the rabbits treated with NH_4Cl.

An extract was prepared of the adrenals enlarged during the NH_4Cl therapy with the method of Swingle and Pfiffner. The efficacy of the extract was estimated in white mice by Bomskov—Bahnsen's technique. In these examinations the hypertrophic adrenals exhibited 11.5 times more cortical hormone than normal adrenals did. These results show that an adequate therapy with NH_4Cl enhances the function of the adrenal cortex to a still greater degree (about 100 per cent) than the ammonia treatment.

Thus the enlargement of the adrenal glands, the hyperfunction of the cortex, and the greater increase of the body weight, showed a parallelism in the rabbits treated with ammonium chloride also.

Hypertrophy and hyperfunction of the adrenal cortex, further a considerable increase of body weight, can be accomplished also by adequate doses of ammonium sulfate, ammonium carbonate(!), sodium-ammonium phosphate, ammonium acetate, ammonium lactate, calcium chloride, hydrochloric acid, lactic acid, acetic acid, sodium dihydrophosphate, and ammonium hydrophosphate.

After these observations fattening experiments were initiated with geese.

First the effect of ammonia was examined. To this end, steeped maize was fed to 20 geese deriving from the same hatching twice a day for 5 weeks. Prior to the onset of the experiment the geese were divided into two groups. Each group consisted of 10 geese. The total weight of each group was about identical. After one week of feeding the geese of one of the two groups were given increasing doses of ammonia of proper quantity and dilution through a gastric sound for 4 weeks. The ammonia solution was administered directly before feeding. The geese of the other group served as controls. The results may be summarised as follows.

The starting weight of the control group was 40.1 kilos. This weight increased during 5 weeks to 60.58 kilos. The total increase of weight was 20.48 kilos yielding an average of 2048 Gr. for one goose of this group. The weight of the group of the geese treated with ammonia rose, during the same period and on the same diet,

from 40.00 kilos to 68.48 kilos, yielding a total weight plus of 28.48 kilos and an average weight increase of 2848 Gr. for one goose. The fattening plus i. e. the difference between the average weight increase of the treated and untreated geese respectively was 800 Gr. i. e. a fattening plus of 40 per cent.

The efficiency of fattening may be expressed for practical purposes by the figure stating how many per cent of the foodstuffs consumed has been converted into body weight, in other words, the ratio weight increase: consumed food. Having achieved these calculations we stated that the utilisation of food was 4 per cent better in the geese treated with ammonia.

As it may be seen the experiments have shown that fattening of geese can, like fattening of rabbits, be markedly enhanced by ammonia therapy. The next problem was the selection of the compound which had best proved itself in the fattening experiments with rabbits and to try the effect of this compound in geese.

In order to enhance the fattening of geese two sorts of pills were prepared. One of them contained 1.0 Gr. ammonium chloride and 0.1 Gr. cholesterol acetate each, the other contained merely 1.0 Gr. ammonium chloride evenly distributed in an indifferent vehicle.

The further experiments with the fattening of geese were accomplished at three private farms. Geese of a common race were put at my command at all of the three farms. Both the experimental geese and the controls derived from an identical hatch. The data of 10 treated geese and those of 10 controls were compared. As a total, 70 geese were treated in the experiments and 50 served as controls. The treatment consisted of the administration of a varying number of the pills mentioned at various intervals whereby all groups received a different treatment. The weight of the animals was measured once a week.

Independently of the treatment applied, the weight increase of the geese treated with any of the compounds was invariably greater than the weight increase of the controls.

The greatest plus was observed with those geese treated for 6 days before the fattening period with one pill daily containing NH_4Cl and cholesterol acetate and during the four weeks of fattening with one pill daily which contained ammonium chloride only. The 10 geese treated by this method displayed a total weight increase of 37.6 kilos during 4 weeks whereas the weight increase of the controls was 23.6 kilos. Thus the treated geese exhibited, in comparison with the untreated animals, a weight plus of 14 kilos corresponding, for one goose, 1.4 kilos i. e. 59 per cent plus increase. The significant difference was 8.04 i. e. relevant.

As for the utilisation of the food it could be established that 13.4 per cent of the maize fed to the control animals had been utilised whereas in the treated group the percentage of utilisation was 21.33 i. e. 7.93 per cent more than in the control group.

In other words: the treated geese reached after 2.5 weeks of fattening the body weight attained by the untreated animals after 4 weeks of fattening.

The average weight of the suprarenal glands was in the treated group 75.6 per cent higher than in the untreated one. Like in our other experiments, the hypertrophy was due to an increase in the number of the cortical cells and their lipoid content. In the musculature of the treated group the percentage of solid constituents was 1.6 higher than in the controls. The difference was due to the fact that the muscles of the treated geese had a higher glycogen content.

The results admit of the conclusion that the treatment applied in the experiments represents a new fattening procedure which excellently lends itself to the fattening of geese and, undoubtedly, other poultry too. The treatment has the advantage of simplicity and cheapness.

In the majority of countries, fat production bases on the fattening of pig. The efficiency of pig fattening is the object of many an economic efforts made in all countries.

The practical experiment of our procedure took place between May 7. and November 30. 1941. In two farms, castrated hogs of identical race, age, and initial weight, were selected for the experiments. The animals were divided in two groups.

The hogs of the first group received once a day, every other day, on the afternoon feeding, 6 Gr. of ammonium chloride partly dissolved in water partly mixed up with the food. The dose corresponded to 0.071 Gr. of the salt per kilo body weight. This therapy was done in the first and second month of the experiment. In the third month there was an interval. In the fourth month the animals were given the same dose of the salt for 3 weeks, then an interval of 1 week followed. In the fifth month a daily dose of 8 Gr. was administered every other day. In the 6th and 7th months no treatment was done.

In the second group of hogs we administered, in the first month, 5 Gr. of ammonium chloride i.e. 0.1 Gr. per kilo body weight every other day. The second month was an interval. In the third, fourth, fifth, and sixth months the daily dose administered for three weeks every other day was 6, 7, 8, and 10 Gr. respectively. The fourth week of each month was an interval. In the 7th month no therapy was applied.

Here are the results of the fattening procedure.

I. Farm of N. M. The total weight of 85 untreated hogs was at the onset of the experiment 7148 kilos representing an average of 84.09 kilos. By the end of the experiment the average weight of a control animal was 187.62 kilos yielding a weight increase of 103.53 kilos.

The quantity of food consumed by one control pig during the 7-month period was 669.93 kilos (fodder produced in the previous year). Thus the control animals utilised 15.46 per cent of the fodder.

The total initial weight of the 83 treated hogs was 6980 kilos yielding an average of 84.09 kilos, like in the control group. The total weight increased during 7 months to 17226 kilos corresponding to an average of 207.5 kilos for one hog. The average weight increase was 123.41 kilos.

The treated hogs consumed 659.82 kilos of fodder of the same year and quality. Thus their utilisation of food was 18.68 per cent.

Ultimately, it may be fairly stated that the average plus-increase of weight was 19.88 kilos per hog in favour of the treated group. The percentage of the increase plus was 19.14. The utilisaton of the treated group was 3.22 per cent better than that of the untreated group.

II. Farm of Cs. P. The group fattened without treatment consisted of 56 hogs. Their initial total weight was 2912 kilos, the average initial weight 52 kilos. The total weight of the group was after the 7-month experiment 8400 kilos i. e. the weight of one hog increased by 150 kilos on an average. The average weight increase was 98 kilos.

The control group consumed 620.80 kilos of fodder produced in 1940. Their utilisation of fodder was 15.78 per cent.

The treated group consisted of 49 hogs. Their total weight was at the onset of the fattening experiment 2465 kilos, the average weight was 50.30 kilos. By the end of the experiment their total weight was 8270 kilos, the average weight 170.75 kilos, the average weight increase 120.45 kilos.

The consumption of fodder was 614.3 kilos per hog in the treated group (fodder produced in 1940). The utilisation was in this group 19.25 per cent.

The comparison of the data showed that, in the farm of Cs. P. the treated hogs exhibited a weight increase exceeding that of the untreated animals by 22.45 kilos i. e. 22.9 per cent on an average. The utilisation of food was in the treated group 3.48 per cent better than in the control group.

As to the period of weight increase, the treated hogs reached the weight ultimately attained by the control animals 5 to 6 weeks earlier.

The final conclusion to be drawn says that the treatment applied resulted in a weight increase plus of 20 to 22 kilos (20 to 23 per cent) in comparison with the weight increase observed in fattened but untreated animals.

Both the treated hogs and the controls were slaughtered in the Szeged City Slaughter-House on consecutive days. After the slaughtering the weight of the various kinds of tissues (flesh, organs, etc.) was officially stated. From these data we have learned that 80 per cent of the weight plus (18.1 kilos) consisted of fat whereas 20 per cent (4.35 kilos) fell to the musculature (flesh).

The fat tissue obtained from both the treated and untreated hogs was melted out in the Fat Plant of Szeged City. There it was stated that the fat tissue of the treated hogs displayed no difference, regarding fat, water, and connective tissue, from that of the controls. These data show that the weight increase brought about by the treatment was due to fat accumulation. The percentage of dry substances was in the muscles of the treated hogs 1.09 higher than in the muscles of the untreated animals; the water content was correspondingly lower. The weight increase of the muscles is, on the basis of our rabbit experiments, due to the fact that the hyper-

trophy of the adrenal glands produced by the treatment gives rise to an accumulation of glycogen in the muscles whereby the nutritive value of the latter increases. The experiments of other authors permit of the conclusion that the treatment mentioned may occasionally bring about protein accumulation. This problem should still be examined.

The adrenal glands (and the other endocrine organs) of the treated and untreated hogs were separately examined. On the basis of the determination of their weight we stated that the adrenals of both treated groups were considerably, about 40 per cent, enlarged in comparison with the normal adrenals. An extract of the cortical substance was prepared of the adrenals of both, treated and untreated, groups by Swingle—Pfiffner's method and the efficacy of the extracts was estimated on infantile white mice deprived of their adrenals with Bomskov—Bahnsen's technique. The adrenals of the hogs treated at the farm of N. M. contained 6.92 times, those of the farm of Cs. P. 7.53 times, as much effective substance as the adrenals of the untreated hogs bred at the same farm. These data show that the treatment applied resulted in a hyperfunction of the adrenal glands.

If infantile white mice deprived of their adrenals were treated with the same number of mouse units of cortex hormone made of the adrenals of treated and untreated hogs, the mice to which the extract of adrenals of treated hogs was administered survived for twice as long a time as the mice treated with the adrenal extract of the control hogs. This result is an evidence for the statement that the hormone obtained from the adrenals of treated animals is more stable and effective than that obtained from the adrenals of untreated animals.

These data undoubtedly show that the weight increase brought about by the therapy applied is a sequel of the hyperfunction of the adrenal cortex.

This statement is in full accordance with the observations of other authors (van Herwerden, Fieschi, Cameron and White, Eaton and his co-workers, Thaddea) who produced increase of body weight in experimental animals by repeated parenteral administration of extracts of adrenal cortex. Verzár and al. have demonstrated that the hormone of the adrenal cortex promotes the absorption of fats, carbohydrates and amino acids (proteins) from the intestinal mucosa.

Having compared our results with the data of literature we give following explanation for the mechanism of our fattening procedure. The moderate and temporary shift of the acid-base balance toward acidity enhances the function of the suprarenal cortex. Latter promotes the absorption of food from the bowels whereby the food is better utilised. This is the factor responsible for the increase in body weight. Besides this, the role of other endocrine factors too is to be taken into consideration (hypophysis, diencephalon, etc.). These relationships of the problem demand further investigation. According to our data, the treatment described may serve as an efficient contribution to the increase of fat production.

Our results are very promising from an economic, pharmaco-industrial, and therapeutic aspect alike.

These fattening experiments had been finished by the end of 1941. The results were written as a monograph early 1942. Since then, the work has been ready for publication it could, however, not been published because of the war and for economic difficulties. The examinations reported form the base of our further experiments in which the chemical influences acting on other endocrine organs have been examined. The results of the latter investigations should be soon published.