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STUDIES ON THE CONTROL OF GROWTH
HORMONE SECRETION IN THE RAT

Thesis for the Degree of M. S.
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Elias Dickerman

1968

THESIS



STUDIES ON THE CONTROL OF GROWTH HORMONE SECRETION
IN THE RAT

ABSTRACT

By Elias Dickerman

I. IN VITRO ASSAY FOR GROWTH HORMONE RELEASING
FACTOR (GH-RF)

A four hour incubation method was developed for assaying rat hypothalamic growth hormone releasing factor (GH-RF). Anterior pituitaries from donor rats were hemisected and distributed randomly into flasks containing 4 ml of protein-free medium 199. Six pituitaries (12 halves) were used per flask. The pituitaries were pre-incubated for 1 hour, the medium was discarded and fresh medium containing neutralized acid extract of rat hypothalamus or cerebrum was added. These were incubated for 4 hours under constant gassing with 95% O₂-5% CO₂, and the medium was analyzed for GH by the standard tibia test.

A log-dose relationship was demonstrated when increasing amounts of hypothalamic extract were incubated with rat pituitary. Graded doses of cerebral extract failed to demonstrate such a relationship, indicating that GH-RF exists as a specific hormone in the hypothalamus. Analysis of pituitary

incubation medium at two dose levels showed log-dose relationships in all cases, indicating that the hormone assayed in the medium was GH. This method is suitable for measuring quantitative changes in hypothalamic content of GH-RF.

II. EFFECTS OF STARVATION ON PLASMA GH ACTIVITY, PITUITARY GH, AND HYPOTHALAMIC GH-RF LEVELS IN THE RAT

The effects of complete food removal for 7 days were measured on plasma GH activity, hypothalamic content of growth hormone releasing factor (GH-RF) and pituitary concentration of growth hormone (GH) in male rats. Control male rats were starved or fed ad libitum for 7 days. In another experiment, the starved rats received replacement doses of L-Na-thyroxine (2.5 ug/100 g body weight/day) beginning on day 2 of starvation. On day 8 all rats were weighed, anesthetized with ether and bled from the abdominal aorta. The pituitaries were removed and individually weighed; the hypothalami were placed in ice cold 0.1N HCl (0.1 ml/hypothalamus). Hypothalamic GH-RF was assayed by the in vitro incubation method described above. Lyophilized plasma, anterior pituitaries, and incubation medium were assayed for GH by the standard tibia test, using a 4 point assay procedure. Statistical analysis of the data showed a significantly lower plasma GH content in starved or

thyroxine-treated starved rats ($P < 0.01$). Pituitary GH content and hypothalamic content of GH-RF were also significantly reduced in the starved rats. These results indicate that starvation in the rat not only lowers the levels of GH-RF in the hypothalamus and of GH in the pituitary, as shown previously, but also leads to a decrease in plasma GH activity.

STUDIES ON THE CONTROL OF GROWTH HORMONE SECRETION
IN THE RAT

By

Elias Dickerman

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

MASTER OF SCIENCE

Department of Physiology

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Dedicated

to

my Family

ACKNOWLEDGMENTS

The author wishes to express his gratitude to Dr. Joseph Meites, Professor of Physiology, for his instruction and inspiration throughout the course of this study. Without his patient guidance this manuscript would not have been possible. Appreciation is expressed to Dr. Andres Negro-Vilar for the informative discussions incurred during the course of this study. An expression of thanks is also extended to the members of the guidance committee, Drs. W. D. Collings, H. D. Hafs, G. D. Riegler, and H. A. Tucker for their help in the preparation of this manuscript.

Special indebtedness is due to Michigan State University and Dr. J. Meites for the financial assistance during this project. Purified ovine GH was kindly supplied by the Endocrinology Study Section, National Institutes of Health, Bethesda, Maryland.

A note of thanks is extended to Mrs. Joan Heaphy for her kind help in preparing this manuscript. Finally, a special thanks to my wife, Katherine, and my daughter, Beyle Sue, for their inspiration, understanding and patience during the time spent in this study.

1. The first part of the document discusses the importance of maintaining accurate records of all transactions.

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8. Accounts payable should be monitored closely to ensure timely payments and avoid penalties.

9. Accounts receivable should be managed effectively to maximize cash flow and minimize bad debts.

10. The final part of the document discusses the importance of maintaining accurate financial statements.

11. These statements provide a clear and concise overview of the organization's financial performance.

12. They are essential for decision-making and for providing transparency to stakeholders.

13. The document concludes by emphasizing the need for ongoing monitoring and reporting.

14. Regular reviews and updates are necessary to ensure the accuracy and relevance of the information.

15. By following these guidelines, organizations can ensure the integrity and reliability of their financial data.

16. This will help them to make informed decisions and maintain a strong financial position.

17. The document is intended to serve as a comprehensive guide for all financial management activities.

18. It is hoped that these guidelines will be helpful and informative for all users.

19. Thank you for your attention and cooperation in this matter.

20. Sincerely,
[Signature]

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INTRODUCTION

The nervous and endocrine systems are responsible for the integration and coordination of the remaining systems of the body. The relationship between these two controlling systems is close and intricate, and only in the last 10-15 years has information clarified this relationship.

It is now known that neuroendocrine mechanisms regulate a wide variety of body functions. The brain is responsible for control of secretions from the anterior and posterior pituitary as well as from the intermediate lobe of the pituitary. Through hypothalamic control of anterior pituitary secretion, the brain regulates thyroid, adrenocortical and gonadal secretions as well as body growth. The control of anterior pituitary secretions is exerted through releasing and inhibiting factors (hormones) in the hypothalamus: corticotropin releasing factor (CRF), thyrotropin releasing factor (TRF), follicle stimulating hormone releasing factor (FSH-RF), luteinizing hormone releasing factor (LRF), prolactin inhibiting factor (PIF), growth hormone releasing factor (GH-RF) and possibly a GH inhibiting factor (GH-IF). Thus, the classical concept of the pituitary as the master gland of the body needs to be revised to include a brain-pituitary relationship.

2.

Evidence for a physiological role for GH-RF has been slow to accumulate. This reflects, primarily, the lack of good and non-cumbersome methods for the measure of the hypothalamic releasing factor (GH-RF) as well as a lack of a sensitive method for the estimation of GH in the body fluids.

It was of interest, therefore, to attempt to develop a short term incubation method for assaying rat hypothalamic GH-RF which would show log-dose response characteristics and would be sensitive enough to detect quantitative changes in hypothalamic content of GH-RF. This study was also concerned with showing the effects of starvation on plasma GH activity, pituitary GH and GH-RF levels in the rat, in an attempt to correlate the previously reported observations of decreased pituitary content of GH and hypothalamic GH-RF with plasma GH levels.

REVIEW OF THE LITERATURE

I. Nervous Control of Anterior Pituitary (AP) GH Secretion

Although the release of GH from the anterior pituitary is generally thought to be under hypothalamic influence, the dependence of GH secretion on the central nervous system (CNS) has been difficult to elucidate because of a unique characteristic of GH. Growth hormone does not have a specific target organ nor does it stimulate a gland to secrete hormones, as is the case with FSH, LH, TSH and ACTH. Growth hormone acts on general growth processes of the body, and these include important influence on protein, fat and carbohydrate metabolism. However, despite this difficulty, several methods have been used to study the influence of the CNS on AP secretion of GH. These methods include one of two categories: (a) those that measure body growth, (b) those that measure pituitary GH content or release of GH from the pituitary. Several methods in each category are considered below.

A. Body Growth as a Parameter of CNS Control of AP Secretion of GH

The description of the hypophyseal portal system by Popa and Fielding (1933), and the observations by Houssay et. al. (1935), Wislocki and co-workers

(1936, 1937, 1938) and by Green and Harris (1949) of the correct direction of blood flow, from the hypothalamus down to the pituitary, led to the suggestion by Green and Harris (1949) that humoral agents are secreted into these hypophyseal portal veins and travel to the pituitary and there exert a regulatory influence on the secretion of anterior pituitary hormones. The indirect approaches to answer this problem consisted in the elimination of hypothalamic influence on the AP by pituitary stalk section or pituitary transplants, and by electrical lesions or stimulation of brain tissue.

Pituitary stalk section in rabbits did not inhibit growth according to Westman and Jacobsohn (1940), although it induced marked gonadal atrophy. A temporary growth delay was observed by Uotila (1939) in rats following stalk section. Pituitary stalk section in goats by Daniel and Prichard (1964) produced severe metabolic disturbances as well as blunted growth of body and pituitary target organs during the first few months after operation. These observations, rather inconclusive, were explained by Harris (1950) to be the result of partial sectioning of the stalk or as a consequence of portal system regeneration.

The observations on brain lesions are perhaps better substantiated. Clinically, growth disturbances

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2. The second part of the document outlines the various methods and tools used to collect and analyze data. It highlights the need for consistent data collection procedures and the use of advanced analytical techniques to derive meaningful insights from the data.

3. The third part of the document focuses on the role of technology in data management and analysis. It discusses how modern software solutions can streamline data collection, storage, and processing, thereby improving efficiency and accuracy.

4. The fourth part of the document addresses the challenges associated with data management, such as data quality, security, and privacy. It provides strategies to mitigate these risks and ensure that the data remains reliable and secure throughout its lifecycle.

5. The fifth part of the document discusses the importance of data governance and the establishment of clear policies and procedures. It emphasizes that effective data governance is crucial for ensuring that data is used responsibly and in compliance with relevant regulations.

6. The sixth part of the document explores the role of data in decision-making and strategic planning. It highlights how data-driven insights can help organizations identify opportunities, assess risks, and make informed decisions that drive growth and success.

7. The seventh part of the document discusses the importance of data literacy and the need for ongoing training and development. It emphasizes that all employees should have a basic understanding of data and be able to interpret and use it effectively in their work.

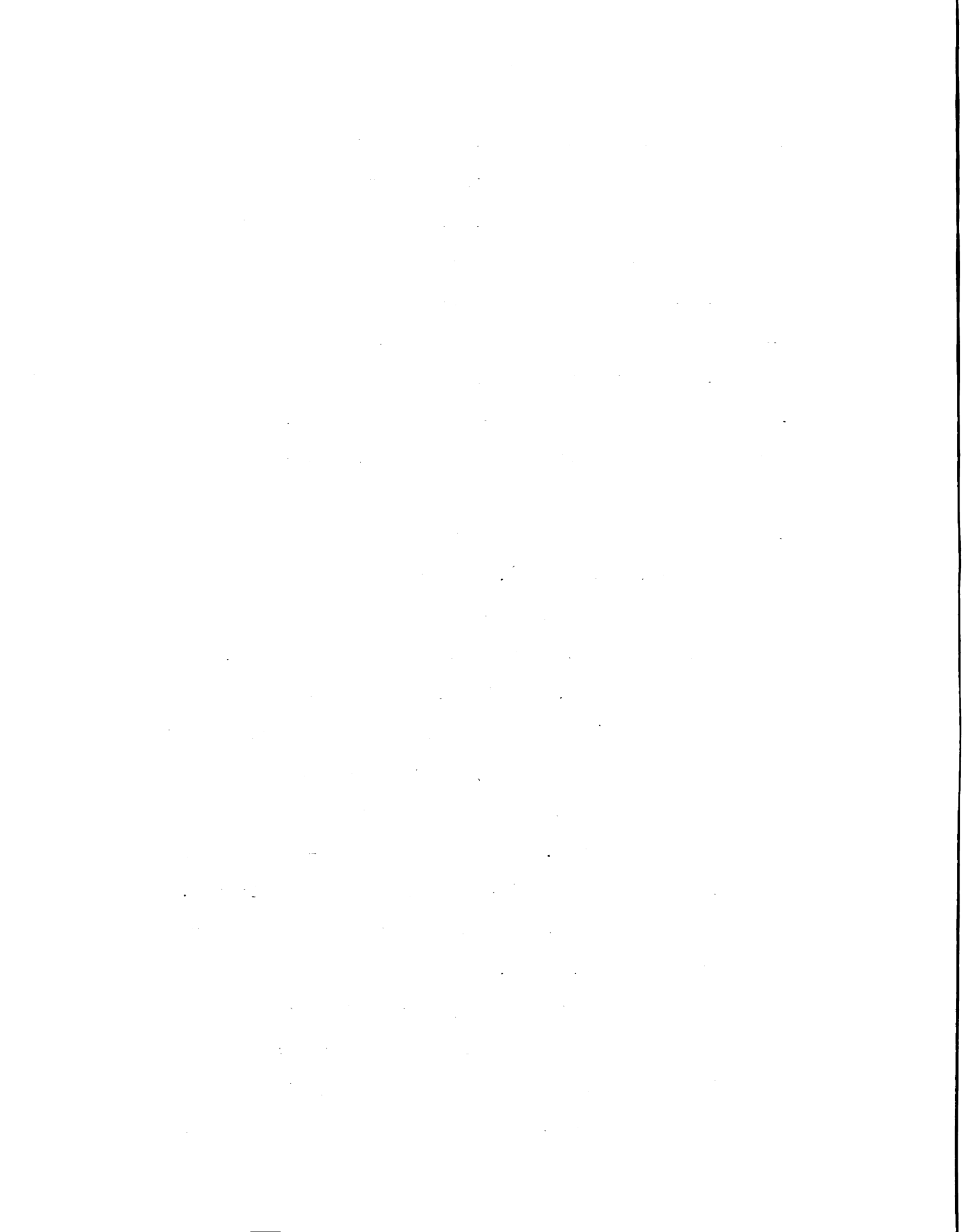
8. The eighth part of the document discusses the importance of data ethics and the need to consider the potential impact of data collection and analysis on individuals and society. It emphasizes that organizations should be transparent about their data practices and should take steps to protect the privacy and rights of individuals.

9. The ninth part of the document discusses the importance of data sharing and collaboration. It highlights how sharing data across different departments and organizations can lead to new insights and innovations, and how collaboration is essential for maximizing the value of data.

10. The tenth part of the document discusses the importance of data archiving and backup. It emphasizes that organizations should have a robust data backup strategy in place to ensure that their data is protected and can be recovered in the event of a disaster or data loss.

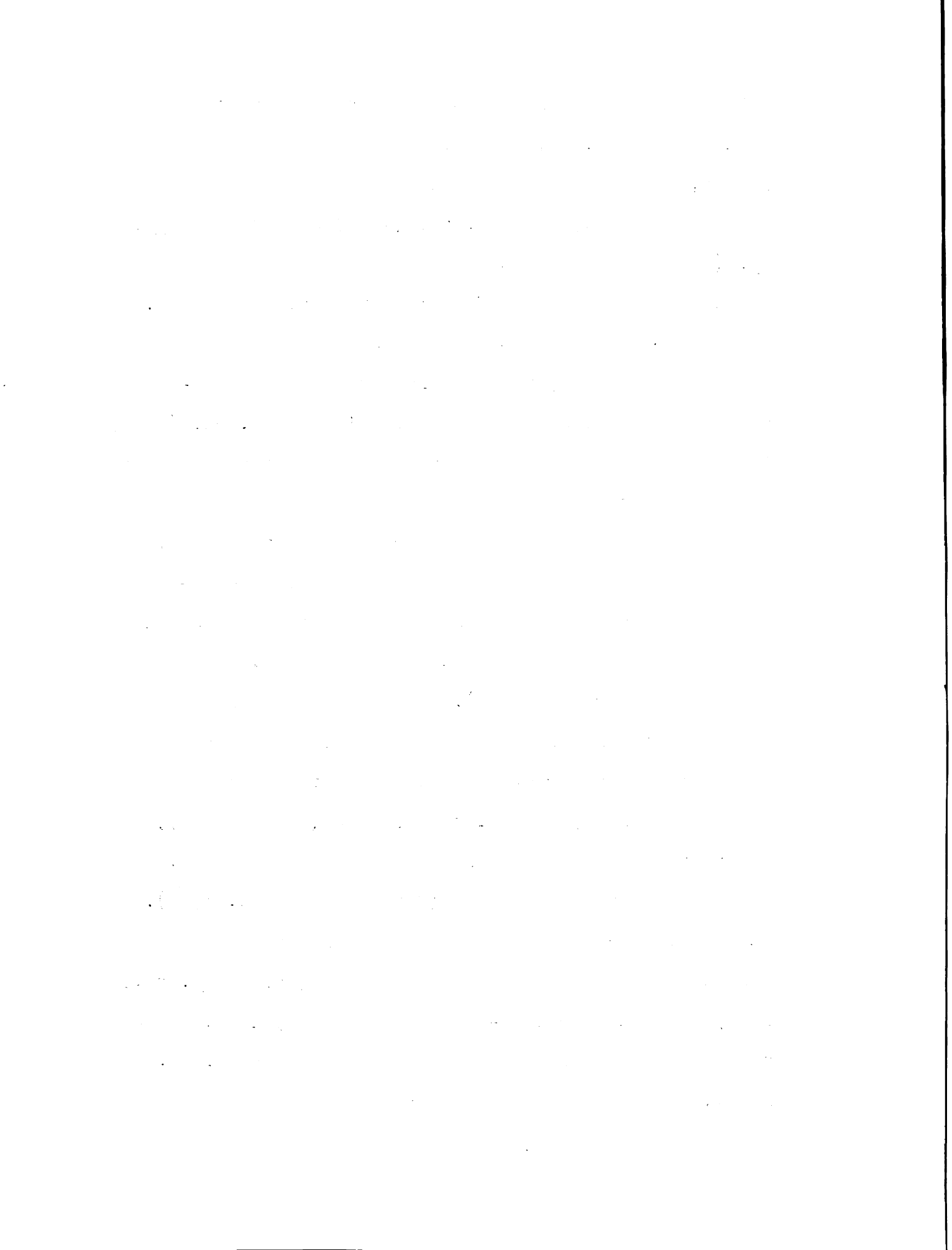
due to brain tumors have been known for many years (Armstrong and Durh, 1922). Cahane and Cahane (1938) injured the hypothalamic area in rats and observed a reduction in body growth. They suggested a possible role for the nervous system in controlling GH secretion. However, difficulties arise in the interpretation of the results obtained. Where extensive lesions are involved, the possibility of involving the areas controlling the secretion of the other AP hormones cannot be excluded. Cerebral lesions may also interfere with food intake and temperature regulation (Bogdanove and Lipner, 1952; Bernardis et. al., 1963). Reichlin (1960 a) showed that lesions of the median eminence and primary portal plexus of the stalk significantly reduced the growth rate of rats. Taking into account the possibility of altered secretions of the remaining AP hormones, Reichlin (1960 b) in a subsequent study injected vasopressin, testosterone and thyroxine to the injured animals. He also used pair-fed controls to exclude the effect of differences in food intake. He found that body growth was not restored to normal following this treatment.

In a more elegant study, where pituitary GH concentration was measured in injured animals, Reichlin (1961) showed that GH content in injured animals was reduced to 15% of that found in non-injured



animals, when measured by the standard tibia test of Greenspan et. al. (1949). These results (Reichlin 1960 a, 1960 b, 1961) and those of Hinton and Stevenson (1962), Bach et. al. (1964) and Endroczi et. al. (1956) suggest that lesions involving the anterior hypothalamus were most effective in retarding growth. This region comprises the area bounded by the supraoptic nucleus, the anterior half of the median eminence and the arcuate nuclei. O'Brien et. al. (1964) found that electrical stimulation of the paraventricular nuclei of weanling kittens caused acceleration of growth as measured by body weight and tibial length.

In general, pituitary transplants to hypophysectomized rats have been able to maintain some degree of growth (Greep, 1936; Martini and de Poli, 1956; Goldberg and Knobil, 1957). Pituitary transplants were made in different areas with lesser or greater success: the anterior chamber of the eye (Goldberg and Knobil, 1957), the kidney capsule (Hertz, 1959), the abdominal cavity (Swelheim and Wolthius, 1962), or the subcutaneous tissues (Meites and Kragt, 1964). The differences in degree of success in part may be related to the site of transplantation (Halasz et. al., 1962, 1963; Nikitovitch-Winer and Everett, 1958) as well as to the age of the pituitary donor (Meites et. al., 1962), the delay in transplantation after hypophysectomy



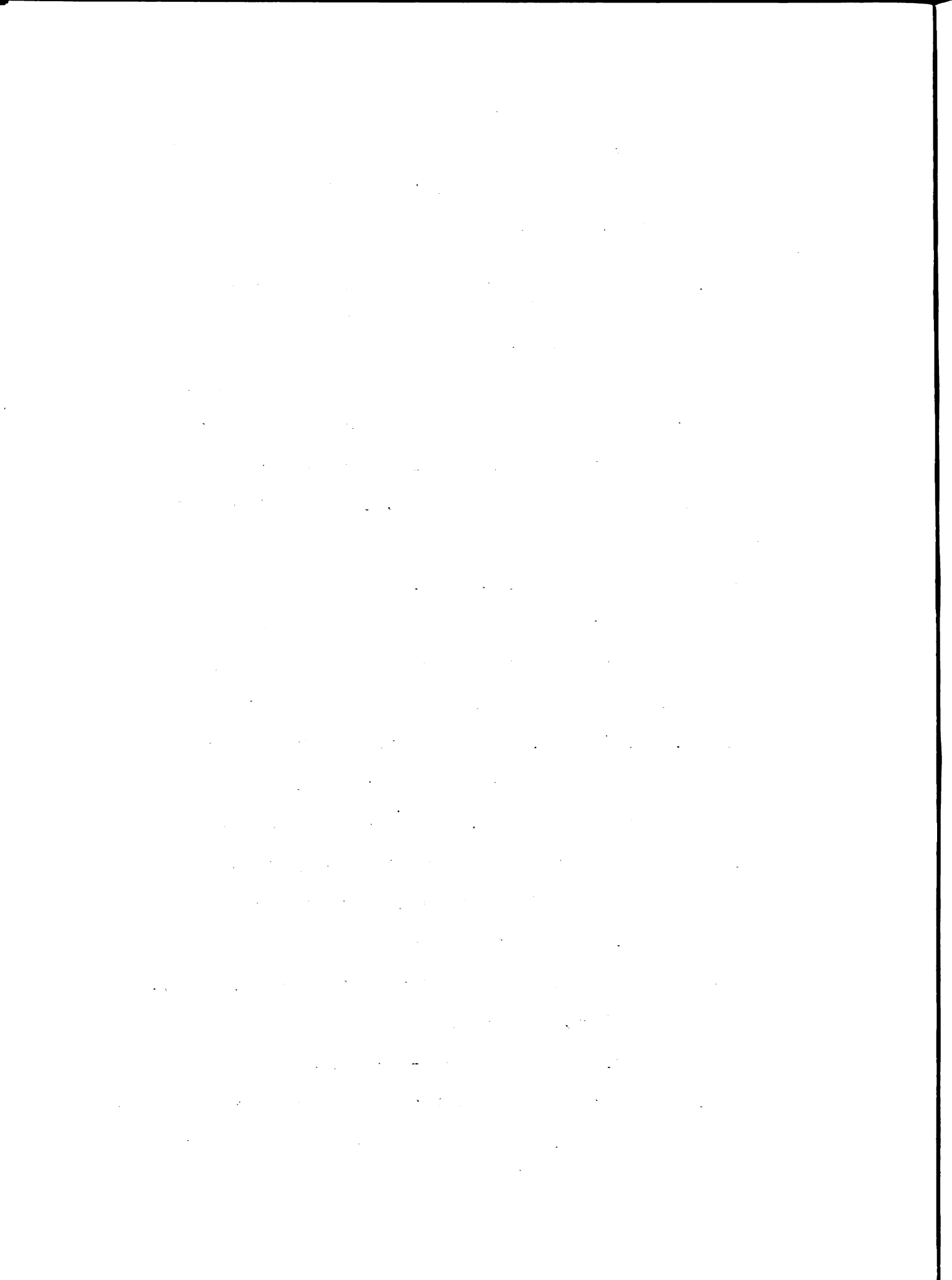
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(Smith, 1961), the amount of viable anterior pituitary tissue present in the grafts, and to post-graft immunological factors.

B. Anterior Pituitary Content or Release of GH as a Function of CNS Control

The direct measurement of pituitary GH content in animals injected with median eminence extracts, as well as the measurement of pituitary content and release of GH into medium after incubation of pituitary tissue with median eminence extracts, constitutes the best evidence for the control of AP synthesis and release of GH by neural tissue.

The first attempt to show the existence of a factor in neural tissue responsible for controlling the release of anterior pituitary GH was that of Franz et. al. (1962). Although the authors concluded that there was growth hormone releasing activity in the hypothalamus of swine, their work and conclusions have been criticized since standard assay procedures were not followed and large variations in response were obtained. Deuben and Meites were the first to show conclusive evidence in this regard (1963, 1964). They reported that neutralized acid extracts of rat hypothalamus produced a 4 to 6-fold increase in GH release by rat anterior pituitary after a 6 day culture. Cerebral cortex failed to increase GH secretion upon



culture. Deuben and Meites (1965) also reported reinitiation of pituitary GH release in vitro by a neutralized acid extract of rat hypothalamus after release had ceased. These findings have been confirmed using in vitro (Schally et. al. 1965; Schally et. al., 1968; Krulich et. al., 1967) and in vivo methods (Pecile et. al., 1965; Muller et. al., 1965; Muller and Pecile 1965; Krulich et. al., 1965; Schally et. al. 1966; Dhariwal et. al. 1966; Machlin et. al. 1967).

The specificity of in vivo assay procedures for hypothalamic GH-RF has been questioned by Rodger et. al. (1967), although dose-response relationships have been reported by Meites and Fiel (1965) and Katz et. al. (1967). Dose-response relationships have not yet been demonstrated for in vitro methods of assay for GH-RF (Schally et. al. 1965; Schally et. al. 1968; Krulich et. al. 1967). It was of interest therefore, to attempt to develop a short term incubation method for assaying rat hypothalamic GH-RF which would be sensitive enough to detect quantitative changes in hypothalamic content of GH-RF.

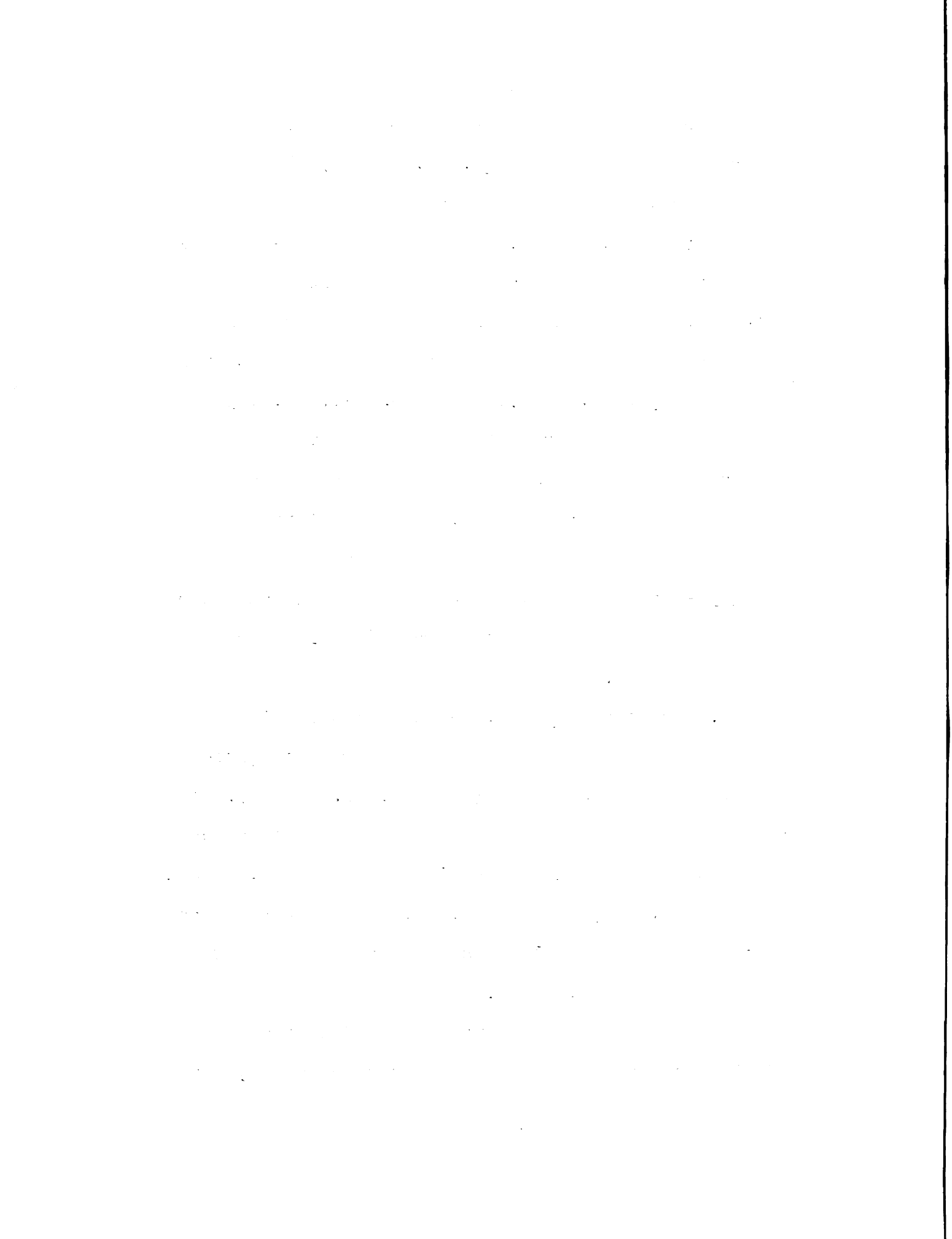
II. Factors Affecting GH Secretion

A. Environmental Factors. The advent of radio-immunological methods for measuring GH in body

fluids greatly advanced our understanding of GH control in humans. Roth et. al. (1963a) showed that moderate exercise stimulated human growth hormone (HGH) secretion. The rise in plasma GH could be blunted by the feeding of glucose prior to the exercise. Abdominal and chest surgery under ether anesthesia was frequently followed by an elevation in HGH (Glick et. al. 1965). Takahashi et. al. (1968) have reported increased HGH associated with the initiation of sleep, not related to changes in glucose, insulin or cortisol. It is of interest to note in this respect, that exercise, moderate or severe hypoglycemia, and cold, all known to elicit GH secretion in humans, failed to do so in rats (Schalch and Reichlin, 1967).

B. Hormonal Factors. Administration of insulin in doses large enough to lower blood glucose resulted in increased HGH (Roth et. al. 1963 b). The increased HGH with insulin induced hypoglycemia has been confirmed by Hunter and Greenwood (1964), Frantz and Rabkin (1964) and others. It is of interest that ethanol induced hypoglycemia does not increase HGH (Arky and Freinkel, 1954).

Thyroidectomy in the rat resulted in a degranulation of pituitary acidophiles (Purves and Griesbach, 1946;



Schooley et. al., 1966), a decrease in growth rate (Koneff et. al. 1949; Schooley et. al. 1966) and a decrease in pituitary GH content (Contopoulos et. al., 1958; Knigge, 1958; and Schooley et. al., 1966). Hyperthyroidism in rats also produced blunting of body growth, degranulation of pituitary acidophiles and a reduction in pituitary content of GH (Solomon and Greep, 1959). The interference to growth by estrogens has been suspected for some time (Gaarenstrom and Levie, 1939; Reece and Leonard, 1939) although the mechanism of action remains uncertain (Meites, 1949a; Sullivan and Smith, 1957; Josimovich et. al. 1967; and Birge et. al., 1967). The study by Birge et. al. (1967) suggests that diethylbesterol incubated with rat anterior pituitary caused suppression of GH release, but had no effect on the amount stored in the pituitary. Androgens, on the other hand, stimulate growth when given in small doses (Rubinstein and Solomon, 1941). The effects of corticosteroids may be similar to those observed with high doses of androgens (Evans et. al., 1943; Marx et. al., 1943; and Geschwind and Li, 1955), in which growth of long bones ceases by the closing of the epiphyses.

C. Food Intake. Reduced food intake or starvation have been reported to decrease pituitary, thyroid, and gonadal weights in the rat (Jackson, 1916;

Jackson, 1917; and Mulinos and Pomerantz, 1941). The resultant decreases in gonadal (Mulinos *et. al.*, 1939) and thyroid functions (Stephens, 1940; Meites 1949 b; and Meites and Wolterink, 1950) apparently are due to a fall in circulating gonadotropins and thyrotropin. The decrease in gonadotropins may be due in part to a direct action of under-nutrition on the hypothalamus, resulting in reduced synthesis and release of hypothalamic releasing factors (Placksek and Meites, 1967; Negro-Vilar, Dickerman and Meites, 1968). Underfeeding has also been reported to result in reduced absolute adrenal weight in the rat (Quimby, 1948).

The decrease in body growth and skeletal length that occurs during starvation in the rat may be due in part to a reduced level of pituitary GH (Meites and Fiel, 1965; Friedman and Reichlin, 1965) and in hypothalamic growth hormone releasing factor (Meites and Fiel, 1965). Since these observations can be interpreted as indicative of increased as well as of decreased release of GH from the pituitary and of GH-RF from the hypothalamus, it was of interest to determine plasma GH activity in addition to hypothalamic GH-RF content and pituitary GH concentration during starvation in the rat.

1. The first part of the document discusses the importance of maintaining accurate records of all transactions. It emphasizes that every entry should be supported by a valid receipt or invoice to ensure transparency and accountability.

2. The second section outlines the procedures for handling discrepancies between the recorded amounts and the actual cash flow. It suggests a systematic approach to identify the source of the error and correct it promptly.

3. The third part of the document addresses the need for regular audits to verify the accuracy of the financial statements. It recommends that these audits be conducted by an independent party to avoid any potential conflicts of interest.

4. The fourth section discusses the importance of keeping all financial records for a sufficient period of time, as required by law. It provides guidance on how to organize and store these records to facilitate easy access and retrieval.

5. The fifth part of the document covers the process of reconciling the bank statements with the company's internal records. It highlights the importance of identifying and resolving any differences between the two sets of records.

6. The sixth section discusses the importance of maintaining up-to-date financial statements to provide a clear picture of the company's financial health. It suggests that these statements should be prepared on a regular basis and reviewed by management.

7. The seventh part of the document addresses the need for proper documentation of all financial transactions. It emphasizes that every transaction should be properly recorded and supported by the appropriate documentation.

8. The eighth section discusses the importance of maintaining accurate records of all assets and liabilities. It suggests that these records should be updated regularly to reflect any changes in the company's financial position.

9. The ninth part of the document covers the process of preparing and filing the annual financial statements. It provides a step-by-step guide to ensure that all necessary information is included and that the statements are filed on time.

10. The tenth and final section discusses the importance of maintaining accurate records of all financial transactions. It emphasizes that every entry should be supported by a valid receipt or invoice to ensure transparency and accountability.

EXPERIMENTAL METHODS AND MATERIALS

I. Animals

A. Experimental Animals

Intact male rats of the Sprague-Dawley strain (Holtzman, Madison, Wisc.) weighing about 290-310g each, were used as control and experimental animals.

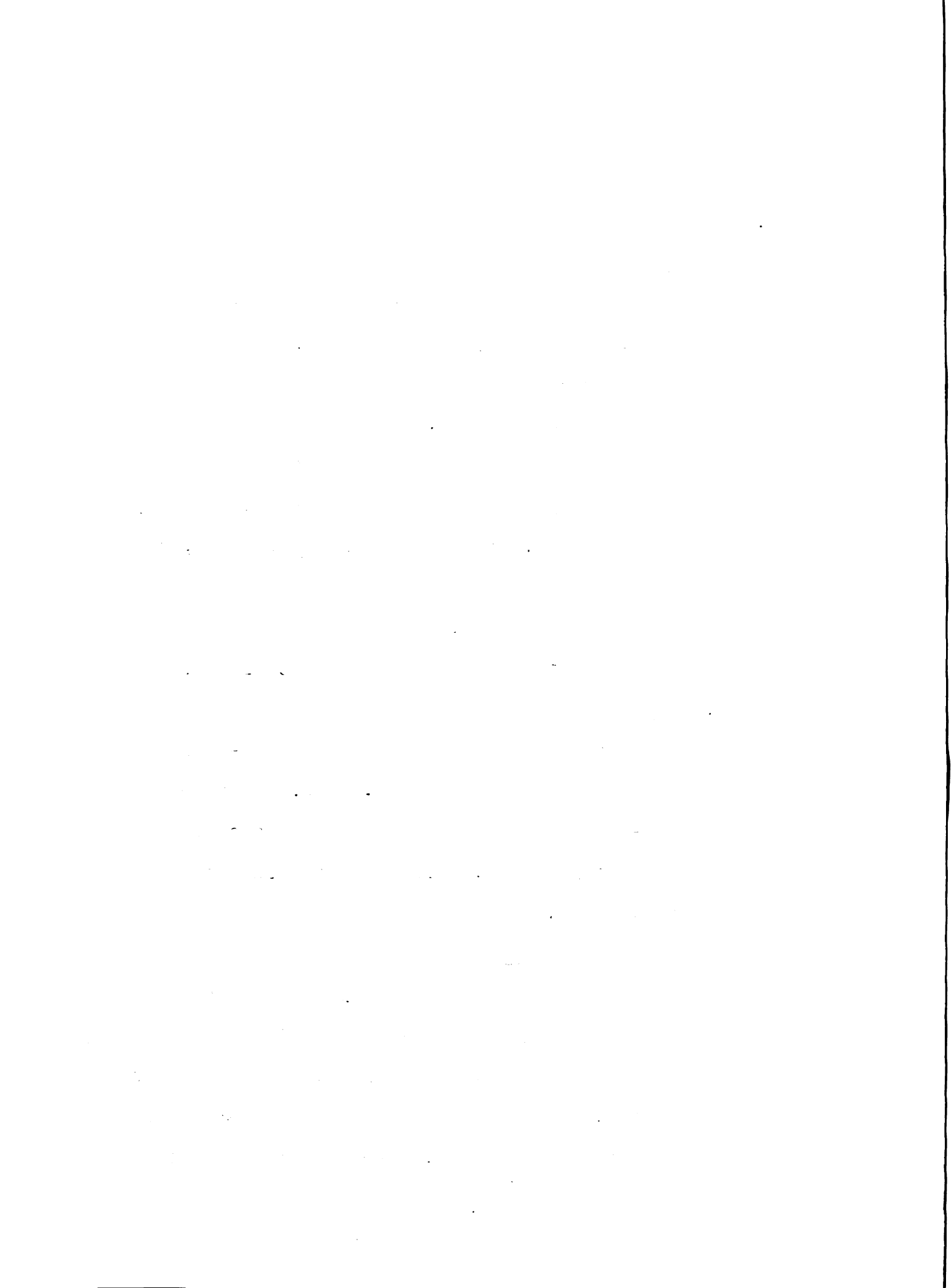
Control animals were maintained on a diet of Wayne Lab Blox pellets (Allied Mills, Chicago, Ill.) and fed ad libitum. Food, but not water, was removed from the experimental animals for 7 days. The rats were weighed at the beginning and end of each experiment.

B. Donor Animals

Mature male rats of the Sprague-Dawley strain (Holtzman, Madison, Wisc.) weighing 200-220g each, were used as hypothalamic and pituitary donors. All donor animals were fed ad libitum.

C. Bioassay Animals

Animals for GH bioassays were immature female rats (Charles River Breeding Laboratories, Wilmington, Mass.) hypophysectomized at 26 days of age. They were used for GH bioassay 15-16 days after operation. The regular diet of



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these animals was supplemented daily with orange slices, carrots and sugar cubes. All bioassay as well as experimental animals were housed in a temperature controlled room ($25 \pm 1^{\circ}\text{C}$) with automatically controlled lighting (14 hr light daily).

II. Preparation of Hypothalamic Extracts (HE), Pituitaries and Plasma

A. Preparation of Hypothalamic Extracts (HE)

Donor rats were killed by decapitation and their hypothalami and/or pituitaries were removed. The hypothalami were placed in ice cold 0.1N HCl (0.1 ml per hypothalamus) and homogenized in a total volume of 0.15 ml per hypothalamus. The homogenate was centrifuged at 12,000g for 40 minutes at 4°C . Just prior to use, the supernatants were placed in protein free medium 199 (Difco Labs., Detroit, Mich.) and the pH was adjusted to 7.4 by adding 1N NaOH a drop at a time and testing with glass electrodes. The same procedure was used in preparing cerebral extracts (CE).

B. Preparation of Pituitary Tissue for Assay

The pituitaries were removed from the control and experimental animals, individually weighed and stored at -20°C . Prior to assay,

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the pituitaries were thawed, homogenized in saline and injected as an aqueous suspension into assay rats.

C. Preparation of Plasma for Assay

Blood was collected from the control and experimental animals via the abdominal aorta with a heparinized syringe. The blood from each group was pooled, centrifuged at 4 C and the plasma obtained immediately lyophilized and stored at -20 C. Lyophilized plasma was reconstituted to the desired volume with saline prior to being injected into the assay animals. A volume of 2 ml daily was injected intraperitoneally into each assay rat.

III. Incubation

The posterior lobe was removed from each donor pituitary and the anterior lobe was hemisected. The halves were randomly distributed in the incubation flasks. A total of 6 anterior pituitaries (12 halves) were placed in each flask. In preliminary experiments it was observed that pre-incubation of the pituitaries increased the precision of the assay, suggesting that during this time release of GH occurred as a result of injury to the tissue. After a number of preliminary

trials to determine the optimal pre-incubation and incubation times, the following procedure was adopted. The pituitaries were pre-incubated in 4 ml of medium 199/flask for 1 hour and the medium was discarded. Four ml of fresh medium containing the neutralized acid extract of hypothalamus or cerebrum was rapidly added to the flasks, and 4 hours later the incubation was terminated. The pituitary tissue was weighed and the medium stored at -20 C until assayed. Incubations were carried out in a Dubnoff metabolic shaker (60 cycles per minute) under constant gassing with 95% O₂-5% CO₂ at 37 C.

IV. GH Bioassay and Statistical Treatment

Growth hormone activity was measured by the standard tibia test of Greenspan et. al. (1949). Aqueous solutions of incubation medium, pituitary homogenate, or reconstituted plasma were injected intraperitoneally once a day for 4 days. Each assay included two or more doses of the control and experimental unknown solutions, as well as two doses of NIH-GH-S8 for reference standards. NIH-GH-S8 was kindly supplied by the Endocrinology Study Section, NIH.

The data were analyzed by linear regression or one way analysis of variance. Breakdown of significance was determined by Duncan's Multiple range test (Bliss, 1967).

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3. The third part of the document focuses on the role of management in overseeing the data collection and analysis process. It stresses that management should ensure that the data is reliable and that the analysis is conducted in a fair and unbiased manner.

4. The fourth part of the document discusses the importance of communicating the results of the data collection and analysis to the relevant stakeholders. It emphasizes that clear and concise communication is essential for ensuring that the information is understood and acted upon.

5. The fifth part of the document concludes by summarizing the key points discussed and reiterating the importance of maintaining accurate records and using appropriate data collection and analysis methods.

EXPERIMENTAL

I. IN VITRO ASSAY FOR GROWTH HORMONE RELEASING FACTOR (GH-RF)

A. Objectives

The purpose of these experiments was to develop a short term incubation method for assaying rat hypothalamic GH-RF which would show log-dose response characteristics and be sensitive enough to detect quantitative changes in hypothalamic content of GH-RF.

B. Procedures

Donor rat pituitary tissue was pre-incubated in medium 199 for 1 hour. The medium was discarded. Fresh medium containing the neutralized acid extracts were then added to the flasks and incubated for 4 hours. Extract equivalent to 0.75, 1.50, 3.00 or 6.00 rat hypothalami were added to each flask containing six pituitaries. This corresponds to 0.125, 0.250, 0.500 and 1.000 hypothalamic equivalent per incubated pituitary. Rat cerebral extract was used as a control. The medium was then assayed for GH by the standard tibia test of Greenspan et. al. (1949).

C. Results

1. Dose response relationship between hypothalamic extract and anterior pituitary (AP) GH release in vitro. Hypothalamic extracts were assayed at 4 doses of 0.125, 0.250, 0.500 and 1.000 hypothalamic equivalent per incubated pituitary. Cerebral extract was assayed at a dose corresponding to the highest dose of hypothalamic extract/incubated AP. It can be seen in Table I and Fig. 1 that when progressively greater amounts of hypothalamic extract were incubated with male rat pituitaries, more GH was released into the medium. Regression analysis of the data showed these differences to be highly significant ($p < 0.001$). Breakdown of significance by a Duncan's Multiple range test showed each point to be significantly different from the next lower point ($p < 0.05$ or $p < 0.01$). GH release by the pituitaries incubated with cerebral extract was significantly less ($p < 0.01$) than released by the lowest dose of hypothalamic extract (0.125 HE/incubated AP).
2. Comparison of cerebral versus hypothalamic extract on AP release of GH. Cerebral and hypothalamic extracts were assayed at two dose levels (0.25 and 1.00 CE or HE/incubated AP).

The first part of the document discusses the importance of maintaining accurate records of all transactions. It emphasizes that proper record-keeping is essential for the integrity of the financial system and for the ability to detect and prevent fraud. The text also mentions the need for regular audits and the role of independent auditors in ensuring the reliability of financial statements.

In addition, the document highlights the significance of transparency and accountability in financial reporting. It states that stakeholders, including investors and the public, have a right to know how their money is being managed. This requires the implementation of robust internal controls and the disclosure of relevant information in a clear and concise manner.

The document further explores the challenges faced by organizations in maintaining high standards of financial reporting. It identifies factors such as complex transactions, rapid technological changes, and the pressure to meet short-term performance targets as potential obstacles. It suggests that organizations should invest in training and professional development to ensure that their staff are equipped with the necessary skills to address these challenges.

Finally, the document concludes by reiterating the importance of a strong ethical foundation in financial reporting. It argues that a commitment to integrity and honesty is not only a moral imperative but also a practical necessity for the long-term success of any organization. By fostering a culture of ethical behavior, organizations can build trust with their stakeholders and ensure the sustainability of their operations.

The document also includes a section on the role of regulatory bodies in overseeing financial reporting. It discusses the need for effective supervision and enforcement of financial reporting standards to maintain confidence in the financial system. It suggests that regulatory bodies should work closely with industry organizations to develop and update standards that reflect the latest developments in the field.

Table I. Dose Response Relationship Between Hypothalamic Extract and Anterior Pituitary GH Release in vitro

Group	HE ^a or CE ^b equivalents/ incubated AP	No. of assay rats	Average tibial width (u) mean ± SE
1	1.000 CE	4	177.6±6.8
2	0.125 HE	4	194.2±4.5 ^{d,e}
3	0.250 HE	4	214.8±4.5 ^e
4	0.500 HE	4	227.9±3.6 ^f
5	1.000 HE	4	244.5±1.6 ^e
6	Hypox ^c assay controls	4	117.0±3.7

^aHE: hypothalamic extract

^bCE: cerebral extract

^cHypox: hypophysectomized

^dCompared against CE

^ep<0.01. Compared against next lower dose.

^fp<0.05. Compared against next lower dose.

Reference Standard: NIH-GH-S8

25 ug = 201.3±2.8

100 ug = 231.8±2.7

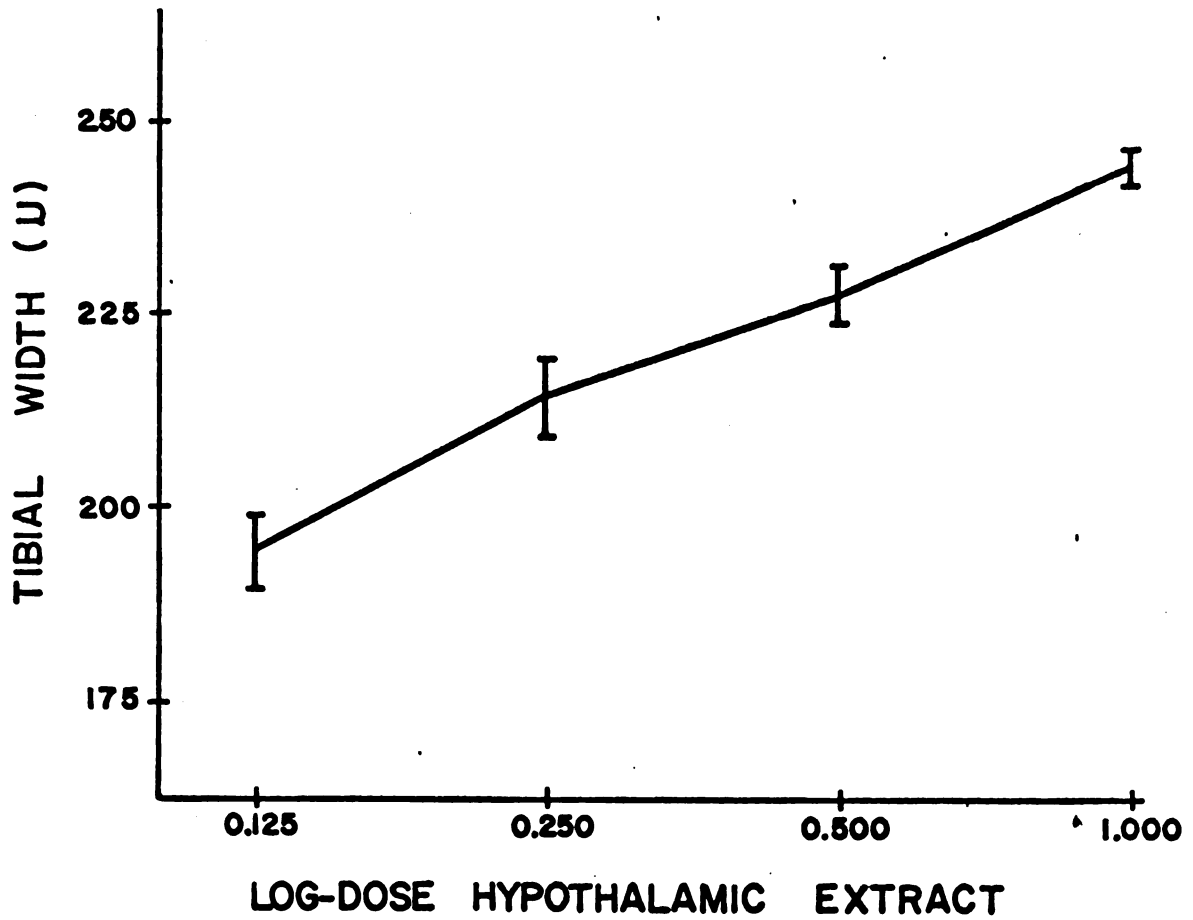


Figure 1. Logarithmic Dose-Response Curve Showing Pituitary GH Release as a Response to Hypothalamic Extract.

It can be seen in Table II and Fig. 2 that when the larger dose of cerebral extract was incubated with male rat pituitary, GH released into the medium was no greater than with the lower dose. On the other hand the larger dose of hypothalamic extract incubated with rat pituitary induced release of significantly more GH into the medium than the lower dose. The amounts of pituitary GH release stimulated by hypothalamic extract were significantly greater ($p < 0.01$) than the amounts released by pituitary upon adding cerebral extract at either dose level. These results compare favorably with those obtained in Experiment 1.

3. Dose response to medium from AP incubated with cerebral extract or medium 199 alone. Medium from AP incubated with cerebral extract or medium 199 alone was divided into low and high doses corresponding to 0.25 and 1.00 AP equivalents/assay rat. These were then injected into each assay rat for 4 days. The results in Table III and Fig. 3 show that cerebral extract did not elicit a significantly greater ($p > 0.05$) release of GH into the medium than medium 199 alone. The difference in response to the low and high

Table II. Comparison of Cerebral Extract versus Hypothalamic Extract on Anterior Pituitary Release of GH

Group	HE ^a or CE ^b equivalents/ incubated	No. of assay rats	Average tibial width (u) mean \pm SE
1	0.25 CE	4	197.7 \pm 6.6
2	1.00 CE	4	204.7 \pm 3.4
3	0.25 HE	4	253.5 \pm 5.1 ^d
4	1.00 HE	4	284.1 \pm 4.6 ^d
5	Hypox ^c assay controls	4	133.2 \pm 5.6

^aHE: hypothalamic extract

^bCE: cerebral extract

^cHypox: hypophysectomized

^dp<0.01. HE versus CE.

Reference Standard: NIH-GH-S8

25 ug = 237.5 \pm 1.6

100 ug = 272.5 \pm 5.1

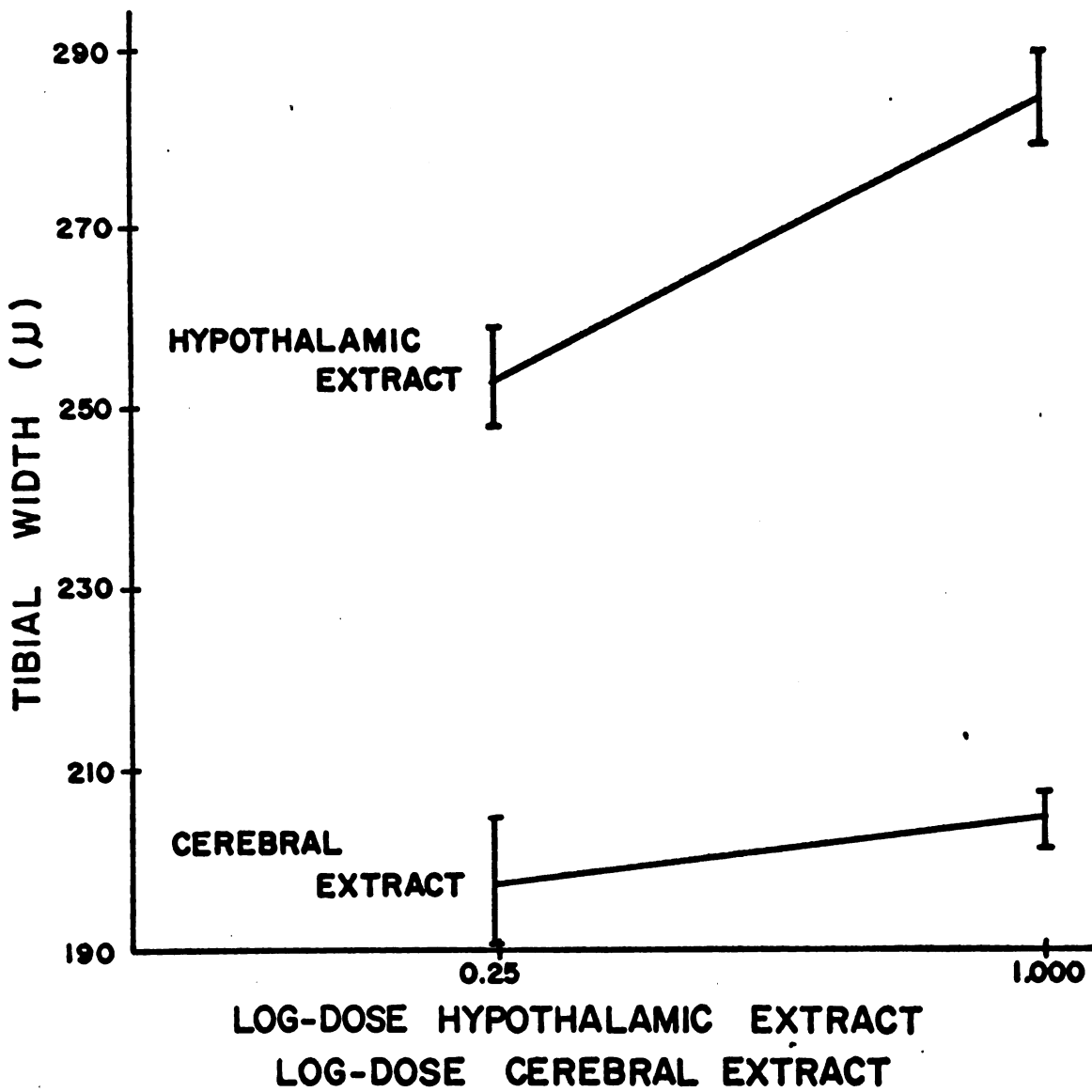


Figure 2. Logarithmic Dose-Response Curves Showing Pituitary GH Release as a Response to Hypothalamic or Cerebral Extract.

dose of medium in each group was significant.

4. Dose response to medium from AP incubated with cerebral or hypothalamic extract. Medium from AP incubated with hypothalamic or cerebral extract was divided into two doses as in 3 above. The results in Table IV and Fig. 4 show that the difference in response to the low and high dose of medium in each group was significant ($p < 0.05$ or $p < 0.01$). Both doses of hypothalamic extract (0.5 and 1.0 HE/incubated AP) elicited significantly greater release of GH into the medium than cerebral extract. The higher dose of HE elicited significantly greater release of GH than the lower dose. These results are in agreement with those in Tables I, II and III.

D. Discussion

The amount of GH released by male rat pituitary in a 4 hour incubation procedure was found to be directly proportional to the logarithm of the dose of rat hypothalamic extract added to the medium. The log-dose response was linear between the levels of 0.125 and 1.000 hypothalamic equivalents/incubated AP. Graded doses of hypothalamic extracts elicited significantly greater

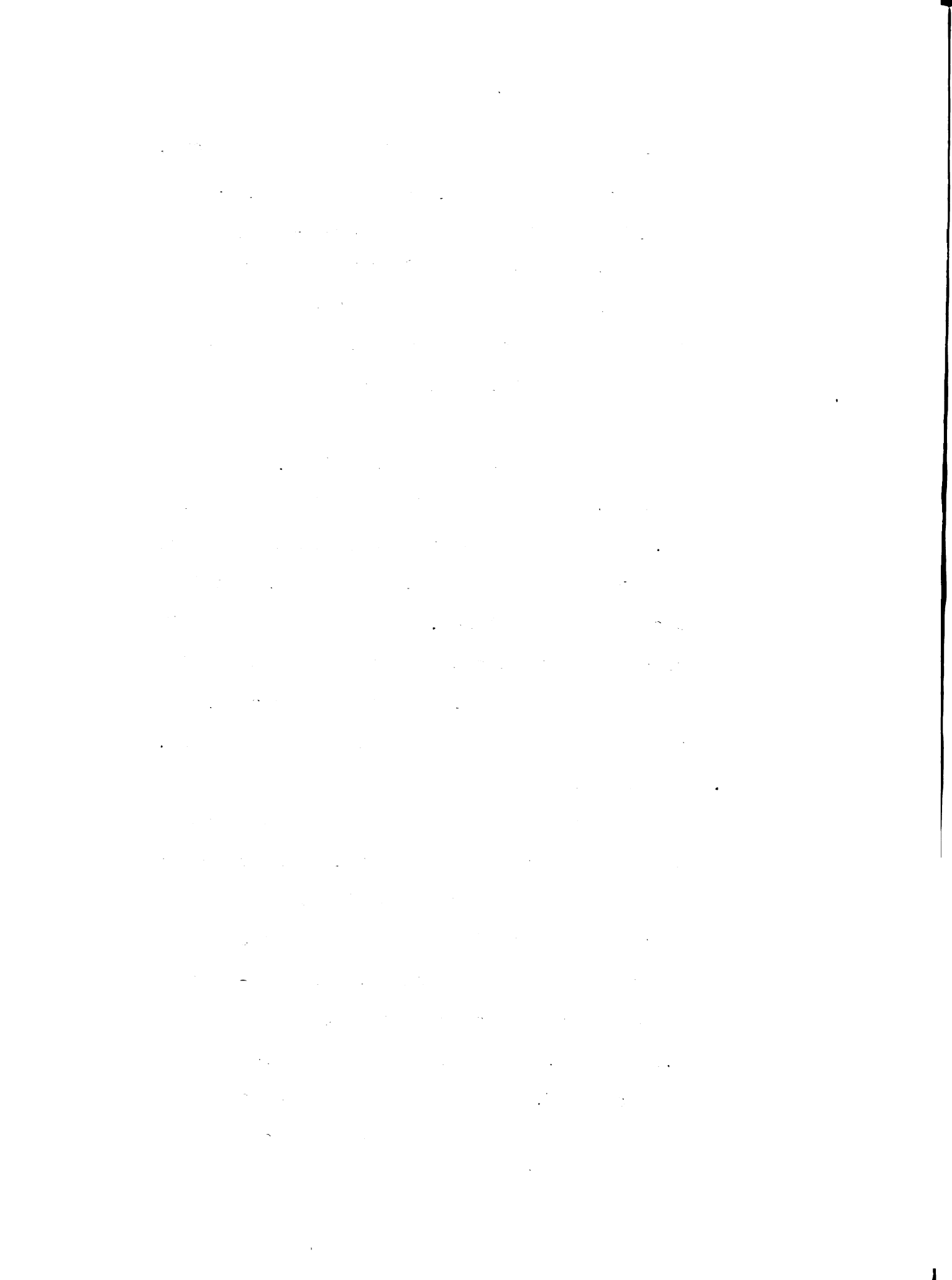


Table III. Dose Response to Medium from AP Incubated with Cerebral Extract or Medium 199 Alone

Group	CE ^a equivalents/ incubated AP	Total Dose of AP equivalents/ assay rat/ 4 days	No. of assay rats	Average tibial width (u) mean ± SE
1	Medium 199	0.25	4	161.1±4.2
2	1.00 CE	1.00	4	191.6±5.8
		0.25	4	152.0±4.3 ^C
		1.00	4	189.4±4.2 ^C
3	Hypox ^b assay controls	----	4	118.8±0.9

^aCE: cerebral extract

^bHypox: hypophysectomized

cp>0.05. Not significant

Reference Standard: NIH-GH-S8

20 ug = 180.9±5.1

80 ug = 227.6±1.1

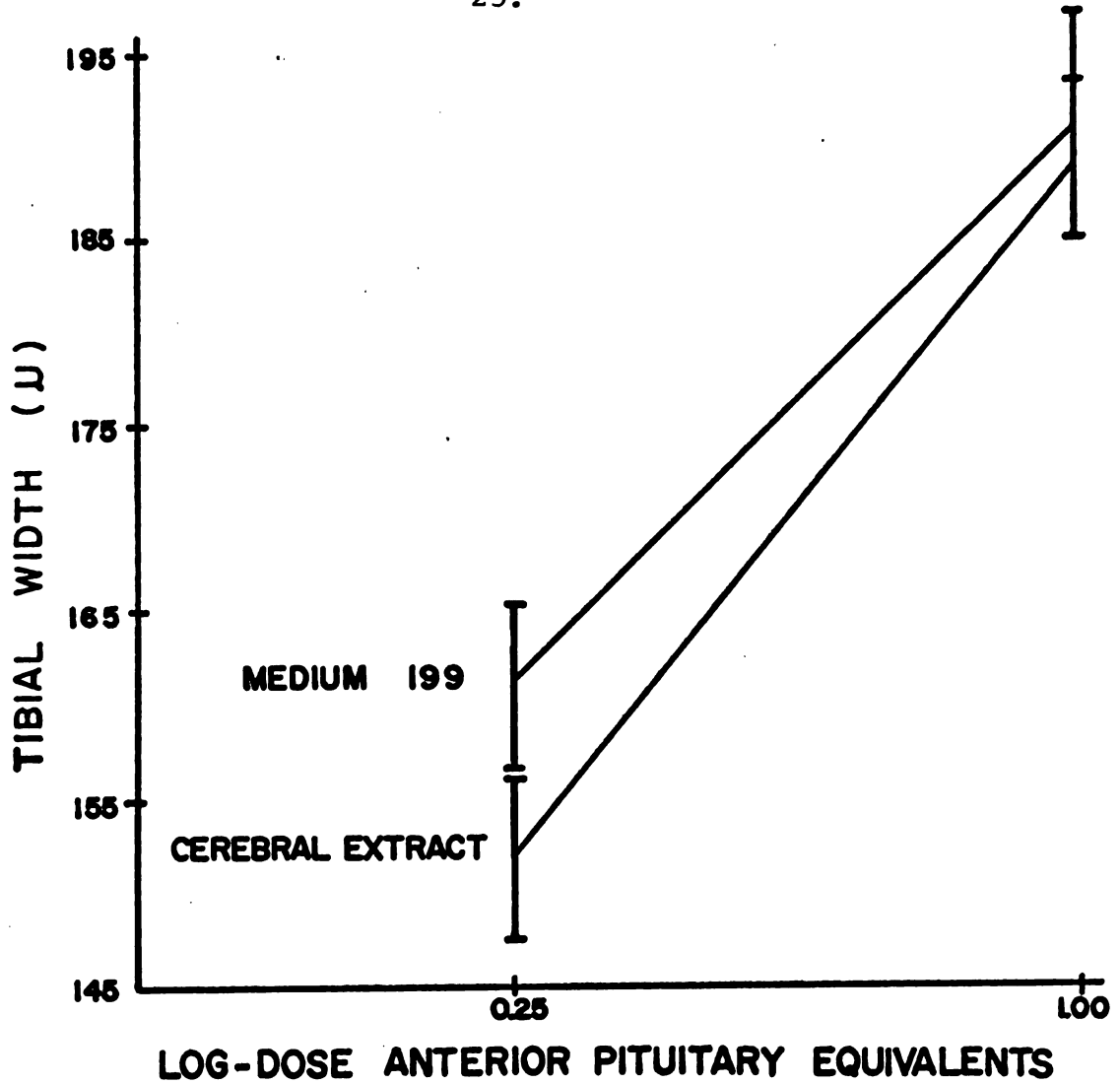


Figure 3. Logarithmic Dose-Response Curves to Medium from AP Incubated with Cerebral Extract or Medium 199 Alone.

Table IV. Dose Response to Medium from AP Incubated with Cerebral or Hypothalamic Extract

Group	HE ^a or CE ^b equivalents/ incubated AP	Total Dose of AP equivalents/ assay rat/ 4 days	No. of assay rats	Average tibial width (u) mean ± SE
1	1.0 CE	0.25	4	129.6±2.5
		1.00	4	168.1±9.7 ^d
2	0.5 HE	0.25	4	152.7±2.2
		1.00	4	191.6±9.4 ^e
3	1.0 HE	0.25	4	182.0±4.2
		1.00	4	216.4±1.9 ^e
4	Hypox ^c assay controls	-----	4	121.3±5.3

^aHE: hypothalamic extract

^bCE: cerebral extract

^cHypox: hypophysectomized.

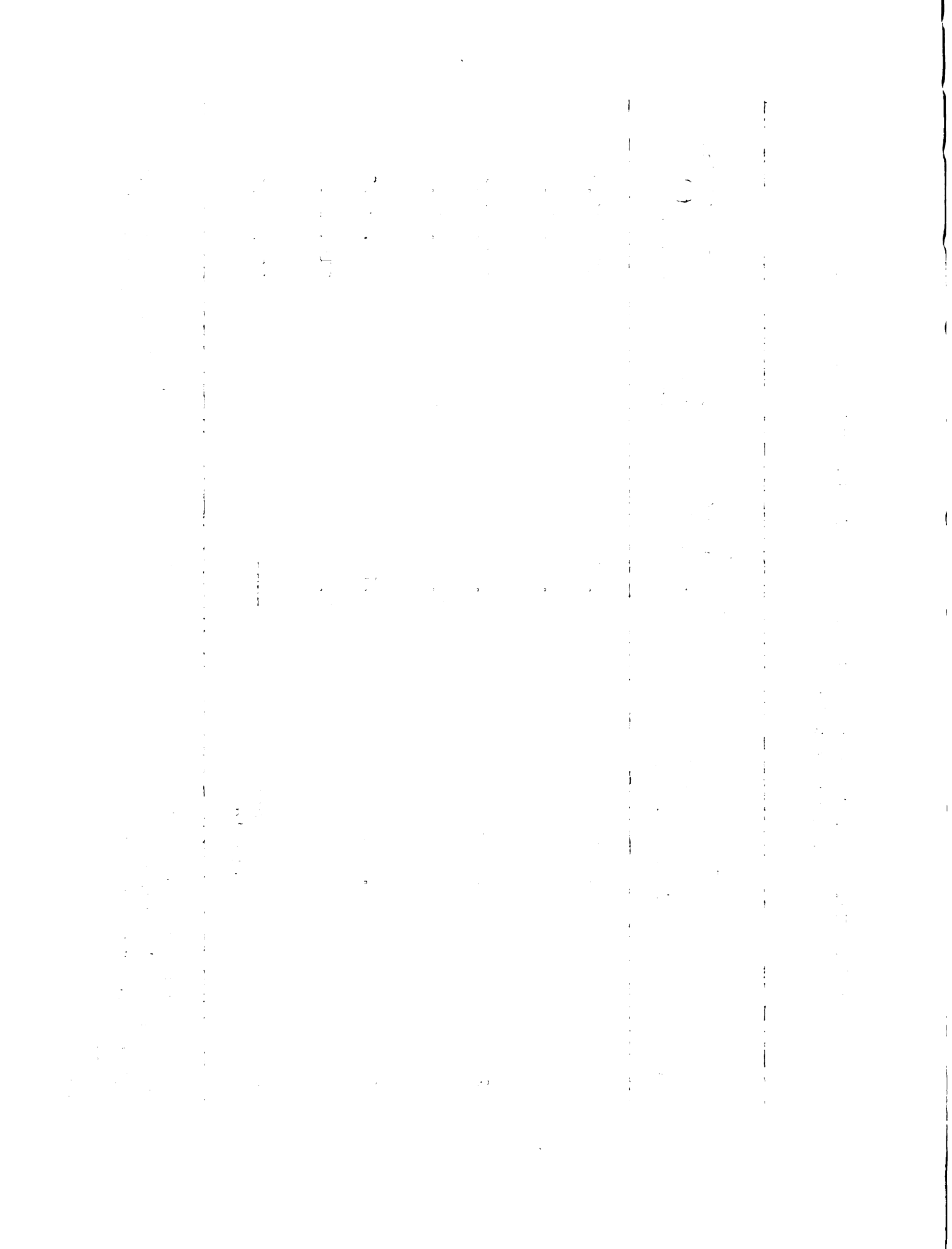
^dp<0.05

^ep<0.01

Reference Standard: NIH-GH-S8

20 ug = 162.8±2.6

80 ug = 209.7±2.3



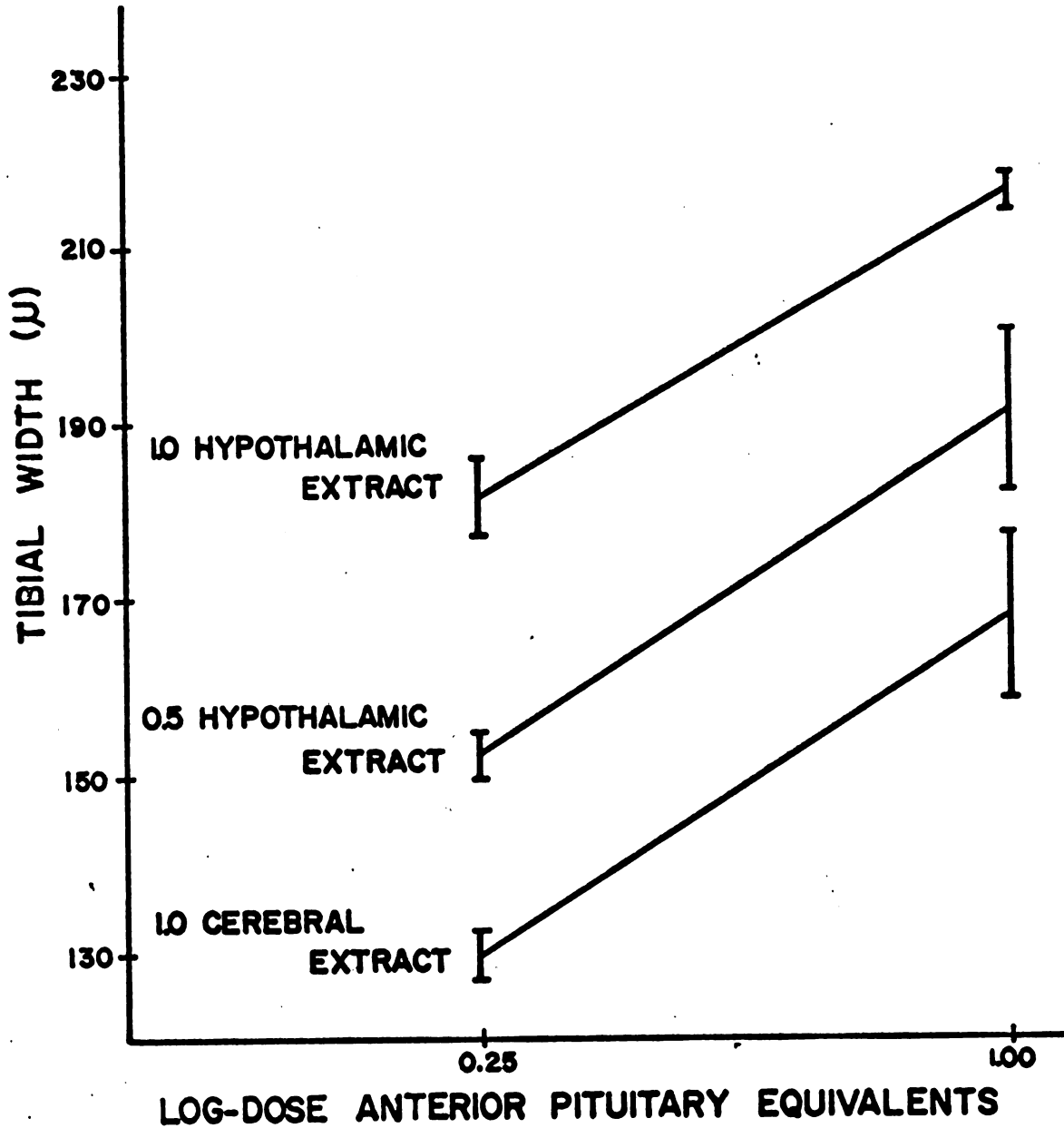


Figure 4. Logarithmic Dose-Response Curves to Medium from AP Incubated with Hypothalamic or Cerebral Extract.

release of GH into the medium in all experiments. However, graded doses of cerebral extract failed to elicit increased release of GH into the medium, indicating that this area of the brain does not contain GH-RF activity. In all experiments, AP incubated with the lowest dose of hypothalamic extract resulted in significantly greater release of GH into the medium than any dose of cerebral extract used. Analysis of the medium at two dose levels showed significant log-dose responses, indicating that the hormone assayed was GH. Some release of GH occurred in incubations of AP with cerebral extract. This is due to spontaneous release of GH since it has been shown that rat pituitary cultures release GH for up to 3 days even in the absence of hypothalamic extract (Meites, Hopkins and Deuben, 1962). There is no evidence that cerebral extracts can induce GH release by the incubated AP (Deuben and Meites, 1964; Deuben and Meites, 1965; Schally et. al., 1965; and Schally et. al., 1968).

Crude hypothalamic extracts can influence the release of anterior pituitary hormones

other than GH (Guillemin, 1956; Schreiber et. al., 1962; McCann, 1962; Talwaker, Ratner and Meites, 1963; Mittler and Meites, 1964). ACTH can reduce epiphyseal cartilage width in young rats (Evans et. al., 1943; Marx et. al., 1943) while TSH can increase it (Fels et. al., 1955). However, intraperitoneal injections of aqueous solutions of ACTH even at high doses have very little effect on the tibial response (Li et. al., 1954), and injections of only very large doses of TSH (500 ug/day/4 days) increase the width of the tibial cartilage plate (Fels et. al., 1955). It appears unlikely, therefore, that either TSH or ACTH in the medium influenced our results. If gonadotropins were present in the medium, they would have reduced rather than enhanced the tibial responses recorded.

Our experimental data support the concept that a specific GH-RF is present in the hypothalamus of the rat, since only such a factor would be expected to release pituitary GH in a log-dose fashion. Our method has been found to be suitable for measuring quantitative changes in hypothalamic GH-RF content produced by different physiological states (see next

1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes that this is essential for ensuring transparency and accountability in the organization's operations.

2. The second part of the document outlines the various methods and techniques used to collect and analyze data. It highlights the need for a systematic approach to data collection and the importance of using reliable sources of information.

3. The third part of the document focuses on the analysis and interpretation of the collected data. It discusses the various statistical and analytical tools that can be used to identify trends and patterns in the data.

4. The fourth part of the document discusses the importance of communicating the results of the analysis to the relevant stakeholders. It emphasizes that clear and concise communication is essential for ensuring that the findings are understood and acted upon.

5. The fifth part of the document discusses the various challenges and limitations associated with data collection and analysis. It highlights the need for a thorough understanding of these challenges and the importance of developing strategies to overcome them.

6. The sixth part of the document discusses the various applications of data collection and analysis in different fields. It highlights the wide range of uses for this type of information and the importance of tailoring the approach to the specific needs of the organization.

7. The seventh part of the document discusses the various ethical considerations associated with data collection and analysis. It emphasizes the need for a strong ethical framework and the importance of protecting the privacy and confidentiality of the data.

8. The eighth part of the document discusses the various legal and regulatory requirements that apply to data collection and analysis. It highlights the need for a thorough understanding of these requirements and the importance of ensuring compliance.

9. The ninth part of the document discusses the various best practices for data collection and analysis. It highlights the importance of using a systematic and consistent approach and the need for ongoing monitoring and evaluation.

10. The tenth part of the document discusses the various future trends and developments in data collection and analysis. It highlights the importance of staying up-to-date on the latest research and technology in this field.

section of thesis). The sensitivity of this in vitro method for assaying GH-RF should be further increased with the availability of a dependable radioimmunoassay for rat GH.

II. EFFECTS OF STARVATION ON PLASMA GH ACTIVITY, PITUITARY GH, AND HYPOTHALAMIC GH-RF LEVELS IN THE RAT.

A. Objectives

The purpose of these experiments was to observe the effects of starvation on plasma GH activity, pituitary GH and hypothalamic GH-RF levels in the rat. An attempt was made to correlate any changes in pituitary and hypothalamic content with plasma GH levels.

B. Procedures

Control animals were maintained on a diet of Wayne Lab Blox pellets and fed ad libitum. Food, but not water, was removed from the experimental animals for 7 days. On day 8, the animals were weighed, anesthetized with ether and bled from the abdominal aorta with a heparinized syringe. The pituitaries and hypothalami were also removed. Blood, pituitaries and hypothalami were prepared as described previously and injected intra-peritoneally into assay rats to test for GH by the method of Greenspan et. al. (1949).

In a separate experiment, the starved animals received a daily subcutaneous injection of L-Na-thyroxine (T_4) (Nutritional Biochemicals

1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes that this is essential for ensuring transparency and accountability in the organization's operations.

2. The second part of the document outlines the various methods and tools used to collect and analyze data. It highlights the need for consistent and reliable data collection processes to support informed decision-making.

3. The third part of the document focuses on the role of technology in data management and analysis. It discusses how modern software solutions can streamline data collection, storage, and reporting, thereby improving efficiency and accuracy.

4. The fourth part of the document addresses the challenges associated with data management, such as data quality, security, and privacy. It provides strategies to mitigate these risks and ensure that data is used responsibly and ethically.

5. The fifth part of the document concludes by summarizing the key findings and recommendations. It stresses the importance of ongoing monitoring and evaluation to ensure that data management practices remain effective and aligned with the organization's goals.

6. The sixth part of the document provides a detailed overview of the data collection process, including the identification of data sources, the design of data collection instruments, and the implementation of data collection procedures.

7. The seventh part of the document discusses the various methods used for data analysis, such as descriptive statistics, inferential statistics, and qualitative analysis. It explains how these methods are used to interpret the data and draw meaningful conclusions.

8. The eighth part of the document focuses on the importance of data visualization in presenting the results of data analysis. It discusses various visualization techniques, such as bar charts, line graphs, and pie charts, and their effectiveness in communicating complex data.

9. The ninth part of the document addresses the ethical considerations surrounding data management and analysis. It discusses the need for transparency, informed consent, and data protection to ensure that the organization's data practices are ethical and compliant with relevant regulations.

10. The tenth part of the document provides a final summary and conclusion, reiterating the key points and emphasizing the importance of data management and analysis in achieving organizational success.

11. The eleventh part of the document discusses the future of data management and analysis, highlighting emerging trends and technologies that are expected to shape the field in the coming years.

12. The twelfth part of the document provides a detailed overview of the data analysis process, including the selection of appropriate statistical methods, the interpretation of results, and the communication of findings to stakeholders.

13. The thirteenth part of the document focuses on the importance of data security and privacy in the context of data management and analysis. It discusses various security measures and privacy policies that can be implemented to protect sensitive data.

14. The fourteenth part of the document provides a final summary and conclusion, reiterating the key points and emphasizing the importance of data management and analysis in achieving organizational success.

Corporation, Cleveland, Ohio) at a dose of 2.5 ug/100g body weight/day for 5 days beginning on day 2 of starvation. Only the plasma of the animals was analyzed for GH activity.

C. Results

1. Plasma GH activity of control and starved rats. Table V and Fig. 5 show the effects of 7 days of starvation on plasma GH activity. In two independent experiments plasma GH activity in control and starved rats was assayed at two dose levels with a fourfold difference between doses (8 or 32 ml of plasma equivalent per assay rat). In both experiments, plasma from control animals elicited a significantly greater tibial response than plasma from starved animals at either dose level ($p < 0.01$).

The starved rats lost an average 87.7 and 88.6 g per animal, respectively, whereas the ad libitum fed controls gained an average 33.8 and 40.4 g respectively. Pituitary weights were also decreased in the starved rats.

2. Effects of starvation and T_4 on plasma GH activity. Starvation has been shown to reduce thyroid activity in rats (Meites and Wolterink, 1950; Yousef and Johnson, 1968)

1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes that proper record-keeping is essential for transparency and accountability, particularly in financial matters. The text notes that without clear documentation, it becomes difficult to track expenses, revenues, and other critical data points.

2. The second section addresses the challenges associated with data management in a rapidly changing environment. It highlights the need for robust systems that can handle large volumes of information while ensuring its integrity and security. The author suggests that organizations should invest in modern technologies and training to overcome these challenges effectively.

3. The third part of the document focuses on the role of leadership in driving organizational success. It argues that strong leaders are those who can inspire their teams, set clear goals, and adapt to changing circumstances. The text provides several examples of successful leaders and their strategies, offering valuable insights for aspiring managers.

4. The fourth section discusses the importance of continuous learning and development. It notes that in today's fast-paced world, skills and knowledge must be constantly updated to remain relevant. Organizations should create a culture that encourages learning and provides opportunities for growth and advancement for all employees.

5. The fifth part of the document explores the impact of technology on various aspects of business operations. It discusses how digital tools have revolutionized communication, marketing, and customer service. However, it also warns of potential risks such as data breaches and cyberattacks, emphasizing the need for strong cybersecurity measures.

6. The sixth section addresses the issue of diversity and inclusion in the workplace. It argues that diverse teams are more innovative and productive, as they bring different perspectives and experiences to the table. Organizations should actively work to create an inclusive environment where all employees feel valued and supported.

7. The seventh part of the document discusses the importance of ethical considerations in business decisions. It notes that while profit is a primary goal, it should not be pursued at the expense of integrity and social responsibility. The text provides guidance on how to navigate complex ethical dilemmas and maintain high standards of conduct.

8. The eighth section focuses on the role of customer feedback in improving products and services. It emphasizes that listening to customers is crucial for understanding their needs and preferences. Organizations should implement effective feedback mechanisms and act on the insights gained to enhance their offerings.

9. The ninth part of the document discusses the importance of strategic planning and execution. It notes that a clear strategy is essential for long-term success, and organizations must have a plan in place to achieve their goals. The text provides a framework for developing and implementing a strategic plan.

10. The final section of the document discusses the importance of resilience and adaptability in the face of uncertainty. It notes that the business environment is constantly evolving, and organizations must be able to pivot and adapt to new challenges. The text offers strategies for building a resilient organization that can thrive in any environment.

Table V. Plasma GH Activity of Control and Starved Rats

Exp.	Treatment & no. of rats	Avg body weight		Avg pit wt of rats mg	No. of GH assay rats	Total Dose (ml of plasma/ assay rat/4 days)	Avg tibial width (u) mean \pm SE
		Initial g	Final g				
I	No food (100)	292.6	204.9	7.2	4	8	192.7 \pm 5.9
	Control-fed <u>ad lib.</u> (55)	286.2	320.0	9.8	4	32	214.3 \pm 2.8
					4	8	232.3 \pm 1.5**
					4	32	265.0 \pm 5.4**
	Hypox ¹ assay controls	-----	-----	----	4	--	132.3 \pm 6.2
II	No food (98)	307.1	218.5	6.2	4	8	199.3 \pm 6.4
	Control-fed <u>ad lib.</u> (43)	305.8	346.2	9.6	4	32	235.6 \pm 4.6
					4	8	235.9 \pm 4.2**
					4	32	264.7 \pm 7.4**
	Hypox ¹ assay controls (4)	-----	-----	----	4	--	125.1 \pm 5.3

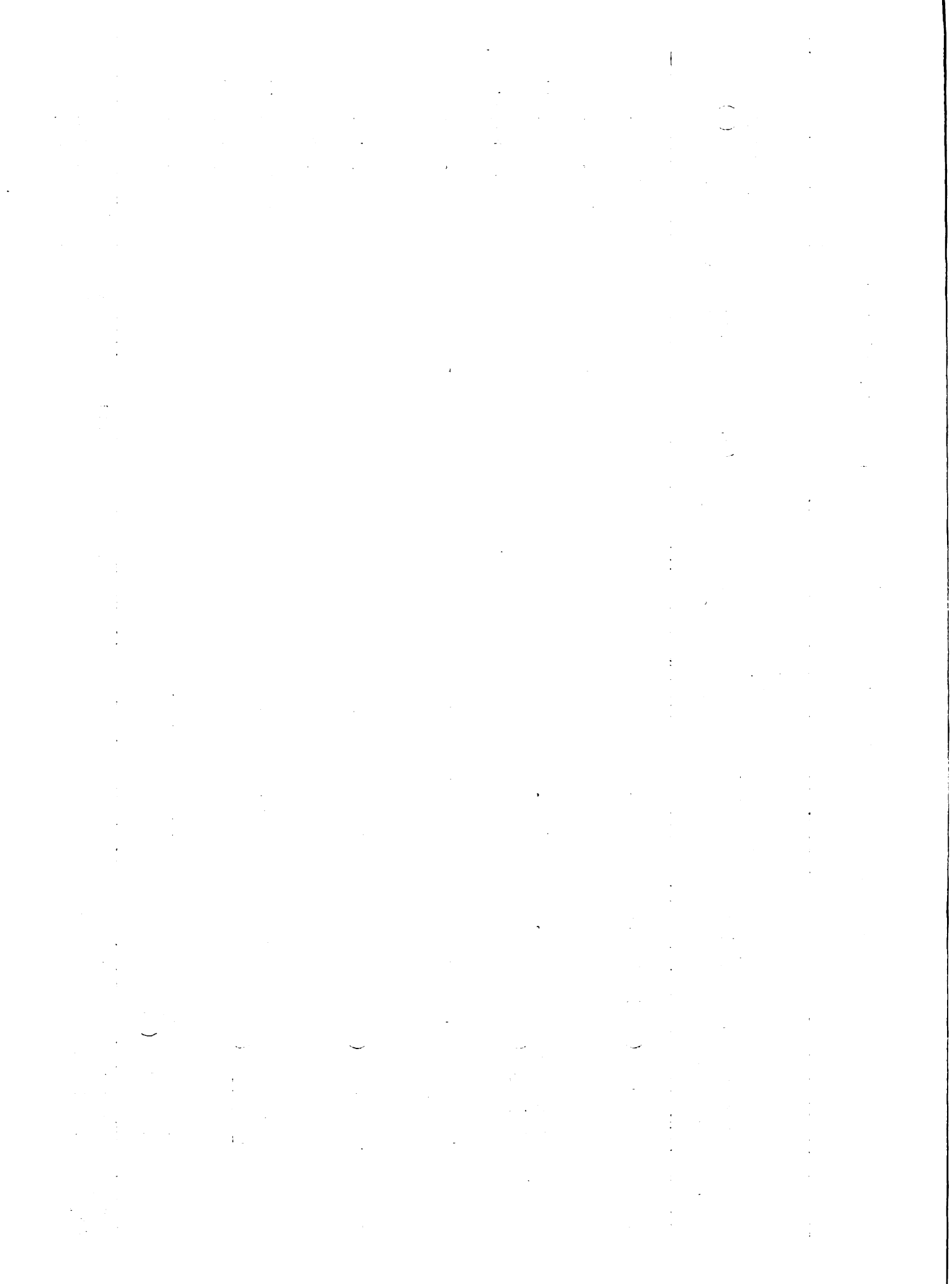
¹Hypox = hypophysectomized

**p<0.01. Control vs no food

Reference Standard: NIH-GH-S8

25 ug = 236.4 \pm 5.1

100 ug = 266.1 \pm 6.5



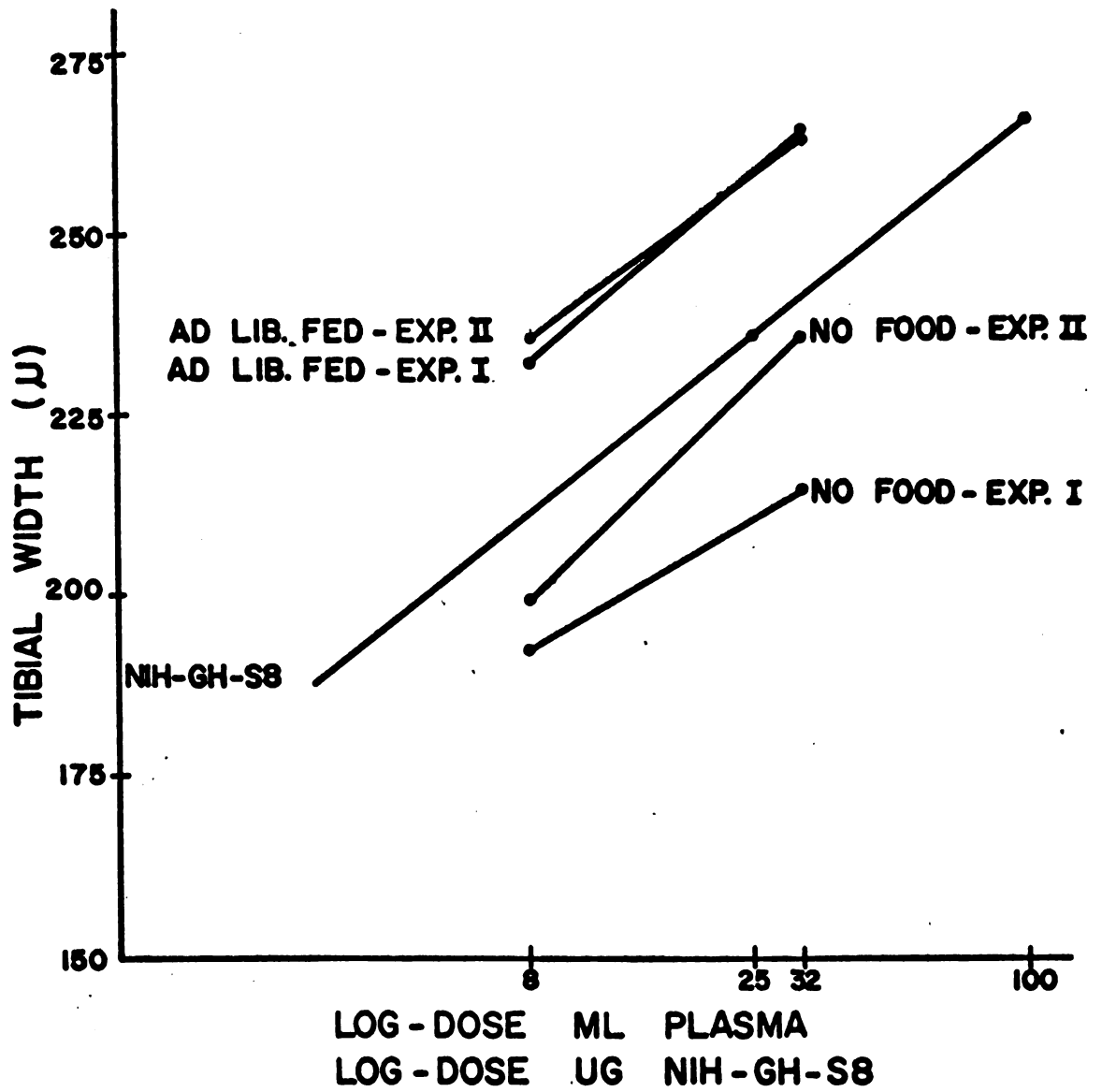


Figure 5. Logarithmic Dose-Response Curves to Plasma from Control or Starved Rats. Standard Curve Extrapolated.

Table VI. Effects of Starvation + T₄ on Plasma GH Activity

Exp.	Treatment & no. of rats	Avg body weight		Avg pit wt of rats mg	No. of GH assay rats	Total Dose (ml of plasma/ assay rat/4 days)	Avg tibial width (u) mean ± SE
		Initial g	Final g				
I	No food + 2.5 ug T ₄ /100 g body wt (110)	315.9	232.3	6.4	5	8	169.1±4.8
	Control-fed <u>ad lib.</u> (50)	327.1	353.8	9.0	5	8	193.3±2.7**
	Hypox ¹ assay controls	-----	-----	----	5	32	232.3±5.8**
						---	127.3±4.2

¹Hypox = hypophysectomized
 **p<0.01. Control vs no food

Reference Standard: NIH-GH-S8
 25 ug = 181.2±2.9
 100 ug = 235.5±5.0

and this probably results in decreased blood levels of thyroxine (Grossie and Turner, 1962). Since the tibial response to GH is decreased in the absence of thyroxine (Schooley et. al., 1966), the starved animals received replacement doses of thyroxine (2.5 ug/100 g body weight/day) during the last five days of starvation. In this way we tried to restore normal levels of circulating thyroxine in the starved rats, thereby reducing the possible effects of thyroid deficiency on GH activity in the plasma.

As can be seen in Table VI, a significant reduction in plasma GH activity was observed in the thyroxine treated starved rats. Body and pituitary weights were also reduced in the starved animals. The reduction in plasma GH activity, body and pituitary weights observed in the thyroxine treated starved rats is comparable to the reductions observed in the previous experiments shown in Table V.

3. Effects of starvation on pituitary GH content. Pituitaries were assayed at two dose levels (2 or 4 mg of anterior pituitary per assay rat). Table VII shows that starvation

Table VII. Effects of Starvation on Relative Pituitary GH Concentration

Exp	Treatment	Avg. body weight Initial g	Final g	Avg pit wt of rats mg	No. of GH assay rats	Total Dose (mg of AP/assay rat/4 days)	Avg tibial width (u) mean ± SE
I	No food	307.2	218.5	6.2	4	2	203.2±3.3
	Control-fed <u>ad lib.</u>	305.8	346.2	9.6	4	2	227.9±3.5**
	Hypox ¹ assay controls	-----	-----	---	4	4	280.6±2.1**
						-	125.1±5.3

¹Hypox = hypophysectomized
 **p<0.01. Control vs no food

Reference Standard: NIH-GH-S8
 25 ug = 237.5±1.6
 100 ug = 272.5±5.1

significantly reduced the concentration of GH in the pituitary ($p < 0.01$). These findings are in agreement with previous reports (Meites and Fiel, 1965; Friedman and Reichlin, 1965). The starved rats lost an average 88.6 g and the ad lib. fed control animals gained an average 40.4 g.

4. Effects of starvation on hypothalamic GH-RF. Hypothalamic content of GH-RF was assayed at two dose levels (.25 or 1 hypothalamic equivalent per incubated pituitary) using the previously described in vitro incubation method. The results in Table VIII show that starvation significantly reduced hypothalamic content of GH-RF ($p < 0.01$). Our results confirm those previously obtained by Meites and Fiel (1965) with an in vivo assay method.

D. Discussion

The data presented here indicate that complete food removal for 7 days in the rat significantly reduces plasma GH activity as well as pituitary concentration of GH and hypothalamic content of GH-RF. These results corroborate the previous observations that

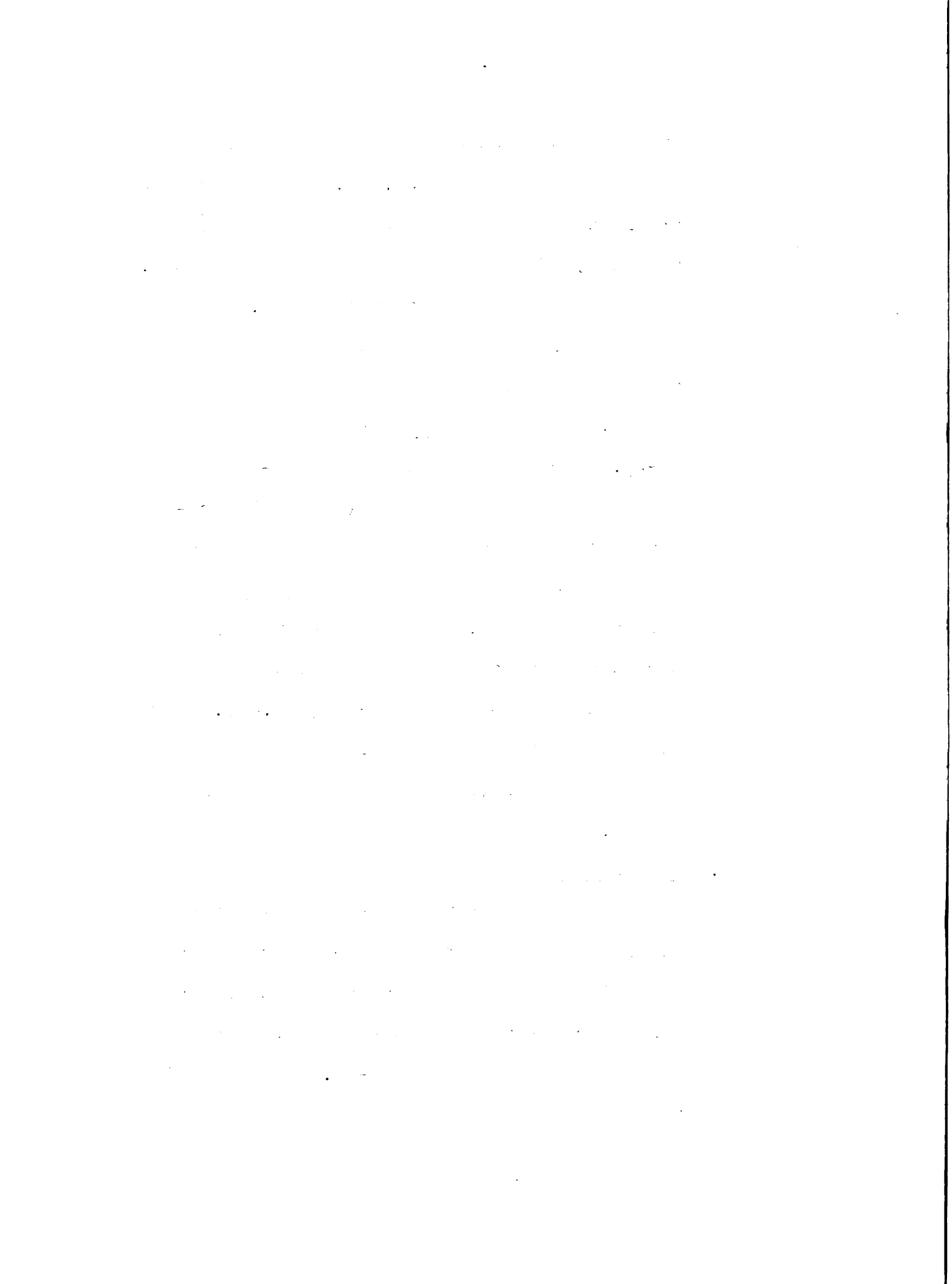


Table VIII. Effects of Starvation on Hypothalamic GH-RF Content

Exp.	Treatment	Avg. body weight		Avg pit wt of rats mg	No. of GH assay rats	Dose (H.E./incubated pituitary)	Avg.tibial width (u) mean ± SE
		Initial g	Final g				
I	No food	307.2	218.5	6.2	4	0.25	191.4±5.7
	Control-fed <u>ad lib.</u>	305.8	346.2	9.6	4	1.00	201.1±5.6
	CCE ¹ controls	-----	-----	----	4	0.25	213.4±3.2**
	Hypox ² assay controls	-----	-----	----	4	1.00	241.7±3.6**
							177.6±6.8
						----	125.1±5.3

¹CCE = Cerebral cortex extract

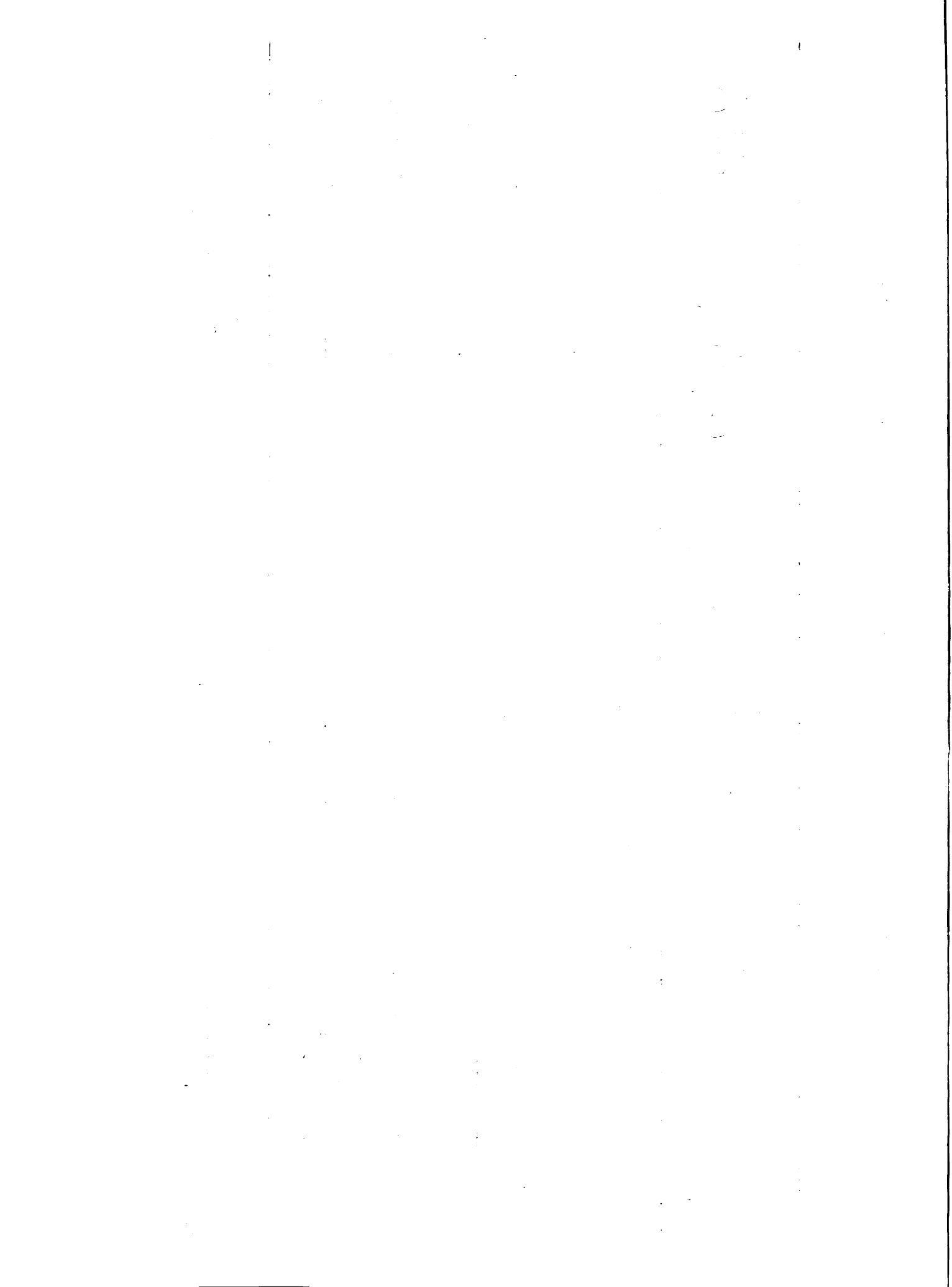
²Hypox = hypophysectomized

**p<0.01. Control vs no food

Reference Standard: NIH-GH-S8

25 ug = 237.5±1.6

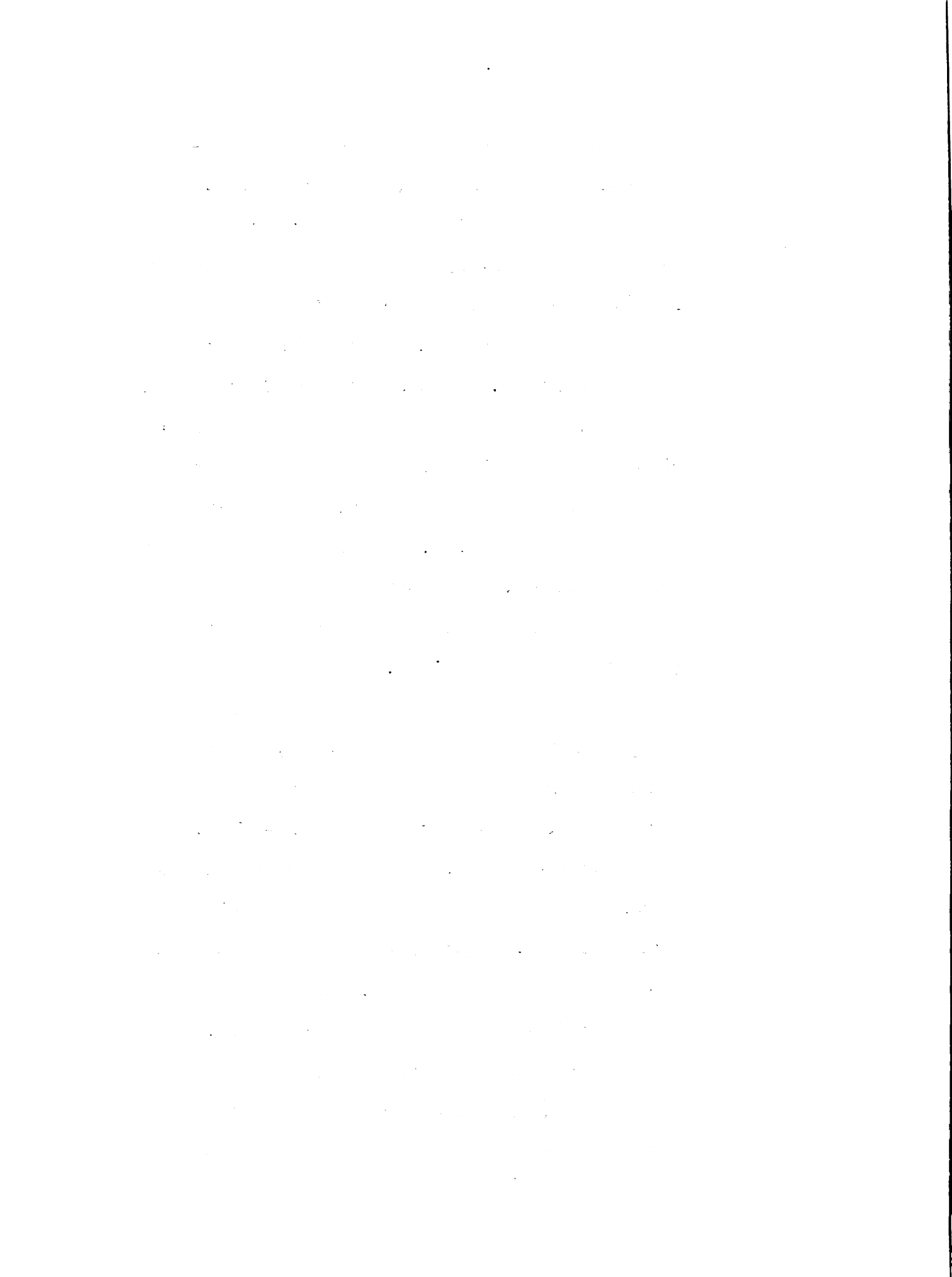
100 ug = 272.5±5.1



starvation in rats results in lower hypothalamic GH-RF content (Meites and Fiel, 1965) and decreased pituitary concentration of GH (Meites and Fiel, 1965; Friedman and Reichlin, 1965), when compared with ad libitum fed controls, and indicate that these changes are reflected in lower concentration of plasma GH activity. Our observation of reduced plasma GH activity in starved rats agrees with a similar independent study carried out in starved rats by Dr. A. Trenkle (Department of Animal Science, Iowa State University, Ames, Iowa) using a radioimmunological assay for GH (personal communication).

Although we have used the term plasma GH activity rather than plasma GH, we have no evidence that the material measured in the blood differs from that in the NIH-GH-S8. As indicated in Fig. 5, the dose-response curves obtained from the plasma of the control and starved rats were parallel to those obtained with purified NIH ovine GH. This suggests that the tibia test is measuring GH activity.

The GH bioassay values found here in the plasma (Fig. 5) are considerably above those reported by radioimmunoassay in the rat



(Schalch and Reichlin, 1966). However, NIH ovine GH was used in our bioassay of rat GH, whereas a purified rat GH was used as the reference standard for radioimmunoassay of rat GH (Schalch and Reichlin, 1966). The ovine GH used in our experiments has a stated potency of 0.79 USP units/mg, whereas a purified rat GH prepared by Dr. S. Ellis (Ames Research Center, Moffett Field, California, personal communication) has a stated potency of 2.7 to 3.9 USP units/mg. Therefore, purified rat GH may be 3.41 to 4.94 times more potent than ovine GH in the rat.

It has been suggested that the tibia bioassay of plasma GH may measure "sulfation factor" activity. Salmon and Daughaday (see Daughaday and Kipnis, 1966) showed that fasting reduces sulfation factor levels in the plasma of rats. Uptake of sulfate in vitro by cartilage from fasted rats was also decreased when the fast was continued for more than 24 hours. Hypophysectomy in rats decreased serum sulfation factor (Salmon and Daughaday, 1957), but GH injections into hypophysectomized rats restored values to

normal levels. However, direct addition of HGH to in vitro incubations containing cartilage from hypophysectomized rats did not stimulate sulfate uptake (Daughaday and Reeder, see Daughaday and Kipnis, 1966). The in vitro stimulation of sulfate uptake was found to be a linear function of the logarithm of the dose of normal serum added to the incubation medium containing cartilage from hypophysectomized rats (Daughaday et. al., 1959). Since a relationship was demonstrated between the dose of GH injected and the rise in sulfation factor activity in the plasma of pituitary dwarfs (Almgvist, 1960), it is believed that GH gives rise to a component of plasma capable of stimulating sulfate uptake by cartilage and incorporating this sulfate into chondroitin sulfate (Koumans and Daughaday, 1963). Serum sulfation factor activity therefore may be an index of GH activity in the plasma (Daughaday et. al., 1959).

Our observations on plasma GH levels are in contrast to those reported on human subjects

by radioimmunoassay. Roth et. al. (1963 b) and Cahill et. al. (1966) reported that prolonged fasting in humans resulted in increased serum GH content. Knobil (1966) however, found no increase in serum GH in fasted monkeys. Machlin et. al. (1968) also reported that plasma GH levels in pigs increased during the first 48 hours of starvation and subsequently fell to lower levels. This may indicate that increased GH secretion during fasting may not occur in all species. In a study closely related to ours, Srebniak et. al. (1959) found a significant reduction in pituitary and plasma GH levels as measured by bioassay in rats fed a protein-free diet for prolonged periods of time. The possibility of a different mechanism for control of GH secretion in the rat as compared to humans is indicated by the recent work of Schalch and Reichlin (1967). They found that stimuli such as forced exercise, moderate or severe hypoglycemia, or cold, all known to elicit release of GH in humans, failed to do so in rats.

The interpretation of our results may

be complicated by the presence or lack of other hormones in the plasma of starved rats, particularly ACTH and TSH. Unpublished observations in our laboratory (Dickerman, Negro-Vilar, and Meites, 1967) showed that absolute adrenal weight decreased in starved rats. These observations confirm previous findings by Quimby (1948). Furthermore, Li et. al. (1954) showed that the tibial response to ACTH is dependent upon the mode of injection of ACTH. Thus, a very high dose of α -adrenocorticotropin, of the order of 100 ug, had very little effect on the tibial response when injected alone intraperitoneally or with GH in an aqueous solution. Fels et. al. (1955) reported that injections of a TSH preparation into hypophysectomized rats (200 ug/day/4 days) increased the width of the tibial cartilage plate from 163u to 192u. Administration of the latter dose with GH gave no increment over the values obtained with GH alone. Since all our assay rats were injected intraperitoneally with aqueous solutions of plasma, anterior pituitary or incubation medium, we believe that the changes in tibial width were due primarily to GH.

CONCLUSIONS

The present experiments support the concept of a hypothalamic factor which controls anterior pituitary secretion of GH, GH-RF. The amount of GH released by male rat pituitary upon incubation was directly proportional to the logarithm of the dose of rat hypothalamic extract added. This factor is not present in the cerebrum of rats, since cerebral extract failed to show a log-dose response and was also unable to increase the secretion of GH above that released spontaneously. This method of measuring GH-RF is sensitive enough to detect physiological changes in hypothalamic content of GH-RF. Thus, it was possible to corroborate the decrease reported in hypothalamic GH-RF by an in vivo method observed after starvation in rats (Meites and Fiel, 1965).

The decrease in hypothalamic content of GH-RF leads to a decrease in synthesis and release of GH from the pituitary and is reflected in a lower plasma GH activity. Thus the rat appears to differ from the primate in its response to starvation. It is also possible that the GH measured in the serum of humans by radioimmunoassay may measure not only biologically active GH, but also biologically inactive GH which is immunologically active.

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2. The second part outlines the various methods and tools used to collect and analyze data. This includes both traditional manual methods and modern digital technologies, highlighting the benefits of automation and data integration.

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4. The fourth part discusses the role of data in decision-making and strategic planning. It explains how data-driven insights can help organizations identify trends, opportunities, and risks, leading to more informed and effective decisions.

5. The fifth part covers the importance of data governance and compliance. It outlines the necessary policies and procedures to ensure that data is handled in accordance with relevant laws and regulations, protecting the organization's reputation and legal standing.

6. The sixth part addresses the future of data management, including emerging trends like artificial intelligence, big data, and cloud computing. It discusses how these technologies will shape the way organizations collect, store, and analyze data in the coming years.

7. The seventh part provides a summary of the key points discussed throughout the document. It reiterates the importance of a data-driven approach and the need for continuous improvement in data management practices.

8. The final part offers concluding thoughts and recommendations for organizations looking to optimize their data management processes. It encourages a proactive and collaborative approach to data, involving all levels of the organization.

REFERENCES

- Almgvist, S., 1960. Studies on sulfation factor (SF) activity of human serum, effect of human growth hormone on SF levels in pituitary dwarfism. Acta Endocrinol. 35: 381-396.
- Arky, R.A., and Freinkel, N., 1954. The response of plasma human growth hormone to insulin and ethanol-induced hypoglycemia in two patients with "isolated adrenocorticotrophic defect." Metabolism 3: 547-549.
- Armstrong, C.N., and Durh, D.P.H., 1922. Three cases of supra-pituitary tumors presenting Frohliid's syndrome. Brain 45: 113-125.
- Bach, L.M.N., O'Brien, C.P., and Cooper, G.P., 1964. Some observations concerning the hypothalamic regulation of growth and of food intake. In: Progress in Brain Research, vol. 5: Lectures on the Diencephalon. W. Bargmann and J.P. Schade (Eds.), Elsevier, Amsterdam.
- Bernardis, L.L., Box, B.M., and Stevenson, J.A.F., 1963. Growth following hypothalamic lesions in the weanling rat. Endocrinology 72: 684-692.
- Birge, C.A., Peake, G.T., Mariz, I.K., and Daughaday, W.H., 1967. Effects of cortisol and diethylbesterol on growth hormone release by rat pituitary in vitro. Proc. Soc. Exptl. Biol. Med. 126: 342-345.
- Bliss, C.I., 1967. Statistics in Biology. Vol. I, McGraw-Hill, New York.
- Bogdanove, E.M., and Lipner, H.J., 1952. Intestinal absorption of glucose in hypothalamic obesity. Proc. Soc. Exptl. Biol. Med. 81: 410-412.
- Cahane, M., and Cahane, T., 1938. Sur le role du diencephale dans le developpement somatique. Rev. Franc. d'Endocrinol. 16: 181-184.

- Cahill, G.F., Jr., Herrera, M.G., Morgan, A.P., Soeldner, J.S., Steinke, J., Levy, P.L., Reichard, G.A., Jr., and Kipnis, D.M., 1966. Hormone fuel interrelationships during fasting. J. Clin. Invest. 45: 1751-1769.
- Contopoulos, A.N., Simpson, M.E., and Koneff, A.A., 1958. Pituitary function in the thyroidectomized rat. Endocrinology 63: 642-653.
- Daniel, P.M., and Prichard, M.M.L., 1964. Observations on the metabolic disturbances, growth and behaviour of young goats after transection of the pituitary stalk. Acta Endocrinol. 45: 84-98.
- Daughaday, W.H., Salmon, W.D., and Alexander, F., 1959. Sulfation factor activity of sera from patients with pituitary disorders. J. Clin. Endocrinol. Metab. 19: 743-758.
- Daughaday, W.H., and Kipnis, D.M., 1966. The growth-promoting and anti-insulin actions of somatotropin. Recent Prog. Hormone Res. 22: 49-93.
- Deuben, R.R., and Meites, J., 1964. Stimulation of pituitary growth hormone release by a hypothalamic extract in vitro. Endocrinology 74: 408-414.
- Deuben, R., and Meites, J., 1965. In vitro reinitiation of pituitary somatotropin release by an acid extract of hypothalamus. Proc. Soc. Exptl. Biol. Med. 118: 409-412.
- Dhariwal, A.P.S., Krulich, L., Antunez-Rodrigues, J., and McCann, S.M., 1966. Separation of GH-RF from CRF. Neuroendocrinology 1: 341-349.
- Endroczi, E., Kovacs, S., and Lissak, K., 1956. Die Wirkung der Hypothalamus-Reizung auf das endokrine und somatische Verhalten. Endokrinologie 33: 271-278.
- Evans, H.M., Simpson, M.E., and Li, C.H., 1943. Inhibiting effect of adrenocorticotrophic hormone on the growth of male rats. Endocrinology 33: 237-238.
- Fels, I.G., Simpson, M.E., and Evans, H.M., 1955. Purification of the anterior hypophyseal thyrotropic hormone. J. Biol. Chem. 213: 311-323.

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- Frantz, A.G., and Rabkin, M.T., 1964. Human growth hormone. Clinical measurements, response to hypoglycemia and suppression by corticosteroids. New Engl. J. Med. 271: 1375-1381.
- Franz, J., Haselbach, C.H., and Libert, O., 1962. Studies on the effect of hypothalamic extracts on somatotrophic pituitary function. Acta Endocrinol. 41: 336-350.
- Friedman, R.C., and Reichlin, S., 1965. Growth hormone content of the pituitary gland of starved rats. Endocrinology 76: 787-788.
- Gaarenstrom, J.H., and Levie, L.H., 1939. Disturbances of growth by diethyl-stilboestrol and oestrone. J. Endocrinol. 1:420-429.
- Geschwind, I.I., and Li, C.H., 1955. The tibia test for growth hormone. In Hypophyseal Growth Hormone, Nature and Actions, R.W. Smith, O.H. Gaebler, and Long, C.N.H., eds. pp. 28-58. McGraw-Hill, New York.
- Glick, S.M., Roth, J., Yalow, R.S., and Berson, S.A., 1965. The regulation of growth hormone secretion. Rec. Prog. Hormone Research 21: 241-270.
- Goldberg, R.G., and Knobil, E., 1957. Structure and function of intraocular hypophyseal grafts in the hypophysectomized male rat. Endocrinology 61: 742-754.
- Green, J.D. and Harris, G.W., 1949. Observation of the hypophysioportal vessels of the living rat. J. Physiol. (London) 108: 359-361.
- Greenspan, F.S., Li, C.H., Simpson, M.E., and Evans, H.M., 1949. Bioassay of hypophyseal growth hormone: the tibia test. Endocrinology 45: 455-463.
- Greep, R.O., 1936. Functional pituitary grafts in rats. Proc. Soc. Exptl. Biol. Med. 34: 754-755.
- Grossie, J., and Turner, C.W., 1962. Thyroxine secretion rates during food restriction in rats. Proc. Soc. Exptl. Biol. Med. 110: 631-633.
- Guillemin, R., 1956. Hypothalamo-Hypophyseal Interrelationships. Charles C. Thomas, Springfield, Illinois.

- Halasz, B., Pupp, L., and Uhlarik, S., 1962. Hypophysiotrophic area in the hypothalamus. J. Endocrin. 25: 147-154.
- Halasz, B., Pupp, L., Uhlarik, S., and Thoma, L., 1963. Growth of hypophysectomized rats bearing pituitary transplant in the hypothalamus. Acta Physiol. Acad. Sci. Hung. 3: 287-292.
- Harris, G.W., 1950. Oestrous rhythm. Pseudopregnancy and the pituitary stalk in the rat. J. Physiol. 111: 347-360.
- Hertz, R., 1959. Growth in the hypophysectomized rat sustained by pituitary grafts. Endocrinology 65: 926-931.
- Hinton, G.G., and Stevenson, J.A.F., 1962. The effect of hypothalamic lesions on growth. Can. J. Biochem. Physiol. 40: 1239-1243.
- Houssay, B.A., Biasotti, A., and Sammartino, R., 1935. Modifications fonctionnelles de l'hypophyse apres les lesion infundibulo-tuberiennes chez le chapeaud. Compt. Rend. Soc. Biol. 120: 725-727.
- Hunter, W.M., and Greenwood, F.C., 1964. Studies on the secretion of human pituitary growth hormone. Brit. Med. J. 1: 804-807.
- Jackson, C.M., 1916. Effects of inanition upon the structure of the thyroid and parathyroid glands of the albino rat. Amer. J. Anat. 19: 305-352.
- Jackson, C.M., 1917. Effects of inanition and refeeding upon the growth and structure of the hypophysis in the albino rat. Amer. J. Anat. 21: 321-358.
- Josimovich, J.B., Mintz, D.H., and Finster, J.L., 1967. Estrogenic inhibition of growth hormone-induced tibial epiphyseal growth in hypophysectomized rats. Endocrinology 81: 1428-1430.
- Katz, S.H., Dhariwal, A.P.S., and McCann, S.M., 1967. Effect of hypoglycemia on the content of pituitary growth hormone (GH) and hypothalamic growth hormone-releasing factor (GHRF) in the rat. Endocrinology 81: 333-339.

[The page contains extremely faint and illegible text, likely bleed-through from the reverse side of the document. The text is too light to transcribe accurately.]

- Knigge, K.M., 1958. Cytology and growth hormone content of rat's pituitary gland following thyroidectomy and stress. Anat. Record 130: 543-551.
- Knobil, E., 1966. Tenth Bowditch Lecture. The Pituitary Growth Hormone: An Adventure in Physiology. The Physiologist 9: 25-44.
- Koumans, J., and Daughaday, W.H., 1963. Amino acid requirements for activity of partially purified sulfation factor. Trans. Assoc. Am. Physicians 76: 152-162.
- Krulich, L, Dhariwal, A.P.S., and McCann, S.M., 1965. Growth hormone activity of crude ovine hypothalamic extracts. Proc. Soc. Exptl. Biol. Med. 120: 180-184.
- Krulich, L., Dhariwal, A.P.S., and McCann, S.M., 1967. Stimulatory and inhibitory hypothalamic factors regulating secretion of growth hormone. Program 49th Meet. Endocr. Soc. p. 87.
- Li, C.H., Geschwind, I.I., Levy, A.L., Harris, J.J., Dixon, J.S., Pon, N.G., and Porath, J.O., 1954. Isolation and properties of alpha-corticotropin from sheep pituitary glands. Nature:173: 251-253.
- Martini, L., and de Poli, A., 1956. Neurohumoral control of the release of adrenocorticotrophic hormone. J. Endocrin. 13: 229-234.
- Marx, W., Simpson, M.E., Li, C.H., and Evans, H.M., 1943. Antagonism of pituitary adrenocorticotrophic hormone to growth hormone in hypophysectomized rats. Endocrinology 33: 102-105.
- McCann, S.M., 1962. A hypothalamic luteinizing hormone-releasing factor. Am. J. Physiol. 202: 395-400.
- Machlin, L.J., Horino, M., Kipnis, D.M., Phillips, S.L., and Gordon, R.S., 1967. Stimulation of GH secretion by median eminence extracts in the sheep. Endocrinology 80: 205-207.
- Machlin, L.J., Horino, M., Hertelendy, F., and Kipnis, D.M., 1968. Plasma growth hormone and insulin levels in the pig. Endocrinology 82: 369-376.

[The page contains extremely faint and illegible text, likely bleed-through from the reverse side of the document. The text is too light to transcribe accurately.]

- Meites, J., 1949a. Relation of food intake to growth depressing action of natural and artificial estrogens. Am. J. Physiol. 159: 281-286.
- Meites, J., 1949b. Effects of starvation in rats and mice on thyroid secretion rate as indicated by uptake of radioactive iodine and thiouracil action. J. Animal Science 8: 642.
- Meites, J., and Wolterink, L.F., 1950. Uptake of radioactive iodine by the thyroids of underfed rats. Science 111: 175-176.
- Meites, J., Hopkins, T.F., and Deuben, R., 1962. Growth hormone production by rat pituitary in vitro. Fed. Proc. 21: 196.
- Meites, J., and Kragt, C.L., 1964. Effects of a pituitary homotransplant and thyroxine on body and mammary growth in immature hypophysectomized rats. Endocrinology 75: 565-570.
- Meites, J., and Fiel, N.J., 1965. Effect of starvation on hypothalamic content of "somatotropin releasing factor" and pituitary growth hormone content. Endocrinology 77: 455-460.
- Mittler, J.C., and Meites, J., 1964. In vitro stimulation of pituitary follicle-stimulating hormone release by hypothalamic extract. Proc. Soc. Exptl. Biol. Med. 117: 309-313.
- Mulinos, M.G., Pomerantz, L., Smelzer, J., and Kurzrok, R., 1939. Estrus-inhibiting effects of inanition. Proc. Soc. Exptl. Biol. Med. 40: 79-83.
- Mulinos, M.G., and Pomerantz, L., 1941. The reproductive organs in malnutrition. Endocrinology 29: 267-275.
- Muller, E.E., and Pecile, A., 1965. Growth hormone releasing factor of a guinea-pig hypothalamic extract: its activity in guinea-pig and rat. Proc. Soc. Exptl. Biol. Med. 119: 1191-1194.
- Muller, E., Pecile, A., and Smirne, S., 1965. Substances present at the hypothalamic level and growth hormone releasing activity. Endocrinology 77: 390-392.

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2. The second part of the document outlines the various methods and tools used to collect and analyze data. It highlights the need for consistent data collection procedures and the use of advanced analytical techniques to derive meaningful insights from the data.

3. The third part of the document focuses on the role of technology in data management and analysis. It discusses how modern software solutions can streamline data collection, storage, and processing, thereby improving efficiency and accuracy.

4. The fourth part of the document addresses the challenges associated with data management, such as data quality, security, and privacy. It provides strategies to mitigate these risks and ensure that the data remains reliable and secure.

5. The fifth part of the document discusses the importance of data governance and the role of various stakeholders in ensuring that data is used ethically and in compliance with relevant regulations.

6. The sixth part of the document provides a detailed overview of the data lifecycle, from data collection to data archiving and deletion. It emphasizes the need for clear policies and procedures to govern each stage of the data lifecycle.

7. The seventh part of the document discusses the importance of data backup and recovery strategies. It highlights the need for regular backups and the use of robust recovery procedures to ensure that data is available in the event of a disaster.

8. The eighth part of the document discusses the importance of data security and the role of various security measures in protecting data from unauthorized access and theft.

9. The ninth part of the document discusses the importance of data privacy and the role of various privacy measures in protecting personal and sensitive information.

10. The tenth part of the document discusses the importance of data retention and the role of various retention policies in ensuring that data is kept for the appropriate amount of time.

- Negro-Vilar, A., Dickerman, E., and Meites, J., 1968. Effects of starvation on pituitary FSH and hypothalamic FSH-releasing factor (FSH-RF) in male rats. Fed. Proc. 28: 269.
- Nikitovitch-Winer, M., and Everett, J.W., 1958. Functional restitution of pituitary graft re-transplanted from kidney to median eminence. Endocrinology 63: 916-930.
- O'Brien, C.P., Happel, L., and Bach, L.M.N., 1964. Some hypothalamic effects of STH-influenced growth and insulin sensitivity in kittens. Federation Proc. 23: 205.
- Pecile, A., Muller, E., Falconi, G., and Martini, L., 1965. Growth hormone releasing activity of hypothalamic extracts at different ages. Endocrinology 77: 241-246.
- Piacsek, B.E., and Meites, J., 1967. Reinitiation of gonadotropin release in underfed rats by constant light or epinephrine. Endocrinology 81: 535-541.
- Popa, G.T. and Fielding, U., 1933. Hypophysio-portal vessels and their colloid accompaniment. J. Anat. (London) 67: 227-232.
- Purves, H.D., and Griesbach, W.E., 1946. Observation on the acidophil cell changes in the pituitary in thyroxine deficiency states, acidophil degranulation in relation to gastrogenic agents and extrathyroidal thyroxine synthesis. Brit. J. Exp. Pathol. 27: 170-179.
- Quimby, F.H., 1948. Organ weights of rats receiving hormone supplements during recovery from chronic starvation. Endocrinology 42: 263-272.
- Reece, R.P., and Leonard, S.L., 1939. Further evidence for a mammogenic factor in the rat hypophysis. Proc. Soc. Exptl. Biol. Med. 42: 200-202.
- Reichlin, S., 1960a. Thyroid function, body temperature regulation and growth in rats with hypothalamic lesions. Endocrinology 66: 340-354.
- Reichlin, S., 1960b. Growth and the hypothalamus. Endocrinology 67: 760-773.

[The text in this image is extremely faint and illegible. It appears to be a multi-paragraph document, possibly a letter or a report, but the content cannot be transcribed or summarized due to the low contrast and blurriness of the scan. The text is organized into several distinct blocks, likely representing paragraphs, but the specific words and sentences are not discernible.]

- Reichlin, S., 1961. Growth hormone content of pituitaries from rats with hypothalamic lesions. Endocrinology 69: 225-230.
- Rodger, N.W., Beck, J.C., Burgos, R., and Guillemin, R., 1967. Variability of response in the bioassay of ovine hypothalamic extracts for a somatotropin releasing factor. Program 49th Meeting Endocr. Soc. p. 88.
- Roth, J., Glick, S.M., Yalow, R.S., and Berson, S.A., 1963a. Secretion of human growth hormone: physiologic and experimental modification. Metabolism 12: 577-579.
- Roth, J., Glick, S.M., Yalow, R.S., and Berson, S.A., 1963b. Hypoglycemia: a potent stimulus to secretion of growth hormone. Science 140: 987-988.
- Rubinstein, H.S., and Solomon, M.L., 1941. The growth stimulating effect of small doses of testosterone propionate in the castrate albino rat. Endocrinology 28: 229-232.
- Salmon, W.E., and Daughaday, W.H., 1957. A hormonally controlled serum factor which stimulates sulfate incorporation by cartilage in vitro. J. Lab. Clin. Med., 49: 825-836.
- Schalch, D.S., and Reichlin, S., 1966. Plasma growth hormone concentration in the rat determined by radioimmunoassay: influence of sex, pregnancy, lactation, anesthesia, hypophysectomy and extrasellar pituitary transplants. Endocrinology 79: 275-280.
- Schalch, D.S., and Reichlin, S., 1967. Stress and growth hormone release. Excerpta Medica 142: 13.
- Schally, A.V., Steelman, S.L., and Bowers, C.Y., 1965. Effects of hypothalamic extracts on release of GH in vitro. Proc. Soc. Exptl. Biol. Med. 119: 208-212.
- Schally, A.V., Kuroshima, A., Ishida, Y., Arimura, A., Saito, T., Bowers, C.Y., and Steelman, S.L., 1966. Purification of GH-RF from beef hypothalamus. Proc. Soc. Exptl. Biol. Med. 122: 821-823.

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3. The third part of the document describes the different types of data that are collected and how they are used to inform decision-making. It notes that a combination of quantitative and qualitative data is often used to provide a comprehensive view of the organization's performance.

4. The fourth part of the document discusses the challenges and limitations of data collection and analysis. It identifies common issues such as data quality, bias, and incomplete information, and offers strategies to address these challenges.

5. The fifth part of the document provides a summary of the key findings and conclusions of the study. It emphasizes the importance of ongoing monitoring and evaluation to ensure that the organization remains effective and efficient in its operations.

- Schally, A.V., Muller, E.E., and Sawano, E., 1968. Effect of porcine growth hormone-releasing factor on the release and synthesis of growth hormone in vitro. Endocrinology 82: 271-276.
- Schooley, R.A., Friedkin, S., and Evans, E.S., 1966. Re-examination of the discrepancy between acidophil numbers and growth hormone concentration in the anterior pituitary gland following thyroidectomy. Endocrinology 79: 1053-1057.
- Schreiber, V., Rybak, M., Eckertova, A., Koci, J., Jirgl, V., Franc, Z., and Kmentova, V., 1962. Isolation of hypothalamic peptide with TRF (Thyrotrophin releasing factor) activity in vitro. Experientia 18: 338-340.
- Smith, P.E., 1961. Postponed homotransplants of the hypophysis into the region of the median eminence in hypophysectomized male rats. Endocrinology 68: 130-143.
- Solomon, J., and Greep, R.O., 1959. The effect of alterations in thyroid function on the pituitary growth hormone content and acidophil cytology. Endocrinology 65: 158-164.
- Srebnik, H.H., Nelson, M.M., and Simpson, M.E., 1959. Reduced growth hormone content in anterior pituitary rats on protein free diets. Proc. Soc. Exptl. Biol. Med. 101: 97-99.
- Stephens, D.J., 1940. The effect of the thyrotropic principle of the anterior pituitary on the thyroid of the undernourished guinea pig. Endocrinology 26: 485-492.
- Sullivan, L.W., and Smith, T.C., 1957. Influence of estrogens on body growth and food intake. Proc. Soc. Exptl. Biol. Med. 96: 60-64.
- Swelheim, T., and Wolthius, D.L., 1962. On the growth hormone production by pituitary transplants. Acta Physiol. Pharmacol. Neerl. 11: 343-349.
- Takahashi, Y., Kipnis, D.M., and Daughaday, W.H., 1968. Increased growth hormone associated with initiation of sleep. Excerpta Medica 157: 17.

1. The first part of the document discusses the importance of maintaining accurate records of all transactions. It emphasizes that proper record-keeping is essential for the integrity of the financial system and for the ability to detect and prevent fraud. The text notes that without reliable records, it would be difficult to verify the accuracy of financial statements and to identify any irregularities.

2. The second part of the document focuses on the role of internal controls in ensuring the reliability of financial information. It describes how internal controls are designed to prevent errors and misstatements, and to ensure that all transactions are properly authorized and recorded. The text highlights that internal controls are a key component of an organization's risk management strategy and are essential for maintaining the trust of investors and other stakeholders.

3. The third part of the document discusses the importance of transparency and disclosure in financial reporting. It notes that providing clear and concise information about an organization's financial performance is crucial for making informed investment decisions. The text emphasizes that transparency is also essential for identifying and addressing any potential risks or uncertainties that may affect the organization's financial health.

4. The fourth part of the document addresses the need for ongoing monitoring and evaluation of financial reporting processes. It states that organizations should regularly review their internal controls and reporting procedures to ensure they remain effective and up-to-date. The text also notes that external audits are an important part of this process, as they provide an independent assessment of the organization's financial statements and internal controls.

5. The fifth part of the document discusses the importance of ethical behavior in financial reporting. It notes that financial reporting is not just a technical exercise, but also a moral one. The text emphasizes that organizations have a responsibility to provide accurate and honest information about their financial performance, and that this responsibility is rooted in the principles of integrity and transparency.

6. The sixth part of the document discusses the role of technology in financial reporting. It notes that advances in technology have made it possible to collect and analyze financial data more efficiently and accurately. The text also notes that technology can help to automate many of the tasks involved in financial reporting, which can reduce the risk of errors and improve the overall quality of the reporting process.

7. The seventh part of the document discusses the importance of communication in financial reporting. It notes that financial reporting is not just about providing information, but also about communicating that information in a way that is clear and understandable. The text emphasizes that organizations should take the time to explain their financial performance and the factors that have affected it, and that this communication is essential for building trust and confidence in the organization's financial reporting.

8. The eighth part of the document discusses the importance of compliance with financial reporting standards. It notes that organizations must adhere to the requirements of these standards in order to ensure the reliability and comparability of their financial statements. The text also notes that compliance with these standards is essential for maintaining the integrity of the financial system and for the ability to detect and prevent fraud.

9. The ninth part of the document discusses the importance of training and education in financial reporting. It notes that financial reporting is a complex task that requires a high level of skill and knowledge. The text emphasizes that organizations should invest in training and education for their financial reporting staff, and that this investment is essential for ensuring the accuracy and reliability of their financial reporting.

10. The tenth part of the document discusses the importance of collaboration in financial reporting. It notes that financial reporting is not just a task for the accounting department, but also a task that involves other parts of the organization. The text emphasizes that organizations should encourage collaboration between different departments and functions, and that this collaboration is essential for ensuring the accuracy and reliability of their financial reporting.

- Talwaker, P.K., Ratner, A., and Meites, J., 1963. In vitro inhibition of pituitary prolactin synthesis and release by hypothalamic extract. Am. J. Physiol. 205: 213-218.
- Uotila, U.U., 1939. On the role of the pituitary stalk of the anterior pituitary with special reference with thyrotrophic hormone. Endocrinology 25: 605-614.
- Westman, A. and Jacobsohn, D., 1940. Endokrinologische Untersuchungen an Kaninchen mit durchtrenntem Hypophysenstiel. Acta Obstet. Gynecol. 20: 392-433.
- Wislocki, G.B. and King, L.S., 1936. The permeability of the hypophysis and the hypothalamus to vital dyes, with a study of the hypophysial vascular supply. Am. J. Anat. 58: 421-472.
- Wislocki, G.B., 1937. The vascular supply of the hypophysis cerebri of the cat. Anat. Rec. 69: 361-387.
- Wislocki, G.B., 1938. Further observations on the blood supply of the hypophysis of the rhesus monkey. Anat. Rec. 72: 137-150.
- Yousef, M.K., and Johnson, H.D., 1968. Effects of heat and feed restriction during growth on thyroxine secretion rate of male rats. Endocrinology 82: 353-358.

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