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Walter Edwin Griesbach (1888-1968)
Life and Work

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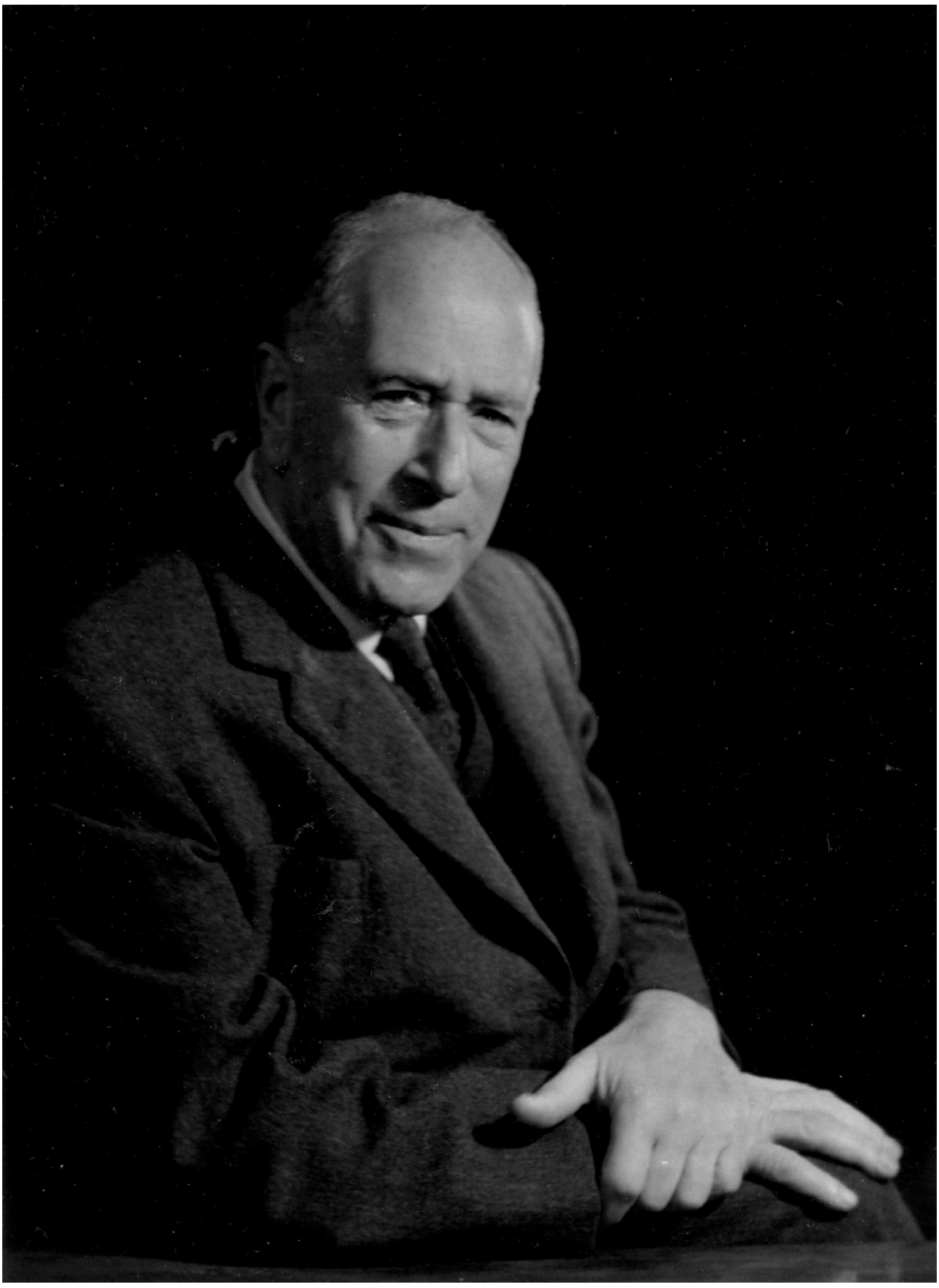

Medico Magistrali

I may not expect that, from the flight of fate, years have passed me by without a trace.
Each one seized the spokes of my wheel,
Spun it around, stopped, and left its mark.
One struck me in the gall bladder, another slowly bowed my neck,
Many of them laid their hands on my face:
Light spread inside me, yet the day's beams faded.
That in turn had its effect on the joints of my sole and foot,
My step grew heavy, my ankle began to twist.
This took the pleasure from vigorous slurping and munching,
It tortured my fingers in claw-like cramp.
One stroked over my hair, so that it was streaked with grey,
And banished me from the daughters to the mothers.
The gloss fades, just as on the antique sideboard –
The dowling splits, the drawer screeches: you're out of fashion!
But stand tall, with lively spirit, when the naked whirlwind
Wildly tears at old trees and clumps of branches,
And invisibly my little bird cuts victoriously through the thunderous song of the giant:
My bird's heart beats powerfully,
Whether it is rejoicing or afraid, for it is not made to linger in limbo.

Poem by exiled poet Karl Wolfskehl, Auckland 1941
For Dr. Walter Griesbach in Dunedin, New Zealand

Table of contents

A. Introduction

The life and work of the physician, endocrinologist, pharmacologist and metabolic pathologist Walter Edwin Griesbach is honoured for the first time in this investigation. This thesis examines not only the scientific history, but also portrays the life of a Jewish doctor and scientist in the first half of the twentieth century. The interweaving of his personal fate with the National Socialist dictatorship is a special aim of this investigation, for it clearly shows in what a cruel and inhuman way the National Socialists in Germany treated their victims. Mere figures and statistics cannot describe the realities of life of a Jewish citizen at that time; only a description of the consequences of contempt and persecution can do justice to individual cases.

So the first part of the work examines the personal fate of Griesbach as it was affected by the State measures of suppression.

In Chapter D (describing Griesbach's life), the study concentrates chronologically on the topics of "Third Reich", "Emigration" and "New Start in New Zealand". It exemplifies the situation of physicians in the Third Reich, during and after emigration, and their re-establishment in other countries.

The medical faculty of the University of Hamburg has in recent years published several works on this theme, and has shown in exhibitions the fate of former doctors of the University. At present further dissertations are being written under the guidance of Professors Dr. Ursula Weisser, Dr. Hendrik van den Bussche and Dr. Werner Selberg on the life of former Jewish physicians at the University of Hamburg[1]. The works mentioned look at the lives and works of colleagues of Walter Edwin Griesbach during his time at the "General Hospital St. Georg" in Hamburg[2].

The current work was suggested by Professor Dr. Hans-Erhard Bock, a colleague of Griesbach in the "General Hospital St. Georg" during the twenties. Griesbach was at the time of their association a Senior Consultant at the hospital, and Bock a medical intern. The investigation was also enthusiastically encouraged and supported by Professor Dr. Ekkehard Kallee. He had met Griesbach at the 1960 Conference on Internal Medicine in Wiesbaden. The two professors therefore knew Griesbach during different times and periods of his medical and scientific career. Professor Bock vividly remembers Griesbach's investigations

[1] Dissertation of Korinna Kauder on Arthur Bornstein (supervised by Prof. Dr. Ursula Weisser) and dissertation of Matthias Andrae on Arthur Lippmann (supervised by Prof. Dr. Hendrik van den Bussche).

[2] „Allgemeines Krankenhaus St. Georg", Lohmühlenstrasse 5, Hamburg, Germany

on metabolism, and on the "Congo-red Method"[3] from the twenties and early thirties. He himself wrote one haematological paper that followed from his work with Griesbach[4]. However, until the time of the completion of this thesis, he knew nothing of Griesbach's scientific research in New Zealand. Professor Kallee, on the other hand, knew only the publications on endocrinology written in New Zealand. It is therefore noteworthy that both professors, from their different perspectives, thought of Walter Griesbach immediately when contemplating the biography of a German-Jewish physician.

This leads to the second aim of this work: the examination of his scientific progress. In chapters E and F the scientific work of Griesbach is evaluated, by separating the research done in Germany and in New Zealand. After introductory chapters on the background of the research institutions in which he was working, the main focus is the appraisal of results in his biochemical publications on glucose metabolism, his haematological publications, and the thyroid and pituitary research.

Chapter C, with which the investigation begins, is an introductory description of the history of endocrinology up to 1940. The aim of this description is to show the knowledge at the time when Griesbach began his scientific work in this young area of research. It therefore illustrates how Griesbach's activity fits into the historical process of endocrinological research.

Griesbach stood out even in his early years, both in clinic and in research by his specialised skills. This is clear from the recommendations of his academic teachers[5], who predicted a distinguished academic career. Griesbach's life up to 1934 confirms this prognosis, which shows all the more clearly the destructive effects on his life of the National Socialist seizure of power. Despite the serious effect of the emigration and his age, Griesbach succeeded in establishing, in a foreign country and a new area of research, a field of study, which was acknowledged and appreciated worldwide. This shows his scientific abilities.

The humiliating treatment in the last years in Germany, the problems of establishing a career in New Zealand, as well as his advanced age, made this part of his life one of the most difficult. Certainly in this connection, the influence of his wife, who supported him energetically, must not be overlooked.

What makes Walter Edwin Griesbach's personality interesting and unusual is the combination of human and scientific achievement in the light of the fate that befell him.

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[3] W. E. Griesbach (1921 b); annual details of publications below without author information will be of Griesbach.

[4] H. E. Bock and G. (1933 c).

[5] Recommendations by Gustav Embden, Frankfurt/Germany, Wilhem Weintraud, Wiesbaden/Germany, and Theodor Deneke, Hamburg/Germany; these documents are available from the estate (E).

An assessment of his person and work in Chapter G, and a summary of the results in Chapter H, close the main part of this investigation.

Preceding the Index of sources and literature cited, Chapter I contains the first complete personal bibliography of Griesbach, covering one book and 76 scientific articles. In the appendix there is a hand-written letter of Griesbach to his New Zealand colleague Herbert D. Purves, dated 06.07.1948, plus four photographs of research colleagues of Griesbach from his time in Germany and New Zealand.

B. Sources and method of evaluation

In this investigation, mainly three groups of sources were used. The first group includes official documents such as birth-, wedding-, naturalisation-certificates, awards and photographs. In general, they reflect these facts correctly apart from typographical errors and the possibility of accidental or deliberate alterations. Apart from falsified documents, subjective implications cannot be found in these sources and they are highly reliable and predictive. They are therefore used in this investigation to verify and catalogue Griesbach's life and work.

The second group of sources were letters, curricula vitae, memoranda, reports, petitions and expert opinions. It is of no importance whether these sources are hand-written or printed, as they are authentic but can lead to subjective interpretations of events. An objective statement of fact, which often can not be verified, might therefore reflect the subjective interpretation, i.e. the feelings of the person who wrote the letter. As the aim of an investigation has to be the factual description of events, theses sources can only be used with caution.

The third group of sources, which were predominately used in this investigation, were the results of written and verbal questions put to contemporaries of Walter and Olga Griesbach. In this study, a long time period – 25 years – lay between the death of Griesbach (1968) and the interviews, which were performed in 1993/1994. The dangers and sources of error of this type of source used are obvious. The memories of more than 25 years after the occurrence are neither exact nor complete. Own wishes and expectations become mixed with memories; sympathy and antipathy affect the content of the statements. Mostly, the statements are positively influenced as they predominately derive from persons, who like to recall pleasant memories. The immense personal involvement in these recollections causes an enormous heterogeneity of the results and the lack of control of their correctness can lead to systematic errors. Nevertheless, sources of this nature can be used in this sort of investigation and they help to portray the person according to his thoughts and actions. If their limited reliability is kept in mind, these sources can furnish important complementally information about a person. A mail questionnaire was hereby a useful tool. Special attention was given to conflicting statements, or statements given by only one person alone. These were therefore marked in the text as "unknown" or "unsubstantiated statement". Collectively, the statements given for this investigation were very helpful in elucidating Griesbach's personality and to confirm facts, and were rarely contradictory. In only one instance did a person not want to give an opinion, which did not concerned Walter Griesbach but his wife Olga Griesbach.

In analysing the life and work of a person, the personal identification of the author with the subject of her investigation must also be taken into account. Naturally, the interests and attitudes of the author influence to a certain degree the image which is created of a person the author never knew herself. The interaction of distance and sympathy forces the author to be aware of her emotions as well as the necessity to preserve her objectivity. A scientific analysis should therefore never be modified by her personal feelings, enthusiasm or rejection of the data.

C. A historical survey of endocrinology up to 1940

1. The three stages of development in endocrinology

The history of endocrinology can be divided into three phases[6]. The first phase, from 1652 until 1839, covers the prehistory of endocrinology, which is associated with the names of Thomas Wharton, Théophile de Bordeu, Julien-César Legallois and Johannes Müller[7]. Until the end of the 18th century, hormones weren't known to be chemically definable substances. Until the beginning of the 17th century, there was no basis for assuming the existence of internal secretions, as the description of the circulation by William Harvey did not appear until 1628 when he postulated the secretion of special substances in the circulating blood[8]. Thomas Wharton's publication "Adenographia" from 1656, which was based on Harvey's previous work, dealt mainly with the anatomy of glands and therefore helped much to advance endocrinological research[9]. Théophile de Bordeu was the first scientist, who publicly assumed in 1775 a sort of internal secretion, instead of a "Consensus partium" based on a neuronal mechanism[10]. Unfortunately, his lectures, which were enlarged and expanded by Julien-César Legallois, were overlooked at the time. In 1830 Johannes Müller was the first to make a distinction between secretion and excretion, and collectively called the spleen, adrenal glands, thyroid gland, thymus and placenta "blood vessel-knots"[11].

The second phase in the history of endocrinology was from 1839 to 1889, when the main definitions of endocrinology were enunciated[12]. Arnold Adolph Berthold could prove in 1849 the existence of internal secretion by transplanting testes in roosters. Therefore, nowadays the birth year of endocrinology is set at 1849, and Berthold is considered its experimental founder[13].

A further milestone was Claude Bernard's differentiation in 1855 between an external and an internal secretion in the liver, such as the external secretion of bile and the internal secretion of dextrose. Because of this differentiation, Bernard is to be considered the founder of the

[6] Schönwetter (1968), 62
[7] The year 1652 is marked by the first lectures of T. Wharton - the basis for his famous book "Adenographia"; see Abderhalden (1950-1952), 4545f.
[8] L.c. 4545.
[9] L.c. 4540.
[10] Leicester (1974), 224.
[11] Abderhalden (1950-52), 4546.
[12] Schönwetter (1968), 62.
[13] Leicester (1974), 224.

doctrine of internal secretion[14]. The importance of internal secretion for medicine became more noteworthy, when Charles-Edouard Brown-Séquard made experiments on himself with extracts of bull testes. Brown-Séquard was a very confident representative of the doctrine of internal secretion, and showed already in 1869, that all glands with or without ducts produce substances which are secreted into the blood and which would cause illness if missing[15]. In the same year that Brown-Séquard published the experiments on himself, Joseph von Mering and Oskar Minkowski proved that the cause of Diabetes mellitus is a pancreatic disorder, a fact which strengthened the doctrine even more[16].

During the third phase of the development of endocrinology, research concentrated on single endocrine organs and their hormones[17]. In 1900, Leonid Wassiljew Ssobolew concluded from his experiments, that the hormone was produced in the islets of the pancreas, and suggested that it be extracted from them. Georg Ludwig Zuelzer was accordingly able to treat patients suffering from Diabetes mellitus in 1908 with these extracts. It was Charles Herbert Best and Frederick Grant Banting, who extracted insulin in 1921[18]. The first hormone to be isolated in crystalline form was adrenaline, which was accomplished independently by Jokichi Takamine and Thomas Bell Aldrich in 1901[19], and three years later it was synthesized by Friedrich Stolz and H. D. Dakin. This was the first synthetic production of a hormone[20]. The designation "hormone" wasn't introduced into the doctrine of internal secretion until 1905 by Ernest Henry Starling[21], and in the same year the existence of another hormone, gastrin was proved by J. S. Edkins[22]. In 1906 the hormone oxytocin was identified by Henry Hallet Dale and has been used in obstetrics ever since the year 1909[23]. It was Nicola Pende who in 1922, at the meeting of the Italian Society for Internal Medicine, for the first time called the young science of internal secretion "endocrinology"[24]. The next hormone to be discovered was the crystalline thyroid hormone, which was extracted from thyroid glands by E. Kendall in 1914. But it wasn't until 1927 that Charles Robert Harington and Georg Barger succeeded in synthesizing thyroxine[25]. The first hormone of the anterior pituitary gland, somatotropic

[14] L.c.
[15] L.c.
[16] Saffran (1992), 126.
[17] Schönwetter (1968), 62.
[18] Saffran (1992), 132.
[19] Vague (1983), 2757.
[20] Leicester (1974), 227.
[21] Karlson (1982), 3-14.
[22] Vague (1983), 2757.
[23] L.c. 2768.
[24] L.c. 2758.
[25] Hall, Glick (1976), 231.

hormone, was discovered in 1921 by Herbert McLean Evans and C. Long[26]. Five years later Bernhard Zondek and Selmar Aschheim described by transplantation experiments of the anterior pituitary gland the existence of substances, which caused the ripening of ovarian follicles and the formation of corpora lutea[27]. Zondek and Aschheim called those gonadotropins "Prolan A and B"[28]. In 1928 the measurement of gonadotropins in urine was named after these two scientists the "Aschheim-Zondek pregnancy test"[29]. At the same time other hormones of the anterior pituitary gland were discovered. Transplantation experiments on animals without pituitaries may be regarded as the basic principle for the identification and later purification of these hormones[30]. With this experimental tool, P. Stricker and F. Grueter were able to identify the hormone prolactin in 1928, and O. Riddle, Bates and Dykshorn isolated it in 1932[31]. The connection between TSH and Thyroxine was understood when M. Aron, L. Loeb, F. Hoffmann and Bassett identified the thyrotropic hormone in 1929[32]. The corticotropic hormone was identified in 1933 by A. Anselmino, L. Herold and F. Hoffmann[33], at the same time as Collip, E. Anderson and Thompson identified the adrenotrope hormone[34]. These results provided the basis for the discovery of the correlation between ACTH and the adrenal gland. In 1934 Adolf Butenandt and Ulrich Westphal, Max Hartmann and Albert Wettstein, Karl H. Slotta and co-workers, Oskar Paul Wintersteiner and W. M. Allen isolated independent of each other the hormone of the corpora lutea (progesterone) in cristalline form[35]. In 1935 Ernst Laqueur extracted testosterone[36] and Tadeus Reichstein 1938 desoxycorticosterone from adrenal glands. The synthesis of the latter hormone has found broad clinical application, apart from its use in Addison's disease[37]. Finally, in 1940, Choh Hao Li isolated the luteinising hormone, LH[38].

The first two phases in the development of endocrinology paved the way for an understanding of hormones and their function in the human body. In contrast to this, the third phase is distinguished by a plethora of discoveries of hormones and their function. Knowledge of the

[26] Vague (1983), 2767.
[27] Abderhalden (1950-52), 4554.
[28] Medvei (1982), 826.
[29] Abderhalden (1950-52), 4554.
[30] L.c., 4555.
[31] Labhardt (1978), 71.
[32] Vague (1983), 2767 and 2760.
[33] L.c., 2767.
[34] Labhardt (1978), 71.
[35] Abderhalden (1950-52), 4556.
[36] L.c., 4555.
[37] L.c., 4558.
[38] Medvei (1982), 827.

structure and the physiology of hormones provided a great stimulus to endocrinology and thus opened up new horizons.

2. Exploration of the pituitary gland

The pituitary gland was already known as an organ in ancient times. Galen postulated its function to be the clearing of mucus produced by the brain. Catarrh of the upper respiratory system would therefore be caused by an excessive production of mucus from the pituitary gland[39]. Andreas Vesal agreed with Galen's opinion and called the gland in connection with its supposed function "Glans cerebri pituitam excipiens"[40]. Galen's theory was accepted until Conrad Viktor Schneider proved it to be wrong in 1660[41]. Schneider's opinion was supported by Richard Lower who wrote in 1672, that the product of the pituitary gland would reach the blood circulation via the "wonder net of the carotids"[42]. In his dissertation "De basi encephali et originibus nervorum cranio egredientium libri V", Samuel Thomas Soemmering used the contemporary designation "Hypophysis cerebri"[43] in 1778 for the first time. With regard to the organ structure the researchers Giovanni Santorini, Jacques-Bénigne Wibslow and Albrecht von Haller described the subdivision of the organ into an anterior and a posterior lobe at the beginning of the 18th century[44].

At the end of the 18th century and the beginning of the 19th century different opinions were expressed concerning the still unknown function of the organ. Johann Friedrich Meckel assumed that the pituitary gland produced a fluid which nourished the brain[45]. Franz Joseph Gall, the founder of phrenology, Carl Gustav and Ernst Burdach assumed different functions of the pituitary gland, whether this be that of a large ganglion, the head end of the nervus sympathicus or that of the top end of the spinal chord[46]. In 1810 Joseph Wenzel suspected the cause of epilepsy to be illness in the pituitary gland[47]. The first descriptions of a pituitary gland tumour that was accompanied by amaurosis[48] originated from P. Rayer and Ward in 1823. The description of the embryological development by H. Rathke led to the breakthrough in the identification of the pituitary, which was now regarded as a gland[49]. The

[39] Medvei (1982), 824.
[40] Schoenwetter (1968), 32.
[41] L.c.
[42] L.c. 33.
[43] L.c. 32.
[44] L.c.
[45] L.c. 33.
[46] Abderhalden (1950-52), 4539.
[47] Schönwetter (1968), 34.
[48] Hirsch (1952), 268
[49] Medvei (1982), 824.

first indications of the existence of different cells in the anterior pituitary gland were brought forward by Adolph Hannover in 1843[50].

The main symptoms of the disease of "Melalacria", as it was known at that time, was described by Cunningham in 1879[51], whereas Pierre Marie gave it the name "acromegalia"[52] in 1886 following the specification of the symptoms. One year later Oskar Minkowski observed an enlargement of the pituitary gland in connection with the clinical disease and Pierre Marie identified acromegalia as a consequence of a pituitary tumour[53]. Roberto Massalongo regarded acromegalia as an over function of the pituitary gland[54], and, at the turn of the century, Carl Benda was able to show that only the anterior pituitary gland is changed as a result of a multiplication of the chromophil cells. Benda is considered to be the discoverer of the eosinophil adenoma of the anterior pituitary gland due to the findings of his histological research[55].

Around 1900 Joseph Babinski and Alfred Fröhlich were able to define an additional disease of the pituitary gland: the "adiopose-genitale syndrome"[56]. J. Erdheim published the first specifications on pituitary gland histology in 1903 and also classified tumours on the basis of the three types of cells that had been discovered so far[57]. In collaboration with the brain surgeon Harvey Cushing, he described tumours of the pituitary gland canal in the following year which he designated as craniopharyngeoma[58].

At almost the same time Victor Alexander Haden Horseley proposed the removal of pituitary tumours via the central cranial fossa[59]. Hermann Schloffer developed the trans-sphenoidal method as a modification in 1906/07, which was further developed by Oskar Hirsch to comprise an operation via endonasal access under local anaesthesia in 1909/10[60].

The pituitary gland associated diseases of hirsutism, dwarfism and cachexia were described in 1910 and 1911 for the first time[61].

Since the twenties the history of the pituitary gland has been increasingly described in connection with the general history of endocrinology, as has been presented in the first chapter of this work. The identification of the growth hormone by Herbert McLean Evans and

[50] Schönwetter (1968), 32.
[51] Vague (1983), 2754.
[52] Melmed (1995), 3.
[53] L.c.
[54] Medvei (1952), 825.
[55] Abderhalden (1950-52), 4576.
[56] Medvei (1983), 825.
[57] Hirsch (1952), 268.
[58] L.c.
[59] L.c.
[60] L.c.
[61] Vague (1983), 2760.

C. Long in 1921 marked the beginning of exploration into the anterior pituitary gland hormones.

As well as the research into hormones, additional pituitary diseases and treatment modalities were described. For example, Bernardo A. Houssay succeeded during the 1930s in healing experimental diabetes in laboratory animals by means of the new method of "hypophysectomy"[62]. A. C. Crooke described basophile and hyaline cells of the pituitary gland[63] in 1935 and M. Sheehan established in 1939 that "pan-hypopituitarism" is caused by postpartal haemorrhage with subsequent necrosis[64].

[62] L.c. 2759.
[63] L.c. 2760.
[64] Medvei (1982), 827.

3. Exploration of the thyroid gland

The thyroid gland was already known in ancient times and was classified together with the salivary glands[65]. Galen, Paracelsus, Andreas Vesal and Bartholomeus Eustachius were extensively involved in the discovery of this organ. In 1541 Vesal called the thyroid "glandes larynges radici adnatae"[66], and Eustachius used the designation "isthmus" for the median section of the thyroid[67] twenty years later.

Thomas Wharton gave the thyroid the name "glandula thyreoideae" in his famous writing "Adenographia" from 1656. Wharton used this designation to describe the rectangular shape of the organ and mistakenly used the plural form as he assumed that the two thyroid lobes worked independently[68]. He saw the task of the gland in the heat retention of the cartilaginous substance of the larynx as well as in the beautification of the throat[69]. In 1706 Giovanni Battista Morgagni discovered the thyroid follicles and their viscous content, the colloid[70]. The disease of hyperthyroidism was described as early as 1761 by Giovanni Battista Morgagni and in 1800 by Antonio Giuseppe Testa[71]. Up to the 19th century the swelling of the thyroid was still considered to be a so-called "bronchocele" and was grouped to the bronchial system[72].

Thus there were many different opinions regarding the function of the thyroid gland prevailing around 1800. Bernhard Nathaneal Schreger considered it to be the regulatory organ for the blood circulation in the brain[73], Johann Heinrich Ferdinand Autenrieth gave it the role of a station in which the blood was prepared for the exchange of gas in the lungs[74]. Joseph Dömling advocated around 1800, a frequently expressed opinion at that time, that the thyroid is the mucous-producing organ to moisten the trachea[75].

In his posthumously published paper, Caleb Hillier Parry described the entire symptoms of goitre with exophthalmia, which was confirmed by Robert James Graves ten years later, and recognised as the pathological syndrome of hyperthyroidism[76]. Carl Adolph von Basedow described the symptoms of exophthalmia, goitre and palpitations as the so-called "Mersburg

[65] Medviei (1982), 846.
[66] Schönwetter (1968), 35.
[67] Medvei (1982), 847.
[68] Schönwetter (1968), 35.
[69] L.c. 36.
[70] L.c. 35.
[71] Abderhalden (1950-52), 4579.
[72] Werner (1991), 3.
[73] Schönwetter (1968), 40.
[74] L.c. 40.
[75] L.c. 36.
[76] Werner (1991), 4.

triad" according to his site of activity. However, the question of the cause of the disease remained unanswered until 1884[77].

At the beginning of the 19th century, attempts were made to elucidate the function of the thyroid by trial extirpation. These mostly failed due to the fact that the parathyroid glands were usually removed in addition to the thyroid itself[78]. Their absence then dominated the resulting symptoms leading along the wrong path.

1848 was of great significance for the exploration of the thyroid gland: Gabriel Gustav Valentin recognised the epithelial lining of the thyroid follicles, Dionysios Panagiotades and K. Wagner introduced the term "follicles"[79]. Alexander Ecker claimed a kind of secretion from the thyroid due to the large blood volume within the organ[80]. Moritz Schiff developed a method of removal and re-implantation of the thyroid in 1856[81], and Jean Nicholas Corvisart defined the disease of tetania five years later[82].

In 1867 Armand Trosseau was able to report of an "erroneous" administration of iodine instead of digitalis in the treatment of thyroid toxicity and the consequences thereof. The advancing differentiation of the various diseases with regard to the thyroid led to the description of "pachydermal cachexia" by J. M. Charcot and Gilbert Ballet in 1877 that was renamed to "myxedema" in the same year by William Odd[83]. In 1880 Paul-Jules Tillaux and Ludwig Rehn began experimenting with the first partial thyroidectomies for the healing of Morbus Basedow[84]. It was Rehn who suspected the hyperfunction of the thyroid to be the cause of Morbus Basedow four years later[85], which was confirmed by Paul Julius Moebius in 1886[86].

The description of an "active principle" and the postulation of the inner secretion by Moritz Schiff was a great step towards the direction of the research methods of the 20th century. Schiff observed during his trials with thyroid transplantations that these administrations prevented the symptoms of cretinism. Thus a substitute therapy was possible[87]. J. M.

[77] Abderhalden (1950-52), 4580f.
[78] Schönwetter (1968), 36.
[79] L.c. 35.
[80] L.c. 36.
[81] Vague (1983), 2752.
[82] L.c.
[83] L.c.
[84] Aberhalden(1950-52),4583.
[85] L.c. 4582.
[86] Hercus(1946), 325.
[87] Leicester(1974), 225.

McKenzie and Fox also advocated this new therapy in 1892 as they had also found the oral administration of thyroid extract to be effective[88].

As a result of histological investigations of Basedow goitres, William Smith Greenfield and Friedrich Müller were able to detect an enlargement and multiplication of the epithelial cells of the follicle and colloid in this disease in 1893[89]. E. Baumann then isolated "thyroidine" from the thyroid in 1895 that was later known as "iodothyrine"[90]. He also noticed that the concentration of iodine reacted in proportion to its activity[91]. As the glands originating from endemic goitre areas contained less iodine, a renaissance of the iodine therapy occurred in the treatment of endemic goitre[92].

The first attempts to avoid thyroidectomy by means of treatment with X-rays, as was proposed by E. D. Williams, Pusey and Caldwell in 1902/03, was not sustainable[93]. Only after the production of radioactive iodine by Enrico Fermi in 1934[94] Saul Hertz was able to enforce the therapeutic application in the case of hyperthyroidism[95], which has been employed as "medical thyroidectomy" until today.

Two additional diseases of the thyroid gland were defined in 1912 and 1914, namely "Hashimoto´s disease", a lymphomatose goitre[96], and the acute purulent thyroiditis by De Quervain[97]. In the same year thyroxine[98] was isolated by E. C. Kendall.

Thyroid therapy was inconceivable without the application of iodine at that time as the first report of a successful iodine prophylaxis for school children from 1917 illustrates[99]. It was also possible to successfully treat Morbus Basedow by repeated administrations of iodine, as was reported by A. Neisser in 1920, with Plummer and Boothey also recommending the preoperative treatment of Morbus Basedow with Lugol´s solution (potassium-iodine solution) in 1923[100]. Plummer described toxic adenoma in 1926 before C. R. Harrington and G. Barger synthesised thyroxine as the second hormone one year later[101].

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[88] Hercus (1946), 325.
[89] Aberhalden (1950-52), 4582.
[90] Werner (1991), 4.
[91] Hercus (1946), 325.
[92] L.c.
[93] Aberhalden (1950-523), 4584.
[94] L.c.
[95] L.c.
[96] Medvei (1982), 850.
[97] Vague (1983), 2763.
[98] Cody (1991), 225.
[99] Hercus (1946), 326.
[100] L.c.
[101] Cody (1991), 225.

M. Aron, I. Loeb and Basset reported the effect of pituitary gland extracts on the thyroids of mammals in 1929[102]. With this and the following investigations, a new epoch in the field of thyroid research commenced. As a result of their experiments on rabbits, Alan Mason Chesney, T.- A. Clawson and B. Webster had established the goitrogenic effect of Brassica seeds one year previously[103]. Charles Hercus and Herbert Dudley Purves continued this research work using different species of Brassica seeds in 1936[104]. Walter Griesbach was able to demonstrate during the continuation of these experiments in 1941 that changes in the pituitaries of rats fed on a Brassica seed diet corresponded to those resulting from partial thyroidectomy[105].

[102] Hercus (1946), 326.
[103] L.c.
[104] L.c. 327.
[105] L.c.

D. Life of Walter E. Griesbach

1. General remarks

In this analysis Walter E. Griesbach's life will be separated into two main sections. At the beginning the main events of his life are listed chronologically. The biographical part is separated into the time before and after the emigration. This seems to be appropriate as the emigration represents a strong demarcation in his life and separates not only the two phases from the point of view of his personal circumstances but also of his career.

About his childhood and youth, apart from other material, mainly the memoirs of his brother George, documents from the estate (E) and reports of relatives were used[106]. Most of the facts about his later years are based on archival material, his estate and reports from relatives, friends and colleagues. Despite these sources, some circumstances and parts of Griesbach's life could not be completely authenticated and therefore have to remain unknown.

The topic of life and career opportunities of Griesbach as a German-Jewish physician during National Socialism and during his emigration to New Zealand will be discussed extensively. Special emphasis is given to the situation of the gradual "exclusion politics" of Jewish doctors during the "Third Reich" and to their classification as so-called "enemy aliens" in New Zealand.

[106] For significance of source materials see Chapter A. Introduction

2. Overview of his life

7.10.1888	Born in New York as first of three children of Samuel Albert and Rosa Anna Griesbach, née Seeligmann
1894	Death of his father
1894	Return of the family to Hamburg
1895 – 1897	Thomsen-Preschool in Hamburg
1897 – 1906	Wilhelm-Gymnasium in Hamburg and "Abitur"
1906	Medical studies in Freiburg/Breisgau, Kiel and Munich Internship during vacations in the Pathological Institute in Hamburg (Director Morris Simmonds)
1909	Physikum in Freiburg/Breisgau Internship during vacations in the Chemical-Physiological Institute in Frankfurt/Main (Director Gustav Embden) and in the Pathological Institute in Hamburg (Director Morris Simmonds)
1910	First publication
1911	State exam in Freiburg/Breisgau, grade "very good"
1911 – 1912	Practical year in Internal Medicine in Freiburg/Breisgau (Director De la Champ) and in Frankfurt/Main (Director Schwenkenbecher) From July 1912 on also trainee and apprentice in the Chemical-Physiological Institute in Frankfurt/Main (Director Gustav Embden)
1912	Scholarship of the "Manfred Bernhard Schiffsche Stipendienstiftung"
1912 – 1913	Conferral of a doctorate in Freiburg/Breisgau "Über Milchsäurebildung im Blute", grade "magna cum laude"
1913	Assistant in the Chemical-Physiological Institute (Director Gustav Embden) Five publications
1914	Junior and Senior House Officer in the Public Hospital in Wiesbaden (Director Wilhelm Weintraud)
1916 – 1918	Army doctor in World War I
1919	Acceptance in the register of the Hamburg Medical Association
1919	Assistant on the Director's ward in the General Hospital of St. Georg (Director Theodor Deneke)

	Research work in the Pharmacological Institute of the University of Hamburg (Director Arthur Bornstein)
1919 – 1921	Consultant at the General Hospital St. Georg, Hamburg
1922	Besides his clinical work, private practice as specialist for Internal Medicine in Hamburg
	Scientific assistant in the Pharmacological Institute (Director Arthur Bornstein)
1922 – 1925	Lung welfare doctor and lecturer at the nurse's training school
1924	Habilitation at the University of Hamburg for Pharmacology with emphasis on metabolic pathology
	Title of the habilitation treatise: "Über die Gesamtblutmenge"
17.5.1924	Inaugural lecture "About Insulin"
1924	Resignation from the Hospital St. Georg
	Assistant Professor at the Pharmacological Institute (Director Arthur Bornstein)
6.10.1924	Marriage to Olga Hallenstein
1926	Successful application as Senior Consultant in the General Hospital St. Georg
1930	Appointment as Associate Professor
1934	Revocation of state doctorate on the basis of §6 of the "Law for the re-establishment of the professional public service"
	Deprivation of his position in the General Hospital St. Georg
	Exception for Griesbach with the limitation: "allowed to treat Jews only"
May 1938	Medical Director of the Department of Internal Medicine of the Israeli Hospital in Hamburg
28.8.1938	Application to study medicine in New Zealand
30.9.1938	Cancellation of medical licence due to the 4th regulation of the "Reich Citizens law" for the "Jewish medical orderlies"
18.10.1938	Acceptance of a research position in Dunedin, New Zealand, shortly followed by an immigration permit
24.4.1939	Arrival in Wellington, New Zealand (journey via London, New York, Perth, Melbourne, Sydney)
June 1939	Start of independent research work on thyroid and pituitary glands

Autumn 1939	Assistant lecturer in the Physiological Institute of the University of Otago, Dunedin
	Research work in the "Thyroid Research Department"
1941	First publications in British Medical Journals
	Official employment in the "Thyroid Research Department"; further part-time lecturing in the Physiological Institute
1945	Full-time employment in the "Thyroid Research Department"
1946	British Citizenship
1948	Research expedition to Berkeley, U.S.A.
1951	Research expedition to London and New York
1953	Official title of a "Research Officer Endocrinology Research" and "Honorary Lecturer in Endocrinology"
1954	ANZAAS conference in Canberra
1957	ANZAAS conference in Dunedin
1959	Part-time retirement
1960	Lecture at the Conference for Internal Medicine in Wiesbaden/Germany on "Regulation of the thyroid gland"
	Lectures in Tübingen, Hamburg-Eppendorf and in the General Hospital St. Georg in Hamburg
5. – 9.7.1960	"International Goitre Conference" in London
18.-23.7.1960	"International Endocrinology Conference" in Copenhagen
	Research excursions to Dallas and Berkeley
1961	Last visit to a conference: London
12/1961	Official full-time retirement
	7 further publications
1967	Admission to the "Deutsche Akademie der Naturforscher Leopoldina", Leipzig/Germany
10.8.1968	Walter E. Griesbach dies in Dunedin/ New Zealand
2.3.1973	Olga Griesbach dies in Dunedin/ New Zealand

3. From birth till emigration from Germany

3.1. Ancestry, childhood and adolescence (1888-1906)

Walter Edwin Griesbach was born on the 7th of October 1888 as the first of three children of Samuel Albert Griesbach and his wife Rosa Anna Griesbach née Seeligmann in New York, in Dakota Flats, 72nd Street[107]. His brother Georg(e) Albert was born in 1890, his sister Alice Henriette Friederike in 1894, after the death of their father[108].

Their father, the son of the merchant Isaac Griesbach and his wife Rahel née Katz, came from Beverungen in Westphalia[109]. He was described as a "warm-hearted, intelligent man with wide-ranging interests"[110]. After participation in the German-French War of 1870/71 he took a position as merchant in a Hamburg firm importing grain sacks from Dundee. As he was responsible for purchasing, he had to move to Scotland with his company. Soon afterwards the firm went bankrupt after speculation with jute, and Albert Griesbach took up a position in 1883 with the largest competitor firm, Robert Lamb & Co., in Dundee/Scotland, with the task of founding the firm Lamb & Griesbach after moving to New York[111].

Their mother, Rosa Anna Seeligmann, who had married Albert Griesbach on 24.7.1885 in Hamburg, was the daughter of the banker Siegfried Seeligmann and his wife Henriette née Bauer, from Hamburg-Altona. Rosa Griesbach is described as a "large, imposing and to some extent intimidating woman"[112]. She was "sensitive but very logical and formal. So it is not surprising that the children had good manners"[113].

Letters were the basic connection between the children and the very busy father, "as their mother herself was scarcely able to speak of him"[114].

After the early death of the father in January 1894 – Griesbach was five years old – and the subsequent birth of the daughter Alice in June, the mother returned to Hamburg in July 1894, as her whole family lived in Hamburg and the cost of living was considerably lower than in New York[115]. Robert Lamb, the father's business partner, paid the mother a generous pension

[107] Birth Certificate, 17.11.1888.
[108] Lassally (WC, written communication); no exact details are known regarding the father's death.
[109] Marriage certificate Samuel Albert Griesbach and Rosa Anna Seeligmann, 24.7.1885 (E, estate).
[110] Griesbach (1980), 4.
[111] L.c.
[112] Brook (WC).
[113] Lassally (VC, vocal communication).
[114] Griesbach (1980), 5; in the estate of Walter E. Griesbach was a birthday letter of his father for his fourth birthday from the year 1892.
[115] L.c. 7.

of $200000. This sum enabled her and the children to live comfortably. Despite the inflation in the 1920's she was able to live on this sum for 43 years. After her death in 1938 the National Socialists seized the remainder of the money[116].
George, two years younger, describes in his memoirs their childhood in Hamburg:

> "We lived in a house in Hamburg, in Johns Allee 31, which my mother bought in 1898 […] because it was two houses away from her nearest and dearest relative, […her] sister Charlotte Hahlo […] our house was high and narrow: ground floor, first and second."

In the cellar was a kitchen, rooms for the cook and the housemaid, a W.C. and a small room which Walter and Georg used as a darkroom for developing films[117].
From George's memoirs, the life of the upper middle class, to which Albert Griesbach's widow and her family belonged, is clearly seen:

> On the ground floor was "a little entrance hall, off which the "salon" for visitors where mother held her Saturday afternoon "Jours" […] The salon had a side wing with a ceiling-high mirror where stood the piano and where my daily practising on the violin took palace, as also my brother's on the piano […] My mother had frequent invitations to dinner parties and, naturally, she had to invite in her turn […] usually 18-20 guests. […] The dignified oaken chairs with their brown, smooth leather seats and backs were then moved from the walls around the table, the enormous linen table covers with their jacquard woven designs were taken out, dishes in silver and plate taken from the safe […] and placed along the table to contain flowers, fruit and sweets".[118]

Despite, or perhaps because of the lack of a father, Rosa Griesbach was a very energetic and conscientious mother. She took care not to give the impression that the family was wealthy, gave the children no pocket money and did not spoil them in the slightest[119].
From "Easter 1895 until Michaelis 1897"[120] Walter Griesbach attended the Thomsen Primary School at The Esplanade 42 in Hamburg[121]. As his German was inadequate, the teacher

[116] L.c.
[117] L.c. 10.
[118] L.c.
[119] L.c. 14.
[120] Certificate of dismissal (E); all school certificates are available in the estate.
[121] C.V. of Griesbach (E).

insisted that only German should be spoken in the family[122]. After primary school Griesbach went to the "Wilhelm-Gymnasium" in Hamburg, and passed his "Abitur" as the best scholar of his class. In May 1906 Rosa Anna Griesbach and her children were accepted as German Citizens[123].

During his whole time at grammar school Walter Griesbach was always among the nine best pupils in his class, and from 1901 until his "Abitur" he was consistently the best pupil. During his school-time he learned Latin, French, Greek and English. His worst marks were always in mathematics, drawing, gymnastics and singing. For his exercise books his marks ranged from "satisfactory" to "poor". Under "behaviour" there are frequent complaints in the first years about "W.'s tendency to chatter"[124], and he was often reproached for "talkativeness"[125].

The absence of a father may also have led to Griesbach's attachment to Dr. Morris Simmonds, their family doctor, who was the same age as his father[126].

Already during his time at school Griesbach visited together with Morris Simmonds[127] the new Pathological Institute in the General Hospital St. Georg, which was headed by Simmonds. Indeed, Simmonds played a major role in Griesbach's decision to study medicine, as Griesbach wrote in 1965: "Simmonds introduced me to medicine"[128]. The fact that Griesbach, in later years worked in the subspecialty of Endocrinology, which was also Simmond's main interest, seems to have been predestined.

Besides considering studying medicine, Griesbach was also attracted to the study of music. Music, particularly the piano, played an important part in his life from his earliest years. Because of the uncertain prospects for professional musicians, however, he decided early-on to study medicine[129].

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[122] Hunter (VC).

[123] Naturalisation Certificate (E); with this act they automatically lost their American Citizenship; see Lassally (VC).

[124] School certificate (E).

[125] L.c.

[126] Even at the age of 79 Griesbach wrote in a very affectionate manner about this obviously extremely formative personality: "I first came to Hamburg with my family and Dr. Morris Simmonds presented himself to us as our "family doctor". From then on, he led us through all the following years, with their inevitable sequences of children's diseases. I remember that my brother and I loved every one of his medical visits. We were so attached to him for his kindness and joviality that my mother got used to making all decisions, like those about schooling, holiday resorts, sports, etc., only after consultating with "our Doctor", whose words we came to look upon as infallible"; see G. (1965 b), 1671.

[127] Regarding Simmonds, Griesbach wrote: „Morris Simmonds gave up his private practice in 1909 and became prosecutor with the title of a professor. With the foundation of the University of Hamburg in 1919 Simmonds became first Professor of Pathology. His special interest was the endocrine organs, especially the pituitary gland. The insufficiency of the anterior pituitary gland was named after him as "Simmond's Disease"; see L.c. 1672 f.

[128] L.c. 1671.

[129] Petersen (VC).

He was not the first doctor in the Griesbach and Seeligmann families. Gustav Seeligmann, his uncle on his mother's side, was a Gynaecologist and Principal Doctor of the Lennox Hill Hospital in New York[130]. It is not known if this influenced him in his choice of a career. Morris Simmonds's influence was the deciding factor.

[130] Griesbach (1980), 4.

3.2. Student time (1906-1912), early scientific works, Army Doctor (1916-18)

Griesbach began his study of human medicine in the winter semester of 1906. He studied mostly in Freiburg im Breisgau, where he sat all his exams; but he spent one semester in Kiel and another in Munich[131].

In October 1907 Griesbach was baptised in the Evangelical-Lutheran Church of St. Johannis in Hamburg-Eppendorf by Rev. R. Kaufmann[132]. It is not known what made him take this step[133]. Religion and belief were of no interest to Griesbach, as were for his whole family and his future wife Olga[134].

He passed his pre-clinical exam ("Physikum") in Freiburg in 1909[135], and worked in the following holidays for the first time in the Chemical-Physiological Institute in Frankfurt am Main. The Head of this Institute was Gustav Embden, whose main research field was glycolysis[136]. This topic in its wider sense was also the subject of Griesbach's first research work, dating from 1910 and bearing the title "Ueber Acetessigsaeure in der Leber diabetischer Hunde; 2. Mitteilung"[137]. The work in Frankfurt was his first in the field of research, although

[131] StAH: Medizinkollegium IV C 82.
[132] Certificate of Baptism (E).
[133] It seems to be very unlikely, that Griesbach converted because of religious reasons. It is much more likely that he took this step to forestall any disadvantages in his profession which could be caused by his Jewish background. It should be noted, that around 1900 despite the increasing emancipation of Jews and their legal equality, social discrimination of Jewish citizens was still apparent. Although the constitution of the German Empire of 1871 declared the total legal equalisation, nevertheless "during the Empire there started a community anti-Semitism of unknown extension"; see Richarz (1989), 11f. Now it was especially jealousy of the education and wealth of the Jewish citizens, which was the reason for anti-Semitic harassment. After the end of World War I and in the following difficult political years, including the burden of reparation payments, there was an increase of anti-Semitism; see Kümmel (1989), 31 and (1985), 60. This had implications also for the academic professions. By 1917 the number of Jewish professorships in medicine had dropped from 20-25 to 13. This represents a percentage of 1 % of the ordinary professorships; see Kröner (1989 b), 39. The average age of the 1918 and earlier appointed German-Jewish professors was at 49 years clearly well above the total German average. This might indicate that "Jewish professors were, if at all, promoted only late in their career"; Kröner (1989 a), 7. Even in the Weimar Republic, when the age of Jewish professors (43.5 years) was the same as the overall average, they could mostly only become associate professorships (deputy principals), and the prejudice against Jewish scientists who were faculty members obtaining a chair was obvious; see Kröner (1989 a), 8. In respect of this difficult situation it is questionable if Griesbach wanted to prevent any difficulties which might have arisen because of this background. It remains a fact, that the reasons for this decision are not known.
[134] "Agnostic [sic], is possibly the correct term. I cannot recall a single occasion of God or religion ever being mentioned; it just didn't exist"; see Brook (WC).
[135] StAH: Medizinalkollegium IV C 82
[136] Well known scientists who researched the processes in yeast extract and similar preparations from muscular tissue at the beginning of the twentieth century and thus contributed to the elucidation of the biological degradation pathway of sugar, were, in particular A. Harden, W Young, C. Neuberg, H. v. Euler, G. Embden, O. Meyerhof, J. Parnas, O. Wartburg, K. Lohmann and C & G. Cori. According to the most eminent researchers in this sector, the glycolytic degradation pathway is also named "Embden-Meyerhof-Schema" or "Embden-Meyerhof-Parnas-Schema" see also Karlson (1988), 226.
[137] G. (1910); the 1. message" did not originate from Griesbach's pen.

even before his first examination in the Pathological Institute in Hamburg he had already acquired basic histological knowledge, which he extended during his clinical studies by dissections and histopathological work[138]. On 31st October 1911, after four years of study in Freiburg, he passed the "Staatsexamen" (state exam) with the grade "very good"[139]. The following practical year he spent first in the medical Clinic in Freiburg under de la Camp, then in Frankfurt under Schwenkenbecher[140]. The completion of part of the practical year in Frankfurt enabled him to do research in Embden's Institute from July 1912 on, first as probationer and then as unpaid assistant. Shortly after his registration as a medical practitioner he was also granted a scholarship from the Manfred Bernhard Schiff Foundation "in recognition of your earlier work in the area of laboratory biology and pathology"[141].

To this work in the Chemical-Physiological Institute was linked, chronologically as well as thematically, the 13-page doctoral dissertation in Freiburg under H. Straub and Axenfeld entitled "Milchsäurebildung aus Kohlenhydrat im lackfarbenen Blute"[142]. This work, which deals with the break-down of glucose to lactic acid in haemolysed blood, fits into the research field of glycolysis and can be regarded as quite important. Griesbach agrees in his thesis with statements of Gustav Embden and his colleagues, that the breakdown of glucose to lactic acid goes through the intermediate stage of glyceraldehyde, and confirms as well as emphasises that both ferments are to different degrees tied to cell structure[143]. The dissertation, which is of great scientific interest, was given the grade "magna cum laude"[144].

Griesbach began his medical career in April 1913 in the Chemical-Physiological Institute in Frankfurt. While he was there, he participated in five publications, almost all connected with glycolysis research[145]. Among his circle of acquaintances were researchers such as Franz Knoop[146] and Paul Ehrlich[147].

During Griesbach's two years at the Institute, the director, Gustav Embden, emphasised again and again Griesbach's astonishing knowledge, his gift of swift assessment and his lively scientific interest, especially considering his youth. Thus in Embden's opinion, he developed more and more into "an independent researcher of the first rank". Not without pride Embden sums up his characterisation as follows:

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[138] G. (1965 b), 1672.
[139] C.V. (E).
[140] L.c.
[141] Letter from Schwenkenbecher to Griesbach (E).
[142] G. (1913 b.)
[143] G. (1913 b), 12; Ferment is the older designation for an enzyme.
[144] C.V. (E).
[145] G. (1913 a, c; 1914 a-d).
[146] Brook (VC).
[147] Adams (1968), 188.

> "I consider Dr. Griesbach one of my most outstanding pupils. My colleagues and I have come to know him also as an excellent personality"[148].

In April of the following year Griesbach moved to the Civic Hospital in Wiesbaden, being headed by the Medical Director Wilhelm Weintraud. Griesbach was entrusted with the direction of a large medical section and the metabolism laboratory[149]. Because of his "outstanding chemical knowledge" and his complete and intimate knowledge of clinical chemistry techniques he was also made director of the hospital laboratory. In his letter of recommendation Weintraud drew attention particularly to Griesbach's "extensive mastery of the pertinent literature" and his "strikingly mature judgement", which allowed him to turn his "lively scientific interest" into practice.

He therefore tackled a wide variety of questions, as for example the measurement of uric acid levels in blood, the formation of sugar in animals and the function of enzymes involved in immune reactions. At the same time he devoted himself "with great zeal to his medical duty" and, for a while, was in charge of the infirmary as well as several wards for internal medicine. Weintraud emphasised particularly Griesbach's "rich experience in the pathology and therapy of internal diseases, including infectious diseases", and his talent for organisation.

Reading Weintraud's final impressions of his pupil Griesbach, especially the great human, medical and scientific potential Griesbach combined in himself, makes one feel sorry about the chances he missed in his future life because of external reasons:

> "For me and the other doctors in the department in the hospital he was always a loyal colleague, and thanks to his extraordinary knowledge in his speciality and to his particular human qualities he was highly valued by us as a person. Considering his special talents and the seriousness with which he pursued his medical calling, I view him as destined to make his mark in scientific medicine. He is capable of successfully filling the post of a laboratory director, and later to be in independent charge of a hospital"[150].

After two years at the hospital Griesbach was conscripted on first of April 1916 as an Army Doctor and took part in the campaigns against France, Russia and Italy[151]. In recognition of

[148] Embden, certificate (E).
[149] C.V. (E).
[150] Weintraud, certificate (E); in the estate was also a photography of Weintraud.
[151] Draft card (E).

his services he was granted the Iron Cross second class and the Hamburg Hanseatic Cross while the war was still in progress[152]. Because of an injury to his foot he was repatriated home in January 1918 as battalion doctor, and remained there until the end of the war[153]. Besides this injury he also contracted severe amoebic dysentery which caused life-long damage to his heart muscle[154].

[152] L.c.
[153] C.V. (E)
[154] StAH: Medizinische Fakultät der Universität Hamburg: Akte Griesbach.

3.3. Resident and Consultant – Research activity 1919 - 1924

After the end of World War I Griesbach took up a post at the St Georg General Hospital. From the beginning he was also active in the Pharmacological Institute of the University of Hamburg. This Institute was situated in the same building as the Pathological Institute, under the direction of Simmonds. On his return to St. Georg Griesbach noted, not without surprise, that Simmonds was the "de facto" director of the 2000-bed establishment. Simmonds' opinion had to be taken into account in all important decisions, and he always gave it "in the nicest manner and with a charming smile"[155]. From this quotation it is again clear how much Simmonds was his role-model. Also typical of Griesbach's later attitude towards colleagues and associates is his emphasising a feature of Simmond's character: "Ability [and] generosity"[156].

In the Pharmacological Institute Griesbach continued, under Arthur Bornstein[157], the research activity already begun in Frankfurt and Wiesbaden, centring on insulin, uric acid and fatty acids[158]. Bornstein was regarded as "the top authority with a splendidly equipped institute"[159]. The advantage of "this Institute ahead of all other German Pharmacological University Institutes", lay in the fact that it was "associated with a large hospital"[160]. In view of this advantage, "a small section was set aside in House L […] in 1922 for patients who, it was thought, would benefit from the specialised knowledge the Institute could provide"[161]. The tasks of the newly-founded university institute consisted in routine examinations for the hospital, the care of the clinical-pharmacological and the pathological-physiological section, with its associated wards, as well as activity in research and lecturing[162]. In addition there were evenings with special lectures in the home of Bornstein, in which personalities like the later Nobel Prize winner Hans A. Krebs participated regularly. Even after he left the hospital and set up a private practice, Griesbach still participated at these evenings[163]. Besides

[155] G. (1956 b), 1673.
[156] L.c.
[157] Arthur Bornstein (1881-1932) was the first professor for Pharmacology after the foundation of the University of Hamburg. In later years, he was increasingly interested in balneology, and founded the Balneologic Insitute in Bad Oeynhausen, which was affiliated to the University of Hamburg. Bornstein died in Bad Oeynhausen at the age of only 51; see Uhlmann and Weisser (1989), 66; van den Bussche (1989 b), 19; Bock (VC).
[158] C.V. (E).
[159] Uhlmann and Weisser (1989), 66.
[160] Hegler (1928), 134.
[161] L.c.
[162] Braun (1989), 344.
[163] Bock (VC).

Simmonds, Bornstein in particular must be mentioned as having great influence on Griesbach as an academic teacher.

Hans-Erhard Bock remembers Griesbach from the twenties and emphasises especially his great modesty. He met everybody with the greatest respect and was always "upfront for everything and everybody, without prejudice". He was especially sympathetic to young people"[164].

In May 1919 Griesbach's name was entered in the register of the Hamburg Doctors' Organisation[165]. From February till October he was an assistant on the director's private patient's ward, and subsequently consultant in the department of internal medicine[166]. Theodor Deneke, under whose directorate he held these positions, described in 1926 his very high admiration of this young colleague. Even when he first entered the hospital, Griesbach had extensive medical experience, and had made a name for himself in science as well. Now he had developed into an experienced specialist in Internal Medicine, and his "outstanding diagnostic capabilities needed special mention"[167]. Griesbach's areas of specialty were at this time physiological and pathological conditions of metabolism and blood. An outstanding achievement of Griesbach's was also the development of a clinically practical method of determining blood volume "in vivo" by the so-called "Congo-red-Method", which found general acceptance and was widely used[168]. Apart from Griesbach's scientific activity, he was also, according to Deneke's description, highly qualified as a consultant or "locum tenens" for the clinic director. As for his human competence, he enjoyed

> "general respect and popularity among his colleagues, and the grateful affection of his patients. He gave an example of serious sense of duty to his juniors, and, whilst on very friendly footing with all, he always knew how to preserve the necessary distance. Dr. Griesbach has all the qualities, medical, human and scientific necessary to direct a large medical department in exemplary fashion"[169].

The above mentioned "Congo-red-Method", a measurement of blood volume, consisted of the intravenous injection of a bolus of the dye Congo red and measuring the dilution factor and

[164] L.c.
[165] StAH: Medizinalkollegium IV C 82.
[166] StAH: Faculty of Medicine of the University Hamburg: File Griesbach.
[167] Deneke (E); Theodor Deneke retired in January 1926. His successor was Carl Hegler; see Andrae (1997), 32-67.
[168] G. (1921 a).
[169] Deneke (E); with regard to Deneke and his "accommodating behaviour during the "Third Reich" see Andrae (1997), 32-67.

the time taken for its elimination. In the course of this investigation a strong red coloration of internal organs occurred in some patients. Hans Hermann Bennhold, who was assigned to Griesbach as a registrar in 1924, investigated this phenomenon and discovered the deposit of Congo-red in amyloid[170]. Amyloid fibres, which was already known, could then and up to knowadays be colour-targeted with Congo-red. Bennhold writes about this discovery:

> "Griesbach was my first clinical teacher in Hamburg, to whom I owe a lot. […] During that time, he was also the only consultant, who instructed me daily and all year long, personally in medicine in the admission ward. I therefore learned a great deal from him. By his determination of the blood volume with Congo-red I was stimulated to pursue some questions raised by this method […] He supported my experiments whenever he could, and encouraged me in the case of set backs. I shall never forget that he never tried to sign as co-author, as is so often the case these days, unfortunately"[171].

In addition to his other activities, Griesbach opened a private practice for Internal Medicine at 15, Brahmsallee in Hamburg, and was also engaged as a specialist for lung diseases as well as second lecturer at the Nursing School[172]. Griesbach was passionately fond of classical music, literature and art, but much less so of politics, and he was never a member of a party or similar organisation. He had an obligatory membership in the German Society for Internal Medicine and the Doctor's Society in Hamburg[173].

In October 1924 the position of an assistant at the Pharmacological Institute, which Griesbach had held until then, was cancelled, and he also ceased his activity in the Nursing School[174]. However, he continued his activities as a lung specialist until the end of 1925[175].

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[170] Bock (VC); and Kallee (1993), 1336.

[171] Bennhold, 19.3.1973 (WM, N); Bennhold is described as „typical national socialist career doctor", who "advanced in his career thanks to his national socialist ideology"; see Andrae (1997), 92. Indeed, he joined the SA in 1933 and was a member of several other national socialist organisations in the following years. Being Head Consultant in the 2. Department for Internal Medicine and the Medical Policlinic of the AK St. Georg, he was one of the predecessors of the displaced Jewish colleague Arthur Lippmann (see chapter D. 4.2.). Hans H. Bennhold became in 1938 the venia legendi, was in 1939 a.o. Professor for Clinical Pharmacology at the University of Hamburg and got in 1942 the chair for Internal Medicine at the University of Tübingen. He was Director of the Medical Clinic in Tübingen until his retirement in 1962 and died in 1976 highly honoured; see Andrae (1997), 92-99. The relationship between Bennhold and Griesbach, especially the invitation of Bennhold followed by Griesbach's visit to Germany in 1960, seems equivocal in the respect of his past; see chapter D. 4.5.

[172] C.V. (E).

[173] StAH: Akte Hochschulwesen; Dozenten und Personalakten I 190.

[174] C.V. (E).

[175] L.c.

3.4. Academic career and marriage to Olga Hallenstein

After more than ten years of scientific activity, mainly during medical studies and clinical duties, Griesbach received on 14 March 1924 the 'Venia legendi' (permission to lecture) for Pharmacology from the University of Hamburg[176]. Up to this point he had already worked for five years in the St. Georg General Hospital and in the Pharmacological Institute of the University. His habilitation bore the title "On the total blood volume"[177] and followed on from several works in the field of haematology, from which the "Congo-Red Method"[178], a method of determining blood volumes, stood out. It is the only publication of Griesbach's included in a book, and appeared in the "Handbook of normal and pathological physiology", Part Two, dealing with blood and lymph. In this script of 32 pages, Griesbach gave a summary of determining volumes of blood and on those in various pathological circumstances. However, the weight of research up to his habilitation lay rather in the area of endocrinology and metabolism, i.e. analyses on uric acid and fatty acids, insulin and sugars. His introductory lecture in Hamburg-Eppendorf, given on 17 May 1925, was typically entitled "On Insulin"[179]. Further lectures in Eppendorf during the next ten years dealt principally with one topic, "The teaching of medical prescriptions, with exercises in prescribing"[180]. Besides his teaching Griesbach was also employed in the hospital and in the Pharmacological Institute, and from 1922 had a private practice in internal medicine.

In December 1924, at the age of 36, Griesbach married the 25-year-old Olga Hallenstein[181] at the Registry office No. 3 in Hamburg. She was the daughter of the leather manufacturer Henry Michaelis Hallenstein and his wife Zara Beatrice née Gotthelf[182]. Olga Hallenstein, born on the family's estate Villa Baroda in Krempe in Holstein[183], was a kindergarten teacher[184]. Olga and her siblings Gladys and Ronald grew up in a well-to-do upper bourgeois Jewish home. Her mother, widowed in 1922, gave her children plenty of room for development, and kept a very open house. Olga, who like Griesbach, played the piano, surrounded herself with many very controversial and extravagant artists. She kept for preference to the cities of Berlin and Hamburg, and knew famous people from film, theatre,

[176] StAH: Akte Hochschulwesen; Dozenten und Personalakten I 190.
[177] G. (1928 a).
[178] G. (1921 a).
[179] StAH: Akte Hochschulwesen; Dozenten und Personalakten
[180] Hamburgische Universität, Verzeichnis der Vorlesungen.
[181] Marriage certificate (E).
[182] "Certified Copy of Entry of Birth for Olga Griesbach" (E).
[183] L.c.
[184] Brook (WC); also: testimony of the Hamburger Fröbelverein (E).

music and literature. It is therefore correct to describe her as "very cosmopolitan"[185]. The intellectual circles in which she moved included such acquaintances as Gustav Gründgens, Marianne Hoppe, Bertold Brecht, Erna Berger and many others[186]. She was also extremely interested in politics and world events. Her critical spirit, her particular gifts and "cold intelligence"[187] never allowed her to show her feelings openly. She shrank from any form of exhibitionism, especially in relation to herself[188]. This, in conjunction with the atheism of the young couple, may be the reason that the marriage was held on a very small scale and only in the Registry Office.

In summary one gains the impression of Olga Griesbach, as well as from her sister Gladys, of being impressive women from early on, and very avant-garde. The two sisters are described as "quite unconventional, free from common prejudices"[189]. Not everybody could accept this unconventional behaviour, which was often misconstrued, and not infrequently, particularly during their emigration, brought difficulties to the Griesbachs, because

> "she certainly had a distinct, down-to-earth, no fuss personality, extremely kind and caring, and there was much love there, though that may not have been obvious to the superficial observer"[190].

Despite the limitations of age and emigration, her individuality and eccentricity, her taste for the extravagant and spectacular are stressed again and again, and "there was never a dull moment with Olga"[191]. Already in Hamburg it was noted that she always addressed her husband as "Griesbach"[192]. Nothing is known about the circumstances which lead to their acquaintance. It is said, however, that Griesbach visited the family for the first time on their estate Krassow in Mecklenburg/Lower Pomerania on his motorbike[193]. Their great common cultural interest may have been the principal factor for their union. Griesbach's outstanding interest in music, literature and graphic art is continually stressed[194]. So it is not surprising that he was considered the best amateur pianist in the whole of Hamburg[195].

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[185] Brook (VC).
[186] Greer (VC).
[187] L.c.
[188] L.c.
[189] Brook (WC).
[190] L.c.
[191] Logan (VC).
[192] Lassally (VC).
[193] Brook (WC).
[194] Bock (VC).
[195] Greer (VC).

Both Griesbachs were musical and highly educated. In Hamburg they were in contact with musical and theatre circles and knew many celebrities of the time, also Yehudi and Yelta Menuhin, the members of the Köchert quartet, Ruggiero Ricci, Janetta McStay, Richard Tauber, Robert Pikler, Hedy Lamar and Lilly Kraus. Many of these friends were also patients of Griesbach´s, kept in contact with them even after their emigration and in later years gave concerts in Dunedin[196].

After their marriage the couple took a flat in the first storey of No. 30 Rothenbaumchaussee in Hamburg[197]. From November 1925[198] Griesbach also conducted his private practice in these premises.

In February 1926 he applied successfully for the position of senior consultant in the Second Medical Station[199] of the St. Georg General Hospital, comprising 235 beds[200]. From this time he was known by Hans Erhard Bock, who about that time was medical assistant, and who describes Griesbach as a very distinguished person, well structured, and acting without ambitious intentions[201]. Besides his employment as Senior Consultant he continued his practice as well as his research in the Pharmacological Institute. When he accompanied a rich patient to British and Dutch India from November 1929 to March 1930 as his personal doctor, and was granted a semester's leave, Arthur Bornstein, the professor of Pharmacology, put in the proposal to give Griesbach the title of professor. This was uncommon in that there had to be a gap of ten years between State Doctorate and the call to a Professorship[202]. Because of this, the proposal was initially declined, but accepted in April 1930, and Griesbach was appointed Senior Lecturer[203]. The three-month trip to India allowed Griesbach to study tropical illnesses at the university clinics in Calcutta, Rangoon and Weltevreden[204]. He summed up these experiences and impressions in a publication[205].

An episode arising from the journey to India shows how much Griesbach was appreciated by his students:

[196] Wassner (WC); also Petersen (WC).
[197] Telefone books in the „Institut für die Geschichte der deutschen Juden", Hamburg.
[198] StAH: Medizinalkollegium IV C 82.
[199] Hegler (1928), 118.
[200] Application documents (E).
[201] Bock (VC).
[202] Written reply of the „Hochschulbehörde" to Arthur Bornstein, StAH: Akte Hochschulwesen; Dozenten- und Personalakten I 190.
[203] "Ausserordentlicher Professor"; L.c.
[204] C.V. (E).
[205] G. (1930).

> "She [Olga] told me that when she was a young wife Walter had had to join an expedition to India. He had 24 light suits with him (always immaculate) and his students all came to bid him farewell. They were so sorry for her being left behind that they took her to lunch and brought her this fruit dish"[206].

From 1924 Griesbach continued his practice away from their private dwelling, renting rooms at 12, Dammtor Street in Hamburg[207]. Griesbach had a very good reputation as an established doctor of Internal Medicine, and was considered the best diagnostician in Hamburg[208]. He had endless patience with children[209]. Although the couple had no children of their own, the love, understanding and wise relationships with children is continually stressed. Admittedly he had problems with some patients or colleagues, for he was "not an uncomplicated character: he could not abide stupid people, was at times moody and demanding, but then again very charming"[210]. As a person and a doctor he was "very soft, warm-hearted and sensitive, a loving, certainly not a vain person"[211] and thus at times quite unworldly. Griesbach's personality and intellect, his wide knowledge and his talents[212], extending far beyond medicine, are often mentioned as exceptional[213].

[206] Howard (WC); the narrator of this occurrence was a good friend and colleague of the Griesbachs. She got the fruit plate as a present before Olga's death and owns it until this day.
[207] Telephone books in the „Institut für die Geschichte der deutschen Juden", Hamburg.
[208] Lassally (VC).
[209] L.c.
[210] Brook (WC).
[211] Greer (VC).
[212] Brook (WC).
[213] "He was a fine, understanding and impressive man, the type you would not hesitate taking into your confidence", see Petersen (WC).

3.5. The time from 1933 – 1938

> *"We scoff at the flags – but we love this country. And just as the Nationalist organisations go with their drums around the roads – with similar justice, with exactly the same rights, we, who were born here, we, who write and speak better German than most of the nationalist donkeys – with exactly the same right we lay claim to river and forest, beach and house, clearing and meadow: it is our land. We have the right to hate Germany – because we love it. We have to be taken into account when people speak of Germany: we, that is communists, young socialists, pacifists, freedom lovers of all levels; we have to be considered when people think of "Germany". How simple to act as though Germany were made up just of national groups. Germany is a divided land, and we are one part of it"* [214].

With the "Law for the re-establishment of the professional public service" of 7 April 1933[215], and in the putting into practice of this law, there began for Griesbach, as for many of his German-Jewish colleagues, an endless period of humiliation, in Griesbach's case on 26 March 1934[216]. The text of this law and its arbitrary interpretation and realisation, formed the basis for getting rid of all public servants who were of "non-Aryan" background[217] or were considered politically unreliable[218]. Only the affected doctors who had served for ten years received redundancy payment. The law allowed for some exceptions, which was ascribed to the insistence of President von Hindenburg[219].

In the introductory sentence of the law the National Socialist "legal intention" is clearly expressed, as "dismissals were to be carried out even when the preconditions prescribed by the law are not present"[220]. The content of Paragraph 6, on the basis of which Griesbach was dismissed, allowed the possibility of by-passing the exception regulations to the paragraph 3:

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[214] Kurt Tucholsky (1929).
[215] 190 orderly and 424 non orderly lecturers were dismissed in the whole of Germany up to 1.12.1934 due to this law; see Gerstengabe (1994), 18.
[216] StAH: Akte Hochschulwesen; Dozenten und Personalakten I 190.
[217] "Non Aryan" meant someone who had one „non Aryan" parent or even grandparent, see Kümmel (1989), 33.
[218] L.c.
[219] On 17.5.1934 this regulation was silently dismissed. It meant that executives were to be excluded if these were already before 1.10.1914 executives, if they had served in World War 1 or if their father or son had died in World War 1; see Kümmel (1989), 34.
[220] L.c. 67.

"Racial extraction"[221]. Based on this law 40 University teachers at the University of Hamburg were dismissed up to 30 September 1934[222]. In the matter of the quantity of dismissals, the University of Hamburg stood in the fourth place after Berlin, Frankfurt and Breslau[223].

With the enforcement regulations of 4.5.1933 and 6.5.1933 the law was extended to non-civil servants such as Honorary Professors, private lecturers, Senior Lecturers and Associate Professors[224]. A distressing aspect is the silence with which this exclusion process was carried out. At the University of Hamburg the dismissals took place "without any visible sign of protest or even of solidarity from the other colleagues. The Rector left it to the faculties"[225]. It is worthy of note that before the final consolidation of the "anti-Semitic laws", it was frequently left up to the Rector or Dean to decide for or against "non-Aryans"[226]. Before 1933 there were almost no National Socialist party-members to be found among the teaching staff of the medical faculty of the University of Hamburg. This does not mean, however, that the professors and lecturers were apolitical or anti-nationalistic. In the Weimar Republic the majority of professors had a conservative attitude, which was evident in the wish to restore the Empire and its political and social order[227]. They were therefore strangely ambivalent towards National Socialism. Even in the summer semester 1933 there was no open anti-Semitism among the regular professors in the Hamburg faculty[228]. Certainly the removal of Jewish and politically undesirable doctors after 1933 cannot be attributed to "blind fate" because the national Socialist state wished it so. Rather it happened so smoothly not least because there were enough devoted party members who from the beginning worked willingly, in some cases with excessive zeal, to bring it about[229]. They were mainly the group of young doctors and lecturers, who deliberately used the medical faculties of the Third Reich as a mechanism for advancing their careers. To reach this goal a connection with the National Socialist Movement was essential, and the so-called "Lecturer's Camp" was almost obligatory for all university teachers, because their appointment as lecturers was made dependent on it[230]. Political opposition from non-Jewish teachers was therefore extremely rare, for among the doctors there were enough convinced party-members who made no bones about getting rid of Jewish

[221] The exact test of paragraph 6 of this law sounds: "to facilitate the administration, executives can be sent into retirement, even when they are not yet invalid. If executives are sent into retirement for this reason, their positions are not to be reoccupied"; see Gerstengarbe (1994), 19.
[222] L.c. 32.
[223] L.c. 33f.
[224] Kröner (1989 a), 4.
[225] Van den Bussche (1989 a), 35.
[226] Kater (1985), 84.
[227] Van den Bussche (1989a), 39.
[228] L.c. 42; there are two exceptions mentioned.
[229] Kümmel (1989), 32, likewise Kater (1985), 85f.
[230] Kater (1985), 32.

colleagues[231]. The "cleansing process" was directed by newly-appointed doctors with a party certificate or some who previously had held comparatively insignificant positions in provincial hospitals[232].

By 24 March 1933 the "bringing into line" of the German doctors was completed. The responsibility for this lay in the hands of the Chairman of the "National Socialist Doctor's Federation"[233], Gerhard Wagner. Three months later the Board of Hamburg Doctors was dissolved[234]. "Merely with the bringing into line of the Doctor's Union, the scientific organisation of Hamburg doctors, which was rich in tradition, Holzmann (in his position as Provincial Director of the "Racial-Political Office" of the national Socialist Party) had difficulty and in the end had no success"[235].

The criticism of the NSDÄB on the part of the Hartmann Organisation was always only on certain points, and was never a criticism of National Socialist ideology, as the common enemy to be fought was considered to be Socialism[236]. The Union of Socialist Doctors[237], founded in 1924, had in its first years of existence scarcely any dispute with the National Socialist way of thinking, but from 1930 it increasingly issued warnings. In July 1932 the doctor and social-democrat politician Käthe Frankenthal[238], one of the chief opponents, spoke in Berlin of "National Socialism – the enemy of public health", and almost at the same time attended a conference of the VSÄ and the Unions in Chemnitz "to counteract the activities of the National Socialist doctors"[239].

As early as first of April 1933 the so-called "day of general boycott of Jews" took place, on which members of the national Socialist groups of the SA and SS warned against entering doctor's practices[240]. The National Representation of German Jews at that time included some 9000 Jewish doctors who according to Nazi criteria were to be classed as "non-Aryan". Jewish doctors were seven percent of the doctor population[241]. On third of April Gerhard Wagner, the chairman of the Doctor's Federation confirmed the "removal of Jews and

[231] Kümmel (1989), 33.
[232] Pross (1989), 139.
[233] Kümmel (1989), 33.
[234] Van de Bussche (1989 a), 45.
[235] L.c. 46.
[236] Gaspar (1985), 48.
[237] L.c.
[238] Käthe Frankenthal (1889-1976) was Social democratic Party Member in the Prussian Parliament, Member of the Berlin City Council and City Doctor of Berlin-Neukölln. She emigrated on the second of April 1933 via different stations in European countries to the USA; see Frankenthal (1985).
[239] L.c. 51f.
[240] L.c. 33.
[241] Kröner (1989 a), 15.

Marxists from the committees and Boards"[242]. Also all Jewish "welfare doctors" had to dismiss their functions[243]. This decision of Wagner's on his own initiative for direct action and subsequent legalisation was typical of the national Socialist system of power[244]. On 22 April 1933 the next blow against Jewish doctors followed when the national Work Ministry announced the end of panel doctors' activity and the prohibition of new admissions of "non-Aryan" and communistically active doctors. The positions thus left free went preferably to young doctors who were loyal party members[245]. Specialist doctors in cities who had a large number of patients, for example Griesbach, were less hit by these measures[246]. Just three months later, in July 1933, an agreement was concluded between the Hartmann Association and the "Organisation of Private Insurance Businesses in Germany" only to pay out for the bills of "non-Aryan" doctors if the doctor belonged to the "privileged non-Aryans" or if "non-Aryan" private patients were treated[247].

On the first of October came the complete exclusion of Jewish doctors even in private insurance companies, the exception being if they treated Jewish patients[248].

The loss of his permission to teach and of his position as Senior Consultant in the General Hospital of St. Georg, and the restrictions imposed on his private practice in the course of only 18 months must have seemed like the collapse of his world to Griesbach. Although no more details are known of his thoughts and feelings at the time, the following words of the surgeon Rudolf Nissen of the Charité in Berlin could apply equally to Griesbach"

> "Everything fades into the background in the face of the filthy insult to one's sense of honour. […] I feel personally hit by this miserable demotion, which is accepted as justified not only by the masses, but also by that class of people who, by their education and acquired experience in life, belong to my professional class"[249].

In the light of this situation in which Jewish citizens found themselves in the years from 1933 on, the award of the "Cross of Honour for Front-Line Soldiers"[250] which Griesbach received

[242] Kümmel (1985), 33.
[243] Baader (1984), 72.
[244] Kümmel (1985), 65.
[245] L.c. 34.
[246] L.c. 71.
[247] Kröner (1989 a), 4.
[248] Kümmel (1985), 71.
[249] The surgeon Rudolf Nissen was a close collaborator of Sauerbruch in Berlin at the Charité; see Kröner (1989a), 9.
[250] „Ehrenkreuz für Frontkämpfer"; Document (E); the document with three copies found in the estate.

form “Reichs”president General Field-Marshall von Hindenburg “in the name of the Führer and Federal Chancellor” must have seemed like a mad joke.

Despite the prohibition to work of March 1934, Griesbach was able to continue in his practice. For this purpose he and 19 others of the 320 Jewish doctors in Hamburg, was provided with a stamped permit which allowed him to practise “exclusively for Jews”[251]. Griesbach, who despite the difficult situation had not lost much of his medical standing, had “a colossal private practice, among all creeds, right up to the highest Nazi officials, and enjoys a prestige and reputation which is amazing”[252]. Griesbach and his wife Olga - probably for security and financial reasons - shifted house and practice in 1934[253] to Mollerstrasse 16 in Hamburg[254]. The house belonged to Olga’s family, and her mother, brother, sister with her small son, and several cousins, lived there too. Olga and Walter Griesbach occupied the ground floor, which was specially adapted for this purpose. The nephew remembers this time:

> “He had a laboratory in the basement at Mollerstrasse where he conducted pathological and biochemical tests on samples from his patients. I remember him showing me slides of leprosy cases (from India). […There was] a consulting room in the flat. In the same room stood his grand […] Steinway. […] I knew that he was very highly regarded as an eminent physician, especially for his diagnostic skills”[255].

The Nuremberg Laws of 15 September 1935 represent the peak of the insults until this time. Jewish citizens were now also officially classed as second class citizens[256]. For those doctors still in practice, these laws brought many restrictions. Female colleagues of many years’ standing had to be dismissed, with the result that the practices of the doctors concerned had to continue without female assistants[257].

With the first and second regulation of the Reich Citizens law of 14.11.1935 the last Jewish medical officials, University lecturers and senior consultants, who were covered by the exception rules of the Professional Occupation Law, lost their positions[258]. The final exclusion

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[251] Bell (WM; E); Griesbach took this stamped permit into the emigration and showed it to Muriel Bell during their talk.
[252] Letter George A. Griesbach’s to Willi Fels, 22.9.1938; Hocken Archives, 121/94, Vol. 47.
[253] StAH: Hochschulwesen, Dozenten- und Personalakten I 190.
[254] Telephone books in the „Institut für die Geschichte der deutschen Juden“, Hamburg; also StAH: Hochschulwesen, Dozenten- und Personalakten I 190.
[255] Brook (WC).
[256] Vogel (1977), 60.
[257] The „Law for the protection of German blood and German honour“ prohibited Jews, to employ German female assistants of ”German or similar blood“ of under 45 years of age. Jewish doctors were furthermore not any more allowed to write opinions for abortions; see Kümmel (1985), 74.
[258] Kröner (1989 a), 10.

of Jewish doctors came with the withdrawal of entry to private insurance companies by the Medical Insurance Union of Germany, affecting about 3000 doctors[259].

After further restricting laws in the first half of 1938[260] came the next blow against Jewish doctors with their exclusion from all treatment in the area of welfare[261]. It is certain that these laws forced Griesbach to give up or restrict his practice. It is therefore understandable that in May 1938 he became director of the Internal Medicine department of the Israelite Hospital in Hamburg, in Eckernförder Strasse[262]. Due to the "Fourth Regulation of the Reich Citizen's Law", valid from 30 September 1938, even more restrictions were applied. It decreed that the appointment of 3152 Jewish doctors still active "in the former Reich" was cancelled. 709 of them, including Griesbach, were permitted, under threat of cancellation, to treat only Jews and their own families, as so-called 'medical orderlies", not as doctors any more[263].

By the end of 1938 the number of such Jewish "medical orderlies" had shrunk to 285[264]. They were forbidden "to culture viruses, to make vaccines and serums, and to undertake blood-tests to diagnose syphilis"[265]. The racist prejudice towards those who were "different and abnormal", which lay behind these prohibitions, matched "a particularly grotesque accusation of the anti-Semitic propaganda since the turn of the century"[266]. The task of the Jewish "medical orderlies" was extraordinarily difficult, as they were often very unequally divided among regions, and had to face a growing number of patients under adverse external conditions[267].

After the pogrom night of 9th November 1938[268] the "naked terror towards Jewish and politically unpopular doctors, politicians in the field of health and health insurance officials"

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[259] Kümmel (1985), 75.

[260] On 5.1.1938 the law to change family and first names came into operation, which peaked in another order from 1.1.1939 with the adding of the first names „Israel" and „Sara" in the official papers; see Vogel (1977), 65. In March 1938 the Jewish communities lost their official character and therefore multiple rebates, and from 26.4.1938 the fortune of Jewish citizens, which they had within and outside of the country, had to be announced; see Vogel (1977), 63. On 22./23. July an identification card for Jews was announced and they were forced to show it in official places; Vogel (1977), 64.

[261] This law was announced in May 1938; see Kümmel (1985), 75.

[262] Anonymous, Physicians Journal for North Germany („Ärzteblatt für Norddeutschland") 1 (1938), 237; C.V. (E).

[263] Kümmel (1985), 34, also Baader (1994), 73.

[264] Baader (1984), 73.

[265] The Jewish doctors were also observed by Dr. W. Illig, as "they were no physicians" any more; see anonymous, Physicians Journal for North Germany („Ärzteblatt für Norddeutschland") 1 (1938), 557; the remark "only allowed to treat Jews" is found on Griesbach´s prescriptions and letter heads (E).

[266] Kümmel (1985), 75f.

[267] L.c.

[268] After the „Reichskristallnacht" all Jews had to pay a financial contribution of 1 billion RM to the German Reich and had to pay all damage from their own funds. From the 1.1.1939 on Jews were not allowed to keep their shops, mail-order businesses, self-employed enterprises, or memberships in an association. This meant in practical terms the loss of existence for hundred thousands and therefore the homelessness for numerous citizens; see Vogel (1977), 65.

increased in a brutal fashion. A considerable number of them were arrested and dragged off to concentration camps. Griesbach, because of his outstanding achievements, was not interned during these outrages, but many male members of his family were[269].

> "The total irrationality and brutality of their fate finalised the intellectual separation, and any who chanced to escape the internment reacted in similar fashion to the trauma. The Jewish citizen saw no other way of explaining this persecution but to hold to the classical model […] of history. He turned back to Jewish history and the Jewish fate. The break with the non-Jewish world was final. The religious community became a community of fate"[270].

From 6 December 1938[271] Jews were no longer permitted to enter theatres, cinemas, concert halls, museums, sporting grounds, public and private baths, certain streets, squares and parks[272]. What this prohibition meant especially for culturally aware people like Walter and Olga Griesbach can only be guessed at, but never really felt, like so much else which happened in that terrible time.

[269] Lassally (WC).
[270] Strauss (1981), 238.
[271] From 3 December 1938 on Jewish enterprises had to be sold or liquidated within a defined period; it was further no longer possible to buy land. Shares had to be deposited in a depot bank and it was forbidden to buy or sell jewellery; see Vogel (1977), 65.
[272] L.c.

4. Emigration and time in New Zealand

4.1. Emigration to Dunedin/New Zealand – 1938/39

> *"And I do not hesitate to acknowledge that from the day when I had to live with essentially foreign papers and documents, I never felt I was really myself, I never felt I belonged to myself. Something of the natural identity with my original and genuine self was destroyed for ever. […] It has not helped me that for almost half a century I trained my heart to beat like that of a 'citoyen du monde'. No, on the day I lost my passport I discovered, at the age of 58, that with your homeland you lose more than just a piece of earth with a fixed boundary"* [273].

The moment when Griesbach first thought of emigration is not known. His becoming director of the Israelite Hospital in Hamburg in May 1938 suggests that the idea of possible emigration occurred only about the middle of that year. Very likely the perception and awareness of reality by his wife persuaded him to this step. Generally, for emigration out of Germany, in the thirties, pertinent factors besides individual psychological grounds were the point in time, age, educational background, and the state of the medical speciality in the country aimed at[274], as well as the family background[275]. The two great waves of emigration of 1933/34 and 1938/39 show different age structures. In 1938/39 they were mainly older doctors in higher positions who, after years of waiting, saw no future in Germany. They were therefore driven by necessity to undertake the difficult conditions of life abroad[276]. It must not be overlooked that the list of great, scientifically eminent emigrants frequently obscures the fact that "the medical emigration was essentially an emigration of doctors"[277].

Although the emigration by the National Socialist regime was basically approved[278], it transpired in later years during the world financial crisis and the imposition of the "tax on

[273] Stefan Zweig (1944).
[274] In the USA it was usage that relatives of emigrants had to provide "affidavits of support" with legal certificates to allow the emigrants the entry into the country; see Strauss (1981), 243.
[275] L.c. 241.
[276] The emigration wave of 1938/39 was the biggest of the German-speaking medical emigration and included 40% of the total of all physicians emigrating. A look at the age spread shows that 25% were over 50 years and the wave affected mainly older age groups; see Kröner (1989), 16.
[277] L.c. 43.
[278] The emigration was seriously impeded by the German authorities; see Vogel (1977),42.

flight from the Reich", which left the emigrants with only 4-6% of their assets[279], that the conditions of emigration were made more difficult. From 1938 on accounts were increasingly frozen[280]. In the years 1938/39 it was especially Great Britain, which accepted a relatively large number of emigrants. With the beginning of the war the European countries were even less prepared to receive refugees, who therefore had to aim more at overseas countries[281].

The Griesbachs, as far as it is known, considered the United States and New Zealand for possible emigration places. Griesbach had been born in the States[282], his uncle Gustav Seeligmann lived there and his brother George wanted to emigrate there from London. On the other hand, close relatives of Olga Griesbach lived in Australia and New Zealand, who were well established and influential. It is known that Griesbach was "insulted" that the practice of medicine in most countries was made dependent on a repetition of the medical exams, which he rejected[283]. In view of the increasing number of German emigrants, the conditions of acceptance were made more rigid on the insistence of local colleagues. Almost everywhere there was a requirement to repeat the final medical examination in the language of the country or after additional medical studies. Sometimes the local medical school exam was demanded, and above all the acquisition of the pertinent citizenship[284].

After the designated time it was also not longer easy to emigrate from Germany at all. For example, in the British mandated territory of Palestine no permission for entry was granted after 1935. In the USA it was only possible to obtain relatively informally the permission to establish a practice in the state of New York. The other states demanded the acquiring of citizenship, which meant a waiting time of at least five years, as well as the repetition of the study[285]. The Commonwealth countries, from 1934 to 1938, required only a one-year repetition of study. From 1938 on, because of the great wave of immigrants and pressure of

[279] The law from 1931 was used in a changed version from 18.5.1934 on, and implicated tax payments over an estate of 50000 RM, if this estate had been owned from 1.1.1931 on. The 'tax rate" for emigrants increased therefore from 25 to 80% and cash transfer was not allowed at all. The emigrant could not take his belongings with him and his assets were blocked. The "re-purchasing" of one's own belongings from the country of emigration was at first subject to a charge of 50%, later a 85% fee to the German "Reich". Therefore the emigrant was left with only 4-6% of his former assets. These humiliating circumstances during emigration meant in facto an expropriation; see L.c. 43f..

[280] Greer (VC).

[281] Emigration countries for physicians were: 22% Great Britain, 18% U.S.A., 13% Palestine, 9 % Turkey, 7% Netherlands and Belgium, 7% Switzerland, 3% France, 3% USSR, 3% Canada, Australia and New Zealand together, and 9% other countries. The fact that relatively few physicians went to neighbouring countries to wait and see, reflects the irrevocability of their decision to emigrate; see Möller (1984), 5.

[282] Around the turn of the century the American Citizenship was lost if one left the country, therefore all three Griesbach children had lost their American Citizenship; see Lassally (WC).

[283] L.c.

[284] Kümmel (1989), 35.

[285] Baader (1984), 75.

national professional bodies, the time was increased to three years[286]. However, Griesbach – almost 50 years of age – applied in a letter of 28 August 1938 to the secretary of the Medical Council in Wellington for permission "to study Medicine at one of the Universities of New Zealand, preferably Dunedin"[287]. Why he sought a repetition of study at the end of 1938 is not recorded. Probably it happened through pressure of time, for in 1938 he received "a friendly warning from an 'Arian' colleague[288] that it would be time to get out of the country"[289]. The political situation in Hamburg in 1938 is described as follows:

> "Until the 'Reichskristallnacht' in November 1938 things in Hamburg, as opposed to other parts of Germany, were relatively easy for Jews and it was only the mass-arrests of November 1938 and the sending of people […] to Sachsenhausen, etc. that convinced many that they HAD to leave Germany. Walter, due to his medical position, was not arrested. I do not think that the Griesbachs actually suffered, again due to his position"[290].
>
> "The reason for all these people leaving so relatively late [was] that the situation in Hamburg as regards anti-Semitism was better than in other parts of Germany, that it was difficult at the time to fully appreciate how bad things were and, finally, that people's lives and livelihoods were invested there; it was their home which was difficult to leave"[291].

The Griesbachs' decision to emigrate to New Zealand instead of the U.S.A. was due to the fact that they received permission to enter New Zealand"[292]. The reason was a post in New Zealand, which Griesbach had received in the following way: The General Secretary of the "Society for the Protection of Science and Learning" had applied to the Dean of the Medical School in Dunedin on 2. September 1938. This Society asked Sir Charles Hercus[293] to keep them informed about free positions in research in New Zealand. This organisation was concerned to find scientists, who in Germany had been driven from posts in the areas of

[286] Doctors with British Certificates were excepted from the repetition of the study; see Beaglehole (1988), 79.
[287] This sentence represents a misunderstanding Griesbach's, because these days there was only one Medical Faculty in New Zealand, namely in Dunedin. In 1964 the second Medical School of the country was founded in Auckland.
[288] Hans Erhard Bock remembers that the pharmacologist Wolfgang Heubner from Berlin sent Griesbach a confidential communication that he was not able to protect him any longer, he would have to emigrate; see Brook (VC). According to Heubner see Kneer (1989).
[289] Logan (VC).
[290] Lassally (WC).
[291] Brook (WC).
[292] Permit To Enter New Zealand, 26.10.1948 (E).
[293] Charles Hercus was from 1937 on Dean of the Faculty of Medicine at the University of Otago in Dunedin, New Zealand; see Chapter F 1.1.

research or teaching on racist, religious or political grounds, in order to find them corresponding positions in a country of the Empire. The Carnegie Corporation undertook the financing of the travel and transport costs as well as the salary of the researcher, for a period of two years. Their condition was that the university which accepted the researcher for these two paid-for years should subsequently assure him of a job[294].

Sir Charles Hercus, since his appointment as Dean in 1937, set himself the goal of establishing research in the Otago Medical School. The Medical School, however, founded in 1873[295], had only restricted means to employ good medical people from the rest of the world, as it was a small university with very limited capacity for research[296]. The request of the "Society for the Protection of Science and Learning", offering to cover the payment of the researchers, was therefore a very good opportunity for building up a research department.

A relative of Olga Griesbach in Dunedin had received a letter about the same time from Griesbach's brother in London asking him to watch for possible work for Griesbach. The letter describes expressly the situation in which Griesbach found himself in the second half of 1938:

> "I have been shown your cable on the situation, and I have strongly encouraged my brother to try to go to your beautiful country. I have willingly undertaken to support him and his wife, as long as it may be necessary, and done all I could to help him over the ghastly shock of having his life's work destroyed, and his usefulness ended by a stroke of the pen […] he is applying for permission to come to New Zealand, a permission, which I suppose to a great extent depends on the council's permission to study. The next thing, which is not clear, and which my brother could not very well say, is, that he is a man of unusual quality, and really one of the most eminent physicians in Germany today. He has, right up to the end, a colossal private practice, among all creeds, right up to the highest Nazi officials, and enjoys a prestige and reputation, which is amazing[297]".

The relative from whom support was sought was Willi Fels, a very well-known and respected personality in Dunedin, who had distinguished himself in University circles as a sponsor and

[294] David Cleghorn Thomson to Charles Hercus, 2.9.1938, Hocken Archives, 121/94.
[295] The Medical School, founded in December 1873, which started its courses in 1875, was the second Medical School in the whole of Australasia. In 1864, Melbourne got its Medical Faculty, Sydney in 1883; see Hercus (1955), 120.
[296] Records from Professor McIntyre, Professor of Physiology 1951-1961, from July 1961, Hercus Papers, Historic Staff Room.
[297] Letter of Georg A. Griesbach to Willi Fels, 22.9.1938, Hocken Archives, 121/94.

patron. He therefore had particular influence in the University and must have also known Sir Charles Hercus[298]. Through these connections he presumably heard of the offer from the British organisation, and the needs of the Medical School in Dunedin. Two other relatives in Dunedin describe the situation in a letter of October 1938 concerning a possible position for Griesbach. The Research Department, they said,

> "is at present in its embryonic stages, but Dr. Hercus is most desirous of seeing it grow, as he considers it a most necessary adjunct to the School. We are of the opinion that work here would be congenial, & there is just a possibility that it might lead to something better, either as regards salary or even a position on the teaching staff […] would appeal most to a man of Walter's scholastic attainments. Further he [Hercus] is almost certain of being able to secure a grant of say £300 p.a. from the Carnegie Institute, with possible travelling expenses in addition, for a period of two years, if someone would guarantee a similar sum for a further two years. It occurred to me that possibly his brother would do this. If he did it would make the appointment one for four years certain, after which he would be 'set' for as long as he cared to stay"[299].

These considerations, which Georg Griesbach undertook from his London base, he conveyed to his brother, and was able to inform the New Zealand relatives of Griesbach's acceptance of this agreement. Georg Griesbach also agreed to guarantee financial support of his brother after the two year stipend from the Carnegie Foundation ran out.

The financial stability for Griesbach's research work in New Zealand and the influential position of the New Zealand relatives must be considered as the reason for the entry permission being granted. The relatives had also contacted the Minister of Customs, who was responsible for entry visas[300]. The situation in New Zealand, a land with a very small population and direct connections with Britain, was difficult in the 1930s, like that of many other countries, because the rise in the number of 'aliens' was ever more drastic[301].

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[298] Willi Fels (1858, Halle/Germany – 1946, Dunedin/New Zealand) was married to Sara Hallenstein, who belonged to the New Zealand part of the family. He was a "member of the League of Nations Union, […] member of the Field Club [and Treasurer and Vice-President of…] the Otago Branch of the Royal Society of New Zealand; see Cooper (1986), 94.

[299] Letter of Percy Halsted to Emil Halsted from 18.10.1938; both were cousins of Olga Griesbach and were related to the N.Z. branch of the Hallenstein family; see Hocken Archives, 121/94.

[300] The responsible minister was Walter Nash.

[301] „Something over fifteen hundred Europeans entered New Zealand between 1934 and 1939. Most of these were Jewish. New Zealand's policy was derived from the principle applied in Britain of "no admission without financial guarantee" […] As Nazi regulations made it increasingly difficult to take money out of Germany, most of these refugees who gained entry to New Zealand were those who had jobs to go to"; see Poole (1982), 8f.

On 12th December Sir Charles Hercus informed the Chancellor of the University of Griesbach's appointment[302]. Consequently Hercus received from the Registrar permission "to accept Dr. Griesbach as a research fellow in the medical school on the understanding that the university is not committed to any expenditure on his account[303]. Hercus then informed the "Society for the Protection of Science and Learning" of the choice of Griesbach in the boundaries of their research programme:

> "As you know this is a small country and the openings in this field are relatively few […] Dr. Griesbach is anxious to come to New Zealand, not to practice but to take up medical research. He has been granted permission to come to New Zealand and our local University Council is prepared to accept him as a Research Fellow in the Medical School subject to suitable financial arrangements being made […] Dr. Griesbach's brother who lives in London […] is prepared to guarantee two years' salary for his brother. I am hopeful that ultimately we will be able to absorb Dr. Griesbach into organised medical research in New Zealand […] if they did [pay the Carnegie-grant] we would thus have finance guaranteed for four years and if the scholar lives up to his reputation I am confident that his future here would be assured"[304].

Griesbach informed the Health Department in Hamburg on the 20.12.1938 of his planned emigration on 21.12.1938[305].
A peculiarity of the Griesbachs stopped them from saying farewell to old friends[306]. Their emigration and the restrictions connected with their departure

> "allowed them to take the furniture[307] and household equipment, but no jewellery or money. They had to wear wedding rings, and these were made for them from the best and heaviest gold, to increase the value. In their passports they had to have the names [Israel…] and [Sara…] added to their first names. One of the Hamburg friends went with her [Olga] to the gangway, and there put his own signet ring on her finger. She wore this ring until her death"[308].

[302] Letter of Sir Charles Hercus to the Chancellor of the University of Otago, 12.12.1938; see Hocken Archives, 121/94.
[303] Registrar of the University of Otago to Charles Hercus, 15.12.1938; L.c.
[304] Charles Hercus to David Cleghorn Thomson, 17.12.1938; L.c.
[305] StAH: Medizinalkollegium IV C 82.
[306] Hunter (VC).
[307] „One was not allowed to take things out of the country unless one paid a sort of duty on them, this applied to silver and jewellery. "Deutsches Kulturgut", i.e. antiques etc. were not allowed out at all"; see Lassally (WC).
[308] Wassner (WC).

The passage to New Zealand took Walter and Olga Griesbach through London to Perth, Melbourne and Sydney where they visited relatives who had emigrated a few months before them[309]. The ship "Awatea" finally brought them from Sydney to Wellington, New Zealand, on 24.04.1939[310].

[309] Greer (VC).
[310] C.V. on the occasion of the enquiry for Naturalisation on 5.5.1946; National Archives of New Zealand, Archives Reference IA 1 115/1898.

4.2. Beginnings in New Zealand 1939 to 1940

> *"I was a great reader at home, in philosophy, literature and matters of social concern. Ideas were very important to me. When I came here, I found that no one knew about the things I had been reading about and were important to me. I had to bury my thoughts. The hardest thing was to suddenly realise that not only people you've known, family and friends are gone, but suddenly you, yourself are nil. Everything you have known is irrelevant […] It can't be shared. What is homesickness? It isn't missing food, it is the thoughts you can't share, the conversations you can't have. So I buried everything that was of no interest to anyone else"*[311].

The arrival in New Zealand meant for most emigrants a total new orientation. Very few of them had a close conception of the conditions of life which awaited them in their land of refuge. The pressure of emigration, the humiliating circumstances in a country they had always regarded as their homeland, the difficulties of being accepted in a new country, did not leave much time for choice. Most of the emigrants knew not much about New Zealand. They were aware of a 'young" country with wonderful fauna and flora, which from the point of view of their traditions was very like the British way of life[312]. Most ignored the fact that the country, which had been occupied by the British only 100 years before, was with its 1.5 million inhabitants very rustic and provincial[313]. It is known that the Griesbachs used to be amused, in later years, about their expectations, especially as regards architecture[314]. One can hardly imagine what it must have meant for people as interested as they were in music, literature and art, to come from a major city like Hamburg with its cultural offerings to Dunedin.

> "Compared to the intensely active cultural life of their cities of origin, what was available in the New Zealand cities of the 1930s was bound to be disappointing for most refugees. Professional theatre, ballet, symphony orchestra or chamber music did not exist. Cafés and restaurants were not yet a common feature of New Zealand city life. But there were professional musicians, amateur theatre, touring theatre

[311] Citation of an anonymous immigrant; see Beaglehole (1988), 48.
[312] L.c. 29f.
[313] L.c. 13 and 4.
[314] Hunter (VC).

> companies, and musicians on tour from overseas. There was also the cinema. The war interrupted many of these activities, especially the music. The supply of new records from Europe stopped, which greatly limited the repertoire of the Broadcasting Service"[315].

In a letter of 1943 to his likewise emigrated friend Arthur Lippmann in Australia, Griesbach described his incomprehension of a medically eminent professor coming to Dunedin:

> "We quite truly cannot understand why a man of his fame[316] and merits takes this job […] – without money, apparature or rooms for scientific work […] I foresee that he might be very disappointed. Quite apart from the living conditions in N.Z. Even the richest people have no domestic help, this place is very cold and continuous fires are needed […] And 7 children! Well he must know, what he is doing. Besides, the people here are very Presbyterian of course, a thing that must by any means be overlooked. But life is cheap and money can perhaps accumulate since there is nothing to spend it on"[317].

Although Griesbach expressed this opinion and in his heart "never really forgave fate for banishing him to New Zealand"[318], he seldom uttered a word of complaint. Certainly he could have agreed with the words of another emigrant, who "desperately missed music and opera and people talking intelligently about politics, philosophy and science, but considered that these losses had to be regarded in the context of what the refugees had escaped from. Not to be able to go to the opera in the evening was a small price to pay for being safe"[319].
Griesbachs, after their arrival in Dunedin on 25.04.1939, lived in "Braemar House", Royal Terrace, not far from the house of their relatives. Not long after they moved into a flat on the first floor of a newly-built apartment block, at Tennyson Court Nr. 8. In this centrally situated

[315] Beaglehole (1988), 42.
[316] The Professor of Physiology mentioned was John Eccles, who won the Noble Prize for his research in the field of Neurophysiology; see Parry (1975), 38.
[317] Letter from Griesbach to Arthur Lippmann, 3.12.1943; StAH, Familienarchiv Lippmann. Arthur Lippmann was from 1908 to 1933, as well as Griesbach, scientific registrar, senior consultant at the polyclinic and finally Professor in the General Hospital St. Georg in Hamburg. Besides establishing and heading the Department of the Internal Medicine Outpatient Clinic, Lippmann was especially involved with the introduction and development of light therapy [for rickets] and with the establishment of a Radiation Department in the General Hospital St. Georg. Arthur Lippmann emigrated in December 1938 to Australia, where family members of his wife lived. Lippmann was admitted in 1941, having overcome difficulties at the beginning, to become one of the earliest emigrant doctors to be allowed to work in his profession without having repeated his medical exams. He died in 1950 in Sydney; for his personal details see the thesis of Andrae (1997), 32-67.
[318] Lassally (VC).
[319] Beaglehole (1988), 43.

flat, with a view over the harbour, peninsula and the Pacific coast, they lived for the rest of their lives[320]. Early on, a friend of the couple wrote:

> "The way of life here must have meant a tremendous adjustment to both of them. Olga's English was better, she was practical and must have been a great help to him – she really looked after him always and referred to him as "Griesbach". We visited them in their modern flat and marvelled that they had been able to bring all their furniture – and his grand piano. Music was their other life"[321].

Financially Walter and Olga Griesbach were not too well off in the early days. As Griesbach himself says at their arrival in New Zealand, "I had only about £100 in my possession, but a few months later I inherited the sum of £2,500 as the result of the death of a relative in America"[322]. Despite the Carnegie scholarship and his later earnings in the Research Department, his difficult financial situation always proved a hindrance to his later research career.

During a stop-over in London, probably at the beginning of 1939, Griesbach had met Sir Charles Hercus, Dean of the Otago Medical School. He offered Griesbach one of the three major research areas in Dunedin: "goitre, hydatids, infantile anaemia"[323]. On his arrival in Dunedin, he filled in the gaps in his knowledge from scientific literature in the Otago University Medical School library. He finally decided to do thyroid research[324]. Research into goitre was of increasing importance for New Zealand, as it is a country like Switzerland or the Southwest of Germany, where endemic goitre is common. The founder of this research direction was Sir Charles Hercus, who also introduced sodium iodide supplementation into New Zealand. From 1932 on, his research focussed on the goitre-inducing effect of cabbage. These experiments were extended further into Brassica seeds[325] from 1932 on, when the scientists Herbert Dudley Purves[326] and later Thomas Henry Kennedy[327] joined the team. From the onset the research was obstructed by financial problems. Following his appointment

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[320] C.V. on the occasion of Application for Naturalisation, Alien Office, 5.5.1946, National Archives of New Zealand.
[321] Howard (WC).
[322] This relative was presumably his uncle Gustav Seeligmann, who was a gynaecologist in New York.
[323] C.V., December 1961 (WC, N).
[324] Griesbach was not allowed to use a library during his last years in Germany; L.c. The description of the TSH (thyroid stimulating hormone) fascinated Griesbach most; this hormone was first isolated by Junkmann and Schoeller in 1932; see Labhardt (1978), 71.
[325] Purves, Endocrinology Research, 1951, ERD Documents.
[326] Herbert Dudley Purves (1908-93) was a chemist and studied human medicine 1935 till 1941 at the suggestion of Sir Charles Purves; see Hubbard (1993).
[327] The chemist Thomas (Tom) H. Kennedy entered the Research Department in 1939; see Purves, Endocrinology Research, 1951, ERD Documents.

as Dean of the Otago Medical School in 1937[328], Sir Charles Hercus initiated the founding of the Medical Research Council of New Zealand in the same year. The commission was the governing body for the Research Departments in Dunedin also providing financial support. The Council was constituted of a board of eight members (including Hercus and Muriel Bell) by means of a government resolution of the Department of Health in Wellington and was legally based on the Health Law of 1920. Hercus´ initiation of this establishment was above all due to his influential connections reaching to the top political levels[329]. The initial government grant amounted to £ 5000 per year[330].

These changes only came into being at the time when Griesbach entered the University. There was still a prevailing situation in which both technical and financial funds were limited and scientists were obliged to pay for the chemicals they require from their own pockets. However, the policy of the new Dean gradually started to show its effect and a balance between research and teaching gradually came into existence[331].

Griesbach, who had decided to research in the field of the thyroid gland, commenced his investigations without knowing that Purves and Kennedy were also working on the same theme. He was provided with a room in the Anatomy Institute for his research as Anatomy was equipped with a good histology laboratory and harboured two very competent technical assistants, Geoff and Loyce Howard. This couple became good friends of the Griesbachs as Loyce Howard still remembers today:

> "It was a light hearted beginning as he practised his English and we corrected his pronounciation […] Geoff could have made slides and photographs then for him […] Dr Griesbach's little presents to Geoff […] all this to show his gratitude"[332].

Stimulated by the publications about TSH, Griesbach wanted to engage in his own research and together with the Physiology Lecturer Muriel Bell, he collected and prepared sheep pituitaries from slaughter houses in the vicinity. Griesbach wanted to approach the thyroid hyperplasia from another aspect, namely from the feedback control of the pituitary gland. He was also the one to steer the subsequent work of the Research Department in the direction of

[328] Carmalt-Jones (1945), 244.
[329] Monroe, C. (VC).
[330] MRC (1987).
[331] Edson, Professor of Biochemistry and Physiology (1961), Hercus Papers, Historic Staff Room.
[332] Howard (NM).

pituitary gland histology and the feedback control pituitary-thyroidea[333]. Purves himself always considered thyroid hyperplasia to be a hyperplasia following iodine deficiency being due to hypophysial causes[334]. The beginning of the war and the difficult political situation finished the pituitary gland investigations even prior to the association with Purves and Kennedy because the employees at the slaughter houses believed Griesbach to be a German spy[335]. The beginning of the war also had an effect on the financial position of the Griesbachs as the danger persisted of the Carnegie scholarship being discontinued. Sir Charles Hercus wanted the work on the pituitary-thyroid cycle to be continued at all costs and,

> "as Physiology at that point (1940) was about to loose almost all its staff, it was possible to divert staff funds to employing Griesbach as a demonstrator, probably initially as a temporary measure, for I can't recall just how long the arrangement may last"[336].

Griesbach was able to earn some money through this assistant teaching in the Institute of Physiology comprising teaching in the subjects Physiology, Biochemistry and Experimental Pharmacology[337]. At the time he was still without an appointment in the research department. The beginning of the war signified once again a period of restraint and uncertainty for the Griesbachs and the other refugee doctors. The medical council raised alarm with reference to the considerable inflow of German physicians to New Zealand. A stop to immigration for the duration of the war was resolved in December 1939, shortly after the commencement of the war. "Feelings ran hot on this issue. Because nearly all the alien doctors were Jewish refugees there were frequent accusations of anti-Semitism, which were denied by the Medical authorities"[338]. In the course of the war the fronts tightened against the doctors who had immigrated to the country. The "Returned Servicemen's Association", supported by the British Medical Association, accused the meanwhile settled refugee doctors of "being defaulters from the war and of usurping the medical practices of New Zealand doctors away

[333] "It was Walter Griesbach who was responsible for the initiation of studies of pituitary cytology in our unit (…) he was installed in the Anatomy Department and had no inkling of the work which we were doing on experimental goitre some two floors below. On the other hand Mr Kennedy and I were at first unaware of the presence of Dr Griesbach. Even after we had discovered each other, there were obstacles placed in the path of our collaboration; see Purves (1974), 548-551.
[334] Macolm, L. (WC).
[335] C.V. December 1961 (WM, E).
[336] Macolm, L. (WC).
[337] C.V. December 1961 (WM, E).
[338] Poole (1982), 58.

fighting"[339]. However, as the number of refugee doctors was approximately 40 during the war, the fuss being made seemed beyond all proportional foundations[340].

With the France's and Great Britain's declaration of war on Germany on 3.9.1939, approximately 1200 people living temporarily or permanently in New Zealand were classified as enemy aliens[341]. From October 1939 onwards, it became necessary to obtain permission from the local Registration Officer before one left one's place of residence for a longer period. In May 1949 considerations were instated to pursue the British and Australian policy and thus controlling the appointments of aliens[342]. Hercus was also interrogated about Griesbach.

In May 1940 the expression "enemy alien" was officially introduced into the regulations and a censorship of the post as well as confiscation of radios ensues[343]. The classification of the enemy aliens took the form of an informal interview with the police. Griesbach was categorised in Class D as were the majority of the classified aliens. This class signified that normal restrictions without additional constraints applied[344]. The categories and their content matter were known to the aliens, but not their own classification. This resulted in a permanent fear of being classified as "B" which would have resulted in internment, instead of the relatively innocuous call "D"[345]. Two incidents from the Life of the Griesbachs are known from this time which emphasised their problems as enemy aliens:

> "Once during the war when they were observed, it knocked on the door and the police wished them a Happy New Year. They were so happy because they knew from then that the police only did its duty in observing them"[346].
>
> "Mrs Griesbach mentioned it only rarely. One evening they were making music with friends with the window open. The police came and they were accused of having giving Morse signals to a submarine in the harbour: German phobia increased on an indescribable scale. The greatest tragedy was the incapability to make a distinction

[339] Beaglehole (1988), 80.
[340] Poole (1982), 58.
[341] The so-called persons had to register with the local police at that time. According to the regulations: an enemy alien was a person of the age of sixteen or above; 1. Who is not a British subject as herein defined; or 2. Who, not withstanding that he may also be a British subject by birth or naturalisation or otherwise, is or at any time has been according to the laws of any State with which His Majesty is at war a national of that State", see L.c. 12.
[342] L.c. 8 and 14.
[343] A list of goods "for enemy aliens, which they might only possess or control with a permit from the Police (…) were explosives; large inflammable liquid; any motor vehicle, boat or aircraft; cameras; any large-scale maps or charts. Special (…) restrictions: as to residence, reporting to the police, registration, occupation, employment, the use or possession of any machine, apparatus, arms or explosives"; see L.c. 5 and 19f.
[344] Class"D" defined restrictions in the sense of the ownership of weapons, maps and charts, radios, cameras and X-ray equipment. The visiting of some locations was prohibited as was the working in certain professions, they were forced to register with the local police and were not allowed to leave their place of residence for longer than 24 hours or to travel more than 24 miles from their place of residence; see Poole (1982), 14.
[345] Approximately 80 aliens were interned around 1940; see l. c. 41 and 81.
[346] Presland (VC).

between German and Jewish. Only a few people realised that they had fled Germany to save their lives. A constant flow of people of Jewish faith had been entering New Zealand since around 1860 (…) there were some grumbles and growls here and there but no anti-Semitism. Some years later I was sitting with her when the television broadcast a report on Jewish pogroms. I expressed my horror and she looked at me and said quietly: "We are used to it." I will never forget these words and the expression in her eyes. I have often seen the same expression in the eyes of Jewish people"[347].

[347] Wassner (WC).

4.3. Years 1941 to 1944 – assistant lecturer in the "Physiology Department" and research work in the "Thyroid Research Department"

The financial situation of Walter and Olga Griesbach was not good in the first years. The basis of their income in the early days of the research activity in Dunedin was the monthly Carnegie scholarship of £200 per month. In addition Griesbach got a salary of £200 per month from his part-time assistant lecturer activity in the Physiology Department of the University of Dunedin[348].

Despite the restriction of time for research which the extra teaching activity caused, Griesbach achieved even up to 1941 significant results from his research. Thus the first two publications in the "British Journal of Experimental Pathology" appeared in 1941. The second of these articles was produced in collaboration with Herbert Dudley Purves and Thomas Henry Kennedy from the "Thyroid Research Department" in Dunedin[349]. On the subject of the circumstances which hindered his research considerably, he wrote on 19th August to his friend and former colleague from Hamburg, Arthur Lippmann in Sydney:

> "I am doing my rather subordinate job and am just stationary […] Some months ago 2 papers of mine were sent to England for publishing, but I don't know, whether they will arrive or be published […] But since then I have been too occupied with the practical course in physiology, I could not work much experimentally"[350].

In a further paragraph of the letter, however, one sees his relief that the way to research was open to him and the repetition of study in his middle years was not necessary.

> "The poor chaps who are going to the medical school for three years have to hear it over and over again, how low the medical education on the continent is and how even these 3 years are not really enough to make them fit for practice here!"[351]

In June 1941, when after two years the Carnegie Scholarship ran out, the New Zealand researchers and the "Medical Research Council" became aware that with Griesbach's work in

[348] Salary slips, Registrar of the University of Otago, Dunedin.
[349] G. (1941 a, b).
[350] Letter from Griesbach to Arthur Lippmann, 19.8.2941; StAH, Familienarchiv Lippmann.
[351] L.c.

the area of pituitary gland histology, Griesbach had begun an important chapter in thyroid gland research. It therefore seemed important to all participants to secure the services of this researcher further. Accordingly Sir Charles Hercus, as chairman of the committee of the "Thyroid Research Department", took the request to the MRC to grant Griesbach a part-time position with a salary of £200 per annum[352].

Thereupon Griesbach received an official appointment on 1st June 1941 in the "Thyroid Research Department", but because of a shortage of jobs he continued to work half-days in the Physiological Institute. The problem of shortage of positions in Physiology was to hinder Griesbach's research activity until the end of the war. In 1943 another attempt was made to tie Griesbach into research with a full-time salary of £500[353]:

> "Dr. Griesbach's part-time services have been of such a great value to the whole research project that it is felt that his full-time services should be secured. It is felt that considerably greater progress would be made if he could devote his whole time [sic] and attention to this important work, and that the relatively small increase in expenditure involved would be amply justified by the results. We are supported in this view by recent reference by Professor Means in the New England Medical Journal and workers throughout the world"[354].

Despite international lack of understanding about the inadequate half-day activity in view of the importance of his research work, the lack of academic teachers forced Griesbach and the MRC to a further postponement[355].

Until his appointment as Emeritus Professor, John Malcolm, as first professor of physiology in Dunedin, was Griesbach's superior during his activity as teaching assistant in the Physiology Institute. Lawrence Malcolm, who himself taught in Physiology, described his impression and his father's relation to Griesbach during their years of co-operation:

> He was "one of the finest science gentlemen I have ever known. Courteous, reliable, yet with a unique sense of humour, and not afraid to damn precisely those whom he thought deserved criticism. Hercus was not spared, nor was Eccles […] My father found in him a very good friend and confidant through the rather difficult forties, and I know they shared many thoughts and ideas. The students liked him, as he was almost

[352] Chairman's Report; TRC, 8.4.1941, Documents of the ERD.
[353] Invoice documents, Registrar of the University of Otago, Dunedin.
[354] Chairman's Report, TRC, 2.4.1943, Documents of the ERD.
[355] In consequence the research may be unable to complete its full program for the year"; letter of Sir Charles Hercus to Watts, Director General of Health, Wellington, 29.11.1943; Hocken Archives, 121/94.

> transparently humble in his approach, never didactic or preaching, and so often interesting as he quoted so much from his own experience. The other members of the staff (there were not that many by 1940!) got on with him very well"[356].

When John Malcolm was appointed Emeritus Professor, John Eccles became the new professor. Griesbach's lack of understanding about the decision of this famous researcher to come to Dunedin has been discussed already[357].
Griesbach himself seems to have had an ambivalent attitude to his activity in physiology. On one hand he often expressed his displeasure, in his letters to Arthur Lippmann, that because of his teaching obligations he could not make the progress in his research which he had visualised. On the other hand, he wrote, for example, in a letter of 3rd December 1943:

> "I shall not be in the Physiology next year. I have been put off the staff, not to embrace [sic] any new man and they are now very much staffed. But if E.[358] is such a nice man this might be reconsidered"[359].

Besides financial difficulties, some further troublesome conditions of life during the war years must also not be overlooked in order to understand this ambivalence.
The research of Griesbach, Purves and Kennedy, which up to this point had attracted notice worldwide, was still somewhat disputed and not universally recognised. The possibilities for research in Dunedin were limited, and many experiments were still not possible due to lack of space or technical equipment.

> "I don't know whether you have read that the active principle of our rape, cabbage etc. seeds, the Thiourea compounds, are now used in U.S. and England for treatment of toxic goitre? It was and is a great disappointment for me that we could not get anybody here to try it; we have predicted action and doses exactly 20 months ago but – well, that's what E.[360] will find here! So research goes on, but rather platonic"[361].

However interested Griesbach was in this research, it seemed to him always a substitute activity. The acceptance of this activity – as long as it was not yet universally recognised –

[356] Malcolm, L. (WC).
[357] Chapter D.4.2.
[358] John Eccles.
[359] Letter of Griesbach to Arthur Lippmann, 3.12.1943; StAH, Familienarchiv Lippmann.
[360] John Eccles.
[361] G. (1943 b); the activity measurement was performed by measuring histological the cellular height.

was often difficult for him as a basic clinician. His remarks to Lippmann on this subject speak for themselves:

> "I have lost all contact with medicine and probably could not get it once more […] for the first time […] I have been invited for a clinical meeting and I did not go because some good friends think this must be a mistake made by a man who has not been here long enough […] My situation – from the hospital site of view – is that of a quack and I cannot do a thing about it. My position would even be more intolerable if I had went through the course and so make myself a possible competition in practice. So they look upon me just as on an old fool, who is of no aware. Of course the Dean[362] […] is quite different to the clinical people; otherwise I could not have stood for it"[363].
> "Since he[364]spread his influence here, my own position has much improved and I have even been invited to join the week senior staff meetings in the Hospital […] This I do now though it seemed quite unbelievable first to use a stethoscope again etc. Today even the Prof. of Medicine found out about my Congo [sic] Red and the Amyloid reaction etc. and was struck by amazement that I should be the author[365]. Perhaps I have been too modest all these years! On the other hand, what could I have done"[366]?

As well as these professional circumstances, which often troubled him, Griesbach's health was not good. Besides the cardiac problems, which had troubled him since the myocarditis he got from the amoebiasis of the First World War and which became worse because of his overweight, he suffered gout, Morbus Menière attacks and lasting, extremely painful migraines with sensory, hemiparetic and paraesthetic aspects[367]. In his letters, concern for his health takes considerable space.
During this period, the difficult political situation must be considered as a further problem. How much the Griesbachs suffered under their designation as enemy aliens is shown by their efforts to be recognised as "stateless":

> "As soon as the law allows, we earnestly desire to acquire citizenship of this our adopted country to which all our loyalty is and will be given. And in the meantime respectfully ask that we be registered as 'Stateless', the only description to which from

[362] Sir Charles Hercus.
[363] Letter of Griesbach to Arthur Lippmann, 4.8.1944; StAH, Familienarchiv Lippmann.
[364] John Eccles.
[365] G. (1921 a); "Congo red method to determine the blood volume".
[366] Letter of Griesbach to Arthur Lippmann, 25.7.1945; StAH, Familienarchiv Lippmann.
[367] Hunter (VC).

> these cuttings, it appears obvious, we, and others in similar position, are legally entitled"[368].

With this proposal the Griesbachs included a newspaper article from the "Sydney Jewish News" of 27.3.1942, in which the registration of German Jewish immigrants as "stateless" is advocated[369].

The final point which added to the unhappiness and frustration of these years was the cultural vacuum, which accelerated throughout the years of war. This vacuum led the Griesbachs into a loneliness which drove both more strongly together[370].

> "We are very lonely; most people who have to stay here in Dunedin for some time go away as quick as possible to the more lively north, so it's quite difficult to make permanent friends. But being unoccupied is 50-75% of my trouble, I am sure. Well, perhaps I should write my memoirs, if there was something to remember!"[371]
>
> "Olga and I are quite alone in this glorious place, with wonderful mean. Olga is "nursing" me wonderfully well, and we are lying in the sun, reading and walking a bit, that's all"[372].

Most of the friends and colleagues of these years were found through their common interest in classical music[373]. Another friend of the Griesbachs, whom they met at the beginning of the 1040s, was the poet Karl Wolfskehl, who also emigrated from Germany to New Zealand[374]. Karl Wolfskehl, who belonged to the Stefan George-circle and who found his second home in

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[368] Letter of Griesbach to the Minister of Justice of N.Z., 14.7.1942; National Archives, Archives Reference AAAR 493 16, J 1940/50/25.

[369] German Jews No Longer Enemy Nationals? On the 25th November 1941 the Nazi German Government issued a Gazette which deprives all persons of Jewish descent who had left Greater Germany, of their German citizenship, and entitled the German authorities to confiscate their remaining properties […] German refugees of Jewish descent could apply to the Commissioner of Police of their place of abode for an alteration in their Alien Registration Certificates regarding their nationality from "German" to "Stateless" on force of the decree that deprived them of their nationality. After the completion of the alteration the refugee would automatically become a friendly alien who is only subject to the restrictions on aliens in general"; "Sydney Jewish News", National Archives, Archives Reference AAAR 493 16, J 1940/50/25.

[370] Lassally (VC) and Hunter (VC).

[371] Letter of Griesbach to Arthur Lippmann, 3.12.1943; StAH, Familienarchiv Lippmann.

[372] Letter of Griesbach to Arthur Lippmann, 24.1.1944; StAH, Familienarchiv Lippmann.

[373] This includes professors of music, with whom Griesbach was making music, as well as music students, i.e. Joan Presland or Pat Petersen. Not the position, simply the love fro music was important, as Joan Presland remembers: "One had the breakthrough with him normally with music"; see Presland (VC).

[374] Karl Wolfskehl, 1869-1948

Auckland, dedicated the poem "Medico Magistrali"[375] to Griesbach and mentioned in a couple of letters his acquaintance with Griesbach:

> "At the moment I recollect only one person who might be a reader, if not a co-worker: I mean the absolutely exceptional Dr. Griesbach, a famous doctor from Hamburg, who is far beyond his medical knowledge, one of the rarest and by all versatility harmonically knowledgeable humanist I had the luck to meet during my at least quantitatively long life […] Dunedin is a small university town on the south island of New Zealand, climatically quite near the south pole. He is teaching and performing research there since a couple of years, likewise on his own"[376].
>
> "Dunedin has a fantastic cultural, academic atmosphere, only found nowadays on the rust rotting continent in Basel or Zurich […] and the crowning of all new human meetings was the acquaintance with one of your colleagues, actually no close one of course, the former in Hamburg situated Professor Griesbach – I would like to know if you have heard of him before – a man of nearly antique stature, being absolutely intellectual without any tenderness, thereby totally close, simple, and, as I believe, with exceptionally medical view, heart and intellect. Although he naturally cannot practise there, he lives from a Carnegie-Scholarship for goitre research, but also teaches, as I believe, at the Dunedin University which has a high standard. Well, you might imagine what it means to meet such a man coming out of isolation"[377].

[375] Medico Magistrali. For Dr. W.G. in Dunedin, Auckland 1941";see Wolfskehl 1960, page 286, also p. 3 of this thesis.
[376] Karl Wolfskehl to Udo Rukser and Albert Theile, 18.6.1945; see Blasberg 1988, page 677f.
[377] Karl Wolfskehl to Rudolf Laudenheimer, 26.6.1942; L.c. 457.

4.4. Research work in the "Thyroid Research Department" and "Endocrinology Research Department" until part-time retirement 1959

> *"A complex building is he, the temple of science. Different are the people walking within it and the spiritual powers, which have led them to this temple […] One of the strongest motives, leading to art and science, is a refuge from the common daily life with all its painful roughness and desolate desert, away from the chains of the permanent changing demands of oneself. It forces the more sensible and sensitive person from his personal life out into the world of objective sight and understanding […] I have often heard that colleagues try to lead back this behaviour to exceptional strong will and discipline; the daily strive for knowledge does not come from a predisposition or program, but from an immediate need"*[378].

In February 1945 Griesbach was appointed with a full salary of £700 to the "Thyroid Research Department" in Dunedin[379]. The problems which were caused by his part-time work in the Physiology Department could also not be solved after the arrival of the new Professor for Physiology, John Eccles. In his function as Dean and Head of the Research Committee, Charles Hercus reports that Eccles wished Griesbach to continue the work and he agrees to this for the duration of the war[380].

The final reason for Griesbach finishing off the lecturing was his health. In October 1944 he was first taken into the public hospital in Dunedin with the suspect of coronary heart disease.

> "I was treated very well in the hospital, with Special Room and Olga there all day long […] Eccles, who is expecting No 8[381]these days, was of course awfully nice, but I must admit that it was naughty the tempo in his Dept. that has given me the knockout […] last week I gave 2 lectures and 2x 6-7 hrs. of "Autorial" [sic] and "Discussion" teaching. At the end of the later I was absolutely exhausted, could hardly speak any more. Well, I am a wreck, of course. It does not seem to hurt the younger people"[382].

[378] Albert Einstein: Mein Weltbild; Editor Carl Seelig 1993, pages 107-109.
[379] Salary slips, Registrar of the University of Otago.
[380] Hercus to Watts, 1.3.1944, Hocken Archives, 121/94.
[381] Refers to the birth of the 8th child of John Eccles.
[382] Letter of Griesbach to Arthur Lippmann, 11.10.1944; StAH, Familienarchiv Lippmann.

The reason, which Griesbach mentions in this letter as a possible trigger to this disease, was the reorganisation of the working hours in the Physiology Department, which were introduced by John Eccles. Griesbach was also influenced by the post-war policy and the discussions about repatriation of the immigrants, as might be seen by the following lines:

> "There is a dreadful stink here anyhow about compulsory repatriation of us at least of the practising doctors. This is on the agenda of the B.M.A.[383] to night. The idiotic Society [sic] Security scheme here gives some of the doctors incomes between 5-7000 pounds and that is good money which should not been wasted on these foreigners. They shall not be allowed to take more out of N/Z. than they brought in: so there you are. So you can organize something in Australia to receive us when deported. The R.S.A.[384] of the Dominion has accepted such resolution for all who came since 1939. So if you did not know who has won this war, now you know"[385].

The regulation mentioned here were discussed in summer 1945 and included the deportation of all enemy aliens originally from Germany, Austria, Hungary or Italy with exactly the amount of money they had at the time of immigration. The rest of their belongings were supposed to be given to widows and orphans of New Zealand soldiers[386]. The section within the "British Medical Association" which was responsible for the region of Otago wanted to deport all refugee doctors in New Zealand to their "own" countries in order to help with post-war rebuilding[387]. De facto only 19, formerly interned doctors were indeed deported[388].
Olga and Walter Griesbach were naturalized as British Citizens on 23rd of July 1946[389]. At that time, when the solutions of the most important questions seemed to appear, Griesbach's health caused special worries. Since his first Angina pectoris-attack of 1944 his work load was diminished, as he was mentioning himself with sadness in his letters to Arthur Lippmann[390].
Griesbach was again in the Dunedin public hospital in 1947 with coronary heart disease, and had in 1949 his first myocardial infarction. From these years of illness arise the following

[383] British Medical Association.
[384] Royal Servicemen's Association.
[385] Letter of Griesbach to Arthur Lippmann, 25.7.1945; StAH, Familienarchiv Lippmann.
[386] Poole (1982), 61; as well Beaglehole (1988), 95.
[387] Beaglehole (1988), 95.
[388] Poole (1982), 90.
[389] Certificate Of Naturalization (E).
[390] Letter Griesbach to Lippmann, 25.7.1945; StAH, Familienarchiv Lippmann.

description of his life circumstances, which document clearly the important help he got from his wife:

> "In 1947 […] I first met Dr. Walter Griesbach who entered our ward following a coronary artery attack […] Wherever Dr. Griesbach was, Olga his wife was too […] Whilst Griesbach (Olga's only name for her husband) was a patient in Dunedin Hospital, Olga would be at his bedside from morning till night. She was wondrously patient and diplomatic, quietly reading, or sometimes dabbling in the ward kitchen on some request on her own – always amazingly unobtrusive […] Gradually as the doctor's health declined, Olga would drive him to work a.m., collect him at lunch time, and return at 1 p.m. Any day of the week around 4.30 p.m. Olga's car could be seen parked at a side door of the Medical School, Olga still reading, smoke drifting by as she patiently waited to lift her husband home"[391].

Despite the restrictions due to his health, the research of Purves, Kennedy and Griesbach gradually developed, as will be demonstrated in the second part of this thesis. It was Griesbach, who made contact with similarly focussed research workers in Berkeley, which was the beginning of an intensive collaboration with common publications[392]. From 5.-25. July 1948 Griesbach went together with his wife on his first journey abroad since the emigration, to visit the Physiology Department in Berkeley. This stay offered Griesbach for the first time a direct contact and exchange with researchers outside of New Zealand. During his stay he met the research team around I. L. Chaikoff, A. Taurog, A. Koneff, R. Goldberg, Penchartz, E. Siperstein and E. S. Evans, with whom he stayed in close contact. The lines written to Arthur Lippmann reflect Griesbach's sorrows at the beginning of the journey as well as his experiences during his stay in Berkeley:

> "In a way it is sad to be back in our sub arctic Dunedin in 5 weeks time. But we do not have enough money to live here without income, naturally. We want to stay for 10 days in Berkeley, where I have to do some things in the Physiology Department, and will then go for the rest of the time to a seaside resort, Carmel. If this is worth all that money? I have played here two piano quintets, which was a very good sufficiency! Also, recently, I played two Brahms quartets in Dunedin, which was even more difficult! So! […I met…] recently Dr. Rudi Wolff, who seems to have been in St.

[391] Monroe, O. (WC).
[392] G. (1954 a), (1963), (1965 a), (1966 b).

> Georg[393]some time, but which I recall even from the time in Freiburg[394]. His son is working in Chaikoff's department and so we came together again and even played quintet in his house, with two professionals and two Griesbachs […] What I have done in Berkeley, was very specialized in respect of our own research topic and would not interest anyone else. For us here it was very helpful, but for them in Berkeley as well, as they did not know the cytology of the pituitary gland and were very interested in our methods of staining the tissue. This is only correct in respect to the Physiology Department, because in the level above them, in H. M. Evans' Department, who discovered the "growth hormone", it looked absolutely different. I have learnt enormously about the pituitary gland there"[395].

Although the work of the New Zealand research team was internationally recognised at that point, nevertheless there was distrust about the results and methods. The new and unique method of including the histology of the pituitary gland to functional hormone deficiencies, with which Griesbach started, as well as other unconventional new methods[396], took some time to convince other research workers. The following sentences of Griesbach's seem not to surprise in this respect, as they clearly show the struggle for recognition of their results:

> "With much work and effort we sent away four publications […] Yesterday I got a letter of Chaikoff in Berkeley, that his people absolutely agreed with my findings about the correlation of Thyroxine –acidophil cells[397]and they want to measure that now quantitatively in blood and with measurements of Thyroid-Thyroxine. I am very pleased about this, as, when I arrived there, I realised that he did not believe what I was telling him about all this. In regard of the millions of cells which I have counted in my days of sickness, this is a certain satisfaction. Our carcinomas[398]were now as well confirmed by Harvard and Beth Israel, Boston. So I seem to be able to retire in peace"[399].

In this context there has to be a reminder about the beginnings of endocrinology research in New Zealand, which started with Hercus during the twenties in order to find a treatment for goitre. Until the start of combining pituitary gland histology to experimentally derived

[393] General Hospital St. Georg, Hamburg, in which Griesbach worked before his emigration, see Chapter 1.3.
[394] Griesbach studied medicine in Freiburg/Breisgau, see Chapter 1.2.
[395] Letter of Griesbach to Lippmann from 16.5.1948 and 7.11.1948; StAH, Familienarchiv Lippmann; the letters were again written in German after the war and the end of the censorship.
[396] One other method is measuring the activity by measuring the height of the cells, (1943 a).
[397] G. (1943 b), (1946 a).
[398] G. (1945 b), (1946 b), (1947 a).
[399] Letter of Griesbach to Lippmann, 14.12.1948; StAH, Familienarchiv Lippmann.

hormone sufficiencies, the research of the "Thyroid Research Department" has not come further than research on goitre. The inclusion of the pituitary gland into this context led the work into the extensive and very young hormone research area[400]. In this field of research the names of Griesbach, Purves and Kennedy were relatively unknown. Therefore, it was obvious that other research workers in this field did not take much notice of this new team in New Zealand:

> "nobody takes any notice, if one does not belong to any famous school etc. one American writer […] speaks of us as a group of workers in remote common [sic; corner?] of the British Empire, not even mentions the names"[401].

What was often humiliating at the beginning, would lead to success within the following years. Important success was reached by finding thyreostatica from the type of thiouracil as a treatment for thyroid disease (1945), the identification of the production locus of all six hormones of the anterior pituitary gland (1951), important results in the research on thyroid carcinomas and the mentioning of an autoimmune cause of exophthalmia in Grave's Disease[402].

In October 1951, the year of their biggest success, the discovery of the production locus of the thyreotrophic and gonadotrophic hormone[403], Griesbach met Kennedy in London and went together with him to a meeting in New York[404]. On first of April 1953 Griesbach got the title of a "Research Officer Endocrinology Research" and "Honorary Lecturer in Endocrinology" and therefore a salary of £1260[405], which should rise to a maximum of £1940 by 1957[406].

The more the research of Griesbach, Purves and Kennedy became important, the more it was necessary to exchange information with other research workers in the same area. Because of Griesbach's health problems, it was more often Purves, Kennedy or younger colleagues[407]of the research department, who went to conferences overseas. Often also foreign researchers visited New Zealand, and in 1957 the conference of the "Association of Scientists in New

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[400] The growth hormone was isolated as first hormone of the anterior pituitary gland in 1921 by Evans and Long; see Romeis (1940), 7-10.
[401] Letter from Griesbach to Lippmann dated 25.7.1945; StAH; Familienarchiv Lippmann.
[402] This research led in 1956 to the description of the so-called LATS (long-acting thyroid stimulator) by Duncan D. Adams and Herbert D. Purves; see Adams (WC).
[403] G. (1951 a, b, d, e, f).
[404] Documents of the ERD.
[405] Salary slips, Registrar of the University of Dunedin.
[406] L.c.
[407] Worthy of mention in this context are Duncan D. Adams, Muriel Livingston, Robert Averill and Nancy E. Sirett; from Purves as the head of the research department it is known that he was very interested in supporting young research workers; see Hunter (VC).

Zealand and Australia" (ANZAAS)[408] took place in Dunedin, after it had taken place in January 1954 in Canberra[409].

On 1st January 1959 Griesbach officially retired[410]. Griesbach, who was at that time point already 71 years old, was much older than the official retiring age of 65 years, as was set by the constitution of the "Medical Research Council". Because of the importance of his research work, this extension was submitted by the MRC and he was until shortly before his death still working in the research department as so-called "associate worker". The importance research and especially medicine had in his life despite his declining health, is made very clear by the following statement:

> "When the time came for Dr. Griesbach to retire he asked for 'Just a broom cupboard for me to work in'. He had to keep on working"[411].

[408] L.c.

[409] Griesbach gave in 1954, in Canberra, a lecture on „The correlation of pituitary cytology and hormone secretion" and Purves on „The results of the study of iodine metabolism with radioactive iodine". These lectures clearly demonstrate the distinct research interests of both; see letter Trikojus to Purves, 30.06.1953; Documents of the ERD.

[410] From this point on he had a retirement income of £970; salary slips, Registrar of the University of Dunedin.

[411] Howard (WC).

4.5. Last years of his life, 1960-1968

Olga and Walter Griesbach got from 16.7.1957 on, backpaid to the 1.11.1953 reparation payments[412] from the Government of the Federal Republic of Germany, which gave relief at a late stage. A friend who was assisting them in obtaining the payments described Griesbach to be in this matter "a bit sarcastic about getting reparation payment"[413]. It is unknown whether these payments are connected with Griesbach's first visit to Germany since the emigration. A circumstance which might have strengthened the decision to visit Germany in 1960[414] might be the congratulations from the University of Hamburg, which Griesbach got for his 70th birthday[415]. Griesbach was always described as very helpful and friendly to German visitors in Dunedin, especially if they were physicians[416]. Walter and Olga Griesbach were also both very early interested and engaged in the 'Goethe Society' in Dunedin, as a Professor of German remembers:

> "As newly ordinate Professor of German language and literature I was also instantly secretary of the 'Goethe Society' in Dunedin and knew therefore the Griesbachs, who were founding members of the Society and attended the meetings of the Society until their death. Walter was probably the oldest in this circle, well educated and highly knowledgeable of literature in a sense which fitted the bourgeoisie, which was seldom found in academics of European origin […] was rather refrained, made a north German impression with his figure and behaviour, elegant Hanseatic and worldly distinguished. His questions following the lectures represented a pensive reflection, a calmness within himself, which fully flourished when a discussion took place in smaller circles. Karl Wolfskehl witnessed him as host and discussion partner in a flat which they did not change until both passed away and which gave a view onto the

[412] Griesbach got as reparation payment for compensation of damage to his career, damage in economic losses, damage due to early cancellation of the life insurance, damage in economic sense for the loss of his practice, a pension until his death. Furthermore, the couple also got paid "Reichsfluchtsteuer" (tax paid to the German government when leaving the country) and "Judenvermögensabgabe" (tax paid for the estate of Jews), "Dego-taxation" and for the emigration costs; see Entschädigungsakte, Amt für Wiedergutmachung, Hamburg; the highest amount was given to Walter and Olga Griesbach in 1956, three years before Griesbach's death.
[413] Logan (VC); he was – as well as the Griesbachs – a founding member of the 'Dunedin Chamber Music Society' and was often invited to the Griesbachs privately to listen together to music and then discuss it afterwards.
[414] An extensive description can be found on the following page.
[415] The way this congratulation letter was set up would have caused Griesbach's annoyance, if he would have known about it, as Bansi, one of its initiators remarked correctly. The congratulation happened after the former Hamburg council chamber president Marcus informed the Professors Christian Kroetz and Hans W. Bansi, and it then went over several other tables including the Dean H. Bürger-Prinz, who was himself not without past in the NS-regime; see StAH, Akte 007.
[416] Hunter (VC).

> city, the peninsula, harbour and sea, whose waves strike onto the sandy beaches on whose promenades I met him a couple of times during the latter years of his life: his view seemed to stretch to the "Landungsbrücken" which in these days hardly made a home coming possible. Ahasver as well, but he has never complained, and although Olga disliked to talk in German, I have never spoken in English with him. He did not seem to know grudge or revenge"[417].

In the last years of his life came the first invitation for a visit to Germany since his emigration. It was issued by his former scholar from the time in Hamburg, Hans Hermann Bennhold. Bennhold was heading the 1960 "German Conference for Internal Medicine" which was taking place annually in Wiesbaden.

Already in Chapter D. 3.3 the respect which Bennhold had towards his former teacher, is mentioned[418].

On the mentioned conference the main subject of interest was the thyroid gland. Griesbach was giving a lecture on "Die Regulation der Schilddrüsenaktivität"[419]. On 21. May 1960 Griesbach held a seminar for members of the Internal Department of the University Clinic of Tübingen[420] as "reports on the work of this Department as far as pituitary gland cytology is concerned"[421].

After a visit to the clinics in Marburg[422] and visits to meet friends and relatives in the area around Frankfurt[423], Walter and Olga Griesbach also went to see the family graves on the Jewish cemetery in Beverungen. As far as a friend reports, Griesbach was pleased by the reception which was held for their welcome. The cemetery was cleared and the stones were cleaned before their arrival. Olga Griesbach, however, felt the cordiality to be insincere[424].

Before Griesbach went to further lectures to Hamburg, he attended in July 1960 the "International Goitre Conference" in London[425] and the "International Endocrinology

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[417] Träbing (WC).
[418] In this context attention must be paid to the inscrutable role played by Bennhold during the "Third Reich", see Chapter D. 3.3.
[419] About his stay in Wiesbaden, Griesbach wrote in his description of the journey: There were 2200 physicians present and I believe that, though the paper was well received, the fact that I had come from as far away as New Zealand mostly impressed the audience and especially such persons as were responsible for the newspaper publicity"; Report of W.E Giesbach M.D. on his leave April 15th – October 18th 1960; Documents of ERD.
[420] Bennhold was medical director of the clinic at this time.
[421] Griesbach, on 1960, Notes only (E).
[422] Bennhold to Griesbach, 25.5.1960 (E).
[423] Kallee (VC).
[424] Wassner (WC).
[425] 5.-9. July; Purves held a position as "Chairman" on one of the meetings; see "Report of W. E. Griesbach M. D. on his leave April 15th – October 18th 1960"; Documents of the ERD.

Conference" in Copenhagen[426]. On 26th July 1960 Griesbach gave a lecture on Arthur Jores invitation students and the medical personnel of the Internal Department of the University Hospital in Hamburg-Eppendorf about his research done in Dunedin. On 16th August[427] another lecture was following in the General Hospital St. Georg in Hamburg, which was initiated by Hans W. Bansi and Hermann Zondeck.

Jores, Bansi and Zondek were fully aware of Griesbach's research in Dunedin, as were all other German research workers who were working on the same topic. Jores and Zondek probably even knew Griesbach before his emigration, which was also the case for some of the American research colleagues[428].

Joachim Kracht, who was also doing research on pituitary gland, met Griesbach in Wiesbaden for the first time and describes him as an "absolutely upright and integer man, of whom one should have high respect. He was a personality, was extremely well balanced and was, as many emigrated Jews, incredibly tolerant and open-minded. At the end of the day a German which one sensed"[429]. It was also "not possible during the 50s, not to hear about Purves and Griesbach in this field of research"[430]. Nothing is known about the impressions and feelings Griesbach had during this one visit to his former home.

After the end of the visit to Hamburg Griesbach and his wife Olga travelled to Dallas, Texas, to meet "my old Berkeley friends Taurog and the Sipersteins"[431], before he stayed for 3 weeks in October in San Francisco. This main intention of this stay was to give lectures and to have "regular meetings with Professor I. L. Chaikoff, Berkeley, and some of his collaborators"[432].

In 1961 Purves and Griesbach visited their last conference together[433], which took place in London, before Griesbach officially retired at the end of this year[434]. In the following years until 1967 he further published 7 research articles, of which 3 were in collaboration with the group in Berkeley[435].

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[426] 18.-23. July; Purves gave here a lecture on "Hypothalamic control of the endocrine system" and presented also the newest results of the experimental thyroid studies. Griesbach remarked on the conferences in Copenhagen and London that "at both meetings, conversations with the people doing research in the same field as our Dunedin group were most fruitful"; see Documents of the ERD.
[427] "Report on overseas travel 1960 by Dr. W. E. Griesbach"; see Documents of the ERD.
[428] One example is E. Oppenheimer, see L.c.
[429] Kracht (VC).
[430] L.c.
[431] "Report on overseas travel, 1960, by Dr. W. E. Griesbach"; see Documents of the ERD.
[432] L.c.
[433] Hunter (VC).
[434] Salary slips; Registrar of the University of Otago.
[435] G. (1963), (1965 a), (1966 b).

In the 1950s and again on the last visit to Hamburg in 1965, Griesbach may have been offered the position of the Head of the Israelite Hospital in Hamburg, but which he always rejected[436].
On 8th March 1967 Griesbach was awarded the membership of the "Deutsche Akademie der Naturforscher Leopoldina" in Halle/Saale[437]. No indication was found that Griesbach has received the offer to be re-admitted to the "Deutsche Gesellschaft für Innere Medizin" or the "Deutsche Gesellschaft für Endokrinologie" during the years after the war.
At the end of 1967 Griesbach's health deteriorated dramatically. From 29.12.1967-18.1.1968 he was again admitted into "Dunedin Public Hospital" with myocardial infarction and he passed away on 10th of August 1968 suffering from pneumonia in "Wakari Hospital", Dunedin[438].
Olga Griesbach died on 2.3.1973 following bronchial carcinoma. Both do not have graves, as according to their beliefs they wanted their ashes to be scattered on the shores of the Pacific near the cemetery of St. Clair Bay in Dunedin[439].

[436] Greer (VC); Proof of this offer could, however, not be found in the archives of the Israelite Hospital in Hamburg.
[437] Reception document from 8.3.1967 (E); the document is written to "Dr. Walter E. Griesbach, Professor of *Pathology,* Dunedin, *U. S. A."*
[438] Records of the Dunedin Public Hospital.
[439] Hugh Gourley Ltd., Funeral Directors, Dunedin, 18.10.1994 (VC).

E. Research work in Germany

1. General remarks

In the second part of this analysis, Griesbach's scientific work will be outlined in detail. His more than 70 publications during the years 1910 until 1933 and 1941 until 1967 have to be seen as being historically as well as thematically separate. The majority of the research work during his life in Germany, which was published from 1910 to 1933, affects the specific field of haematology and biochemistry. Biochemistry, which was created as a specificity only at the beginning of the 20th century[440], was forced to change for five times due to the changing standard of knowledge and increasing within only fifty years: At the end of the 19th century the main effort was the discovery of the structures of sugars, amino acids, nucleic acids and other low molecular weight natural products. During the first ten years of the 20th century the discovery of the role of phosphate for the metabolism as well as the beta-oxidation of fatty acids took place. The main interest of the international research from 1920 till 1940 was the demonstration of the structure and the isolation of vitamins and hormones. This is insofar of special interest, as the terminology of "hormone" was described only in 1905 by Ernest Starling[441] and "vitamin" in 1911 by Casimir Funk. In the thirties and forties of the 20th century, the research areas of glycolysis and fermentation were fully discovered. Also during this time the uric acid and citrate cycle were finally described[442].

This overview clearly reflects that the content of Griesbach's publications was assigned to the timely topics in research in the individual time. Therefore, his publications on the metabolism, especially on the sugar and uric acid metabolism of the years 1910 till 1933, contributed to the exploration of the glycolytic and uric acid degradation path.

The publications during the years 1941 till 1967, which were produced during his exile in Dunedin, can be allocated to the special topics of endocrinology, histology and pathology. They deal with the biological effect and suppression of hormones, conditions of hormone deficiencies and their substitution, as well as the discovery and description of their stimulation localisation within the anterior pituitary gland.

Therefore, the analysis of all of Griesbach's publications will be separated regarding their content. Only those specific areas will be extensively addressed, which were at their time

[440] Karlson (1994), 13f.
[441] Karlson (1982), 3-14.
[442] Karlson (1994), 13f.

regarded as important. These publications include the research areas of metabolism, haematology, thyroid gland and pituitary gland histology.

As in Griesbach's life and work his academic teachers played an immense role, introductory chapters were added to describe the research institutions and his academic teachers as well as the research topics they were working on during the particular time. The arrangement of these chapters is made chronologically analogous to the time Griesbach was working there. With a keen sense Griesbach managed to wok in institutions which enjoyed a good reputation and research of world class standard was performed. This again reflects Griesbach's acquired taste to aim for the highest standards and to interact with research workers of high standard.

2. Institutions and co-workers

2.1. "Chemical-Physiological Institute", Frankfurt, Head of Institute: Gustav Embden

Gustav Georg Embden was born on 10.11.1874[443] in Hamburg as the son of the lawyer Dr. Georg Heinrich Embden[444]. He studied medicine at the universities in Freiburg, Munich, Berlin and Strasburg. Already during his student times he was working in the Physiological Institutes of Johannes v. Vries[445]and Chr. Bäumler in Freiburg, J. G. Gaule in Zürich[446], Franz Hofmeister[447]and Ernst Ewald in Strassburg[448]and Paul Ehrlich in Frankfurt/Main[449]. Embden's „scientific affections" were especially "nurtured and engrossed"[450] during his participation in Hofmeister's laboratory. In 1903 Embden became an assistant in the Physiology Institute in Strasburg, which was founded and headed for long years by Felix Hoppe-Seyler[451]. Research work done by Franz Hofmeister in his institute also set the pattern for Embden's own research. Hofmeister influenced in his Strasburg' Institute the doctrine of the intermediary metabolism significantly. Nearly all publications of his scholars from the Institute addressed this field, but none of them "developed so consistently and broadly" as Gustav Embden[452]. In 1904 Embden was appointed by Carl von Noorden[453]to the head and shortly later to the director[454] of the newly founded Chemical Laboratory of the Public Hospital in Frankfurt/Main. The laboratory was expanded after five years and reallocated into

[443] Schmauderer (1970-1980), 359.
[444] Lehnartz (1959), 473.
[445] Schmauderer (1970-1980), 359.
[446] Lehnartz (1959), 473.
[447] BLÄ II, 363.
[448] Schmauderer (1970-1980), 359.
[449] Lehnartz (1959), 473.
[450] Schmitz (1933), 1442.
[451] Felix Hoppe-Seyler (1825-1895), who had been lecturing before this time in Strasburg also in Tübingen, was raised the claim for an independent speciality for physiological chemistry and proposed separating Physiology into Biophysics and Biochemistry; he is therefore thought to be the founder of the term "Biochemistry". In 1877 Hoppe-Seyler founded the 'Journal of Physiological Chemistry'. With this journal they aimed to concentrate the research done into the field of Biochemistry in one journal; see Karlson (1977), 717.
[452] Schmitz (1933), 1442.
[453] Ernst Schmitz (1933), 1442, describes the research team of von Noorden and Embden: "It was of special fortune that this versatile metabolic pathologist conjoint with the experienced research worker and imaginary physiologist".
[454] BLÄ II, 363.

the "Physiological Institute"[455]. In later years the Institute became independent from the Public Hospital and became the "Public Chemical-Physiological Institute"[456].

In 1907 Embden published his State doctorate in Experimental Pathology in Bonn[457], based on his research work in Frankfurt[458]; two years later he was appointed Assistant Professor. After the foundation of the University of Frankfurt/Main in 1914[459] Gustav Embden was appointed Professor of Physiology in his re-named "University Institute for Vegetative Physiology"[460]. Since the turn of the century physiological chemistry specialised more and more on the "development of biological functions with chemical methods", on which Embden had "eminent influence"[461]. His research focused on two big, distinct but logically linked areas. Firstly, he worked on the intermediary stages of the liver metabolism. Secondly, his main interest was the physiological-chemical correlation of muscular contractions[462].

Embden realised early, that experiments on living animals produced unclear results. On the other hand, post-mortal tissue represented only unsatisfactory material, as the organic structure was destroyed[463]. For these reasons he already developed during his time in Strasburg a technique which allowed them to study on live organs, a method which based on their artificial perfusion[464]. This method, which also permitted the recognition of the oxidative desaminisation as one step in the breakdown of amino acids, formed the basis for Embden's[465] as well as Griesbach's biggest success in this field of research. Embden recognised that sugar could be synthesized from lactic acid and that, analogous to the beta-oxidation as described by Franz Knoop, acetic acid and acetone were products of a pathologic glucose metabolism.

Embden's work on the intermediary products of the carbohydrate metabolism led his interests into the chemical processes during muscular activity[466]. During this research, he recognised that during muscular activity the phosphor acid metabolism is increased[467]. In 1924 Embden was able to isolate a hexosediphosphate as an intermediatory metabolic product which he

[455] Schmauderer (1970-1980), 359.
[456] BLÄ II, 363.
[457] BLÄ II, 363.
[458] Schmauderer (1970-1980), 359.
[459] Lehnartz (1959), 473.
[460] BLÄ II 363.
[461] Lehnartz (1959), 473.
[462] Schmauderer (1970-1980), 360.
[463] L.c.
[464] Embden was using the liver of endothermic animals, which could be held in a satisfactory condition thanks to his specially developed perfusion method. This enabled him to study the metabolic function of the isolated liver, and made the discovery of carbohydrate- and acetone body-formation as well as –degradation possible; see Lehnartz (1959), 474.
[465] Schmitz (1933), 1442.
[466] Schmauderer (1970-1980), 360.
[467] Schmitz (1933), 1443.

called “Lactacidogen”[468]. The isolation of this product made it possible to demonstrate that glucose needs to be chemically esterified before it could further reduced to phosphor acid[469]. In 1927 he discovered hexose-monophosphate in the muscular cell, which was named after him “Embden Ester”[470]. During their twenty years of research work, Embden and his co-workers were able to isolate important phosphor-incorporating intermediate products of the carbohydrate metabolism in the muscle and thus established a new huge research field within biochemistry. Embden was the first to recognise the fast reversibility of chemical processes during muscular contraction[471]and tried to demonstrate the last connection between contraction and chemical procedures in the muscle[472]. Embden’s research projects focused on the isolation of glycerine phosphor acid and phosphor-glycerine acid as intermediate products of the anaerobic carbohydrate degradation.

Hence, the foundation stone was laid for the ultimate clarification of the metabolic intermediate products[473]. In the course of his final experiments from 1932 to 1933, Embden and his colleagues detected all stages of glycogen degradation including lactic acid in muscles[474].

On 25.7.1933 Gustav Georg Embden died at the age of 59 in Nassau/Lahn[475].

Gustav Embden succeeded in achieving, “in rare completion the combining of the characteristics of the teacher and the researcher” and was “loved and venerated”[476] by his students. He loved “developing and debating his problems in detail with chosen students he was close to”[477], which must have been extremely exiting for the young scientists.

Griesbach encountered Embden and his institute for the first time during his studies. After he had passed his intermediary preclinical examination[478], he did some research work for Embden in Frankfurt during his summer vacation, hence his first publication: “Über Acetessigsäure in der Leber diabetischer Hunde”[479] originated in this institute. He also spent part of his practical year in Frankfurt/Main and therefore was able to continue working in

[468] Embden, Griesbach and E. Schmitz presumed that the primary product of lactic acid, which they called “Lactacidogen”, would play a special role within the glycolysis. The proof of its existence was brought in their publication “Über Milchsäurebildung und Phosphorsäurebildung im Muskelpresssaft”; (1914 c); see also Schmauderer (1970-1980), 360.
[469] Schmauderer (1970-1980), 360.
[470] L.c.
[471] L.c.
[472] In diesem Zusammenhang widerlegte Embden die damals herrschende Hypothese, dass Milchsäure die Muskelkontraktion auslöse und gleichzeitig ihre primäre Energiequelle sei; vgl. Lehnartz (1959), 474.
[473] L.c.
[474] Schmauderer (1970-80), 360.
[475] Lehnartz (1959), 473.
[476] Schmitz (1933), 1442.
[477] L.c. 1443.
[478] StAH: Medizinalkollegium IV C 82.
[479] G. (1910).

Embden's institute[480]. As an acknowledgement of his research that he continued during this period simultaneously to his clinical training, Griesbach was awarded the Manfred Bernhard Schiff-Scholarship 1913[481], which provided the financial basis for a further publication[482]. After he received his licence to practise medicine[483], Griesbach worked initially as a medical intern and later, in the same year, as a medical trainee for Embden[484]. The contents of the dissertation that Griesbach presented in Freiburg were chiefly based on the research activities in this institute[485].

Griesbach attracted the attention of Embden from the onset by virtue of his "astonishing knowledge, his keen perception and his lively scientific interest", which Embden found amazing especially in view of his youthfulness. Embden attested Griesbach that he had developed into an "independent high-ranking scientist" over the years whom he considered to be "one of his most brilliant students"[486].

The influence that Embden exercised upon Griesbach must be designated as enduring and formative. Embden's field of study in respect of glucose metabolism is also the subject matter of Griesbach's publications.

[480] C.V. (E).
[481] Letter Schwenkenbecher, 13.12.1912 (E).
[482] G. (1914 b).
[483] Adams; Griesbach´s hand-written C.V. (E).
[484] C.V.(E).
[485] G. (1913 a).
[486] Embden, 1.2.1926, certificate (E).

2.2. "Institute of Metabolism" in the Municipal Hospital of Wiesbaden, Head of Institute: Wilhelm Weintraud

Wilhelm Weintraud was born on 13.3.1866 in Offenbach/Main[487]. His doctorate was conferred in 1890[488] after he had been an assistant for F. D. V. Rechlinghausen[489]. In the same year he entered his first position in the Medical Clinic in Strasburg[490] under Bernhard Naunyn[491], where he habilitated in 1893 on the topic of Internal Medicine. The years 1894 to 1896 led him subsequently as senior physician to the Charité in Berlin where he worked under Karl Gerhardt. A. Kast became his teacher[492] while Weintraud was in charge of the "Internal Polyclinic" at the Medical Clinic[493] in Breslau[494] during the period from 1896 to 1897. From 1898 to his suicide on 7.9.1920[495], Wilhelm Weintraud was the senior physician[496], later director of the Department for Internal Medicine[497] in the Municipal Hospital in Wiesbaden. One of his first acts was the establishment of a laboratory for metabolism from where "a great range of efficient and good work emerged"[498].

At the end of the last century as Weintraud entered the clinic, queries pertaining to metabolic changes in the case of hunger, febrile conditions and under the influence of diverse organic illnesses became the focal topic of research within the internal medical area. Weintraud´s interests lay towards metabolic illnesses in a more restricted sense, namely gout and Diabetes mellitus[499]. In the scope of his publications special mention is made of his great "work on diabetes" and also of the investigations into the changes in uric acid secretion due to the feeding of granatus animal tissues of the thymus[500]. Completely new aspects could be initiated as a result of this work. Weintraud´s publications on liver disease, diabetes mellitus as well as the contributions to the physiology and pathology of the metabolism of uric acid were regarded as "fundamental"[501]. His studies on the endogenous and exogenous formation of uric

[487] DBJ 2 (1924-42), 764
[488] Bumenfeld (1920), 1188.
[489] BLÄ I, 1827.
[490] L.c.
[491] Brandenburg (1920), 968.
[492] BLÄ II, 1658.
[493] Blumenfeld (1920), 1188.
[494] BLÄ I, 1827.
[495] L.c.; Weintraud suffered increasingly from depression during his latter years; his knowledge of his incurable cardiac disease may have been the cause for his suicide; see Blumenfeld (1920), 1188.
[496] BLÄ 1, 1827.
[497] DBJ 2 (1923-32), 764.
[498] Blumenfeld (19209), 1188.
[499] L.c.
[500] Brandenburg (1920), 968.
[501] BLÄ II, 1658.

acid were also considered to be "extremely interesting"[502]. The work on uric acid led Wilhelm Weintraud towards a therapy-oriented direction in later years. In this context his well known publications on Atophan[503] are worthy of special mention. The characterisation of the "atophans" in its particular reaction on the uric acid metabolism (and the introduction of the atophan) as a remedy for gout[504] traces back to him.

The capabilities of Weintraud did not only lie in the field of research. He was also an "excellent diagnostician and a popular, warm-hearted physician". From his character "fine, likeable (and) versatile educated", he was gifted with "an extreme power and high desire to work"[505]. The relationship to his students can only be described as "unusually auspicious", and it was always "a great pleasure for him […] that this or that student, who had been working under his direction, had held a presentation"[506].

Griesbach's first contact to Weintraud was in 1914 due to his internship in the Municipal Hospital in Wiesbaden. Parallel to his duties as resident, he also conducted numerous research works, initially for Embden in Frankfurt, later for Weintraud in Wiesbaden. For a short period he was appointed with the direction of this institute[507]. Griesbach's early withdrawal from the Wiesbaden hospital was not due to professional reasons but "due to his conscription to military service", as Weintraud wrote in his final appraisal. Weintraud praised, in particular, Griesbach's excellent chemical knowledge" and emphasised that he was completely familiar with the technology of clinical chemistry" in this appraisal. As a result of his extensive mastery of the relevant literature and his "outstandingly mature judgement" an independent opinion to the current metabolic problem was possible due to his "lively scientific interest". Weintraud also praised Griesbach's "great human interest" and his "special human qualities" and held him "with respect to his special gifts and the seriousness, with which he pursued his studies and his complete medical training as assigned to occupy a scientific position in the field of medicine. He would be able to occupy both the position of a Head of a Laboratory in the medical field as well as occupying the position of the Director of a Hospital"[508].

No communal publications resulted from Griesbach's time with Weintraud. However, the conclusion cannot be made that Weintraud had no influence on the scientific moulding of

[502] Brandenburg (1920), 968.
[503] BLÄ II. 1658.
[504] Brandenburg (1920), 968.
[505] L.c.
[506] Blumenfeld (1920), 1188.
[507] C.V. (E)
[508] Weintraud, 30.11.1918, certificate (E)

Griesbach. The research of Griesbach in the twenties, in particular on uric acid and Atophan[509] allow the clear recognition of the sustained influence of his mentor Weintraud.

[509] G. (1919 b), (1920 a-d), (1923 b), (1933 b).

2.3. "Chemical-Physiological Institute", General Hospital St. Georg in Hamburg[510], Head of Institute: Arthur Bornstein

Arthur Bornstein was born on 14.4.1881 in Berlin. After studying in Berlin and Kiel and his conferral of a doctorate in 1903 in Kiel, Bornstein spent his resident time in Berlin, Geneva and Göttingen. The post doctorate qualification followed 1908 in Göttingen[511]. In the following year he was engaged in the construction of the Elbtunnel in Hamburg as a "physician specialised in compressed air". From 1910 Bornstein was head of the Chemical Physiological Department of the St. Georg General Hospital in Hamburg[512]. The department was located in the Pathological Institute and was completely reconstructed during the years 1913 to 1915[513].

When the University Hamburg-Eppendorf was founded in April 1919, there was a long dispute concerning the occupancy of the pharmacological chair. The representatives of the St. Georg General Hospital[514] were eventually able to prevail who had proposed Arthur Bornstein on the grounds that he was a "prime worker with an excellently equipped institute in the location"[515]. On 5.5.1919 Bormann became the first professor for pharmacology in the newly founded University of Hamburg[516].

The space was not available for the relocation of the institute to Eppendorf and the University Pharmacological Institute remained in the St. Georg General Hospital until the end of Bornstein´s tenure[517]. The advantage possessed by the institute[518] according to Bornstein in

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[510] Korina Kauder wrote a dissertation on Arthur Bornstein at the "Institut für Geschichte der Medizin in Hamburg under the supervision of Professor Ursula Weisser.

[511] BLÄ II, 150.

[512] Braun (1989), 343.

[513] The interior equipment and instruments suffered during in the reconstruction due to the war situation and "later only a small portion of the assigned instruments and apparatus could be acquired". The rooms for chemistry work were located in the ground floor of the institute, the rooms used for animal experiment on the first floor and the storage rooms, the rooms for large machines and a room designated for experiments involving the metabolism of animals were situated in the basement; see Bornstein (1925), 100.

[514] The GH St. Georg, as the general hospital in Lohmühlenstraße in the district of St. Georg was generally known, was built in 1823, and is the oldest hospital in Hamburg. It was completely newly designed from 1898-1915 under the medical director Theodor Deneke when it attained its current form consisting of a large, mostly two-storey pavilion construction; see Hegler (1928), 118.

[515] Ullmann and Weisser (1989), 66.

[516] Braun (1989), 343.

[517] L.c. 344.

[518] Routine examination of patients, the care of the clinical-pharmacological and pathological-physiological department with wards, lectures in the University Hospital Hamburg-Eppendorf as well as the institute's own research program were among the duties of the institute. Two assistants, a reader, two voluntary assistants, four technical assistants and six attendants; self-employed Hamburg physicians were also part of the staff; see Braun (1989), 343.

comparison with all the other German pharmacological institutes was that it stood "in organic connections with a large hospital"[519].

In 1930 Bornstein founded the second German Balneological Research Institute[520] of that period in Bad Oeynhausen, which provides an insight into the versatility of his interests. According to the words of his student Hans Erhard Block[521], Bornstein was an extremely capable and unique researcher and teacher personality. Not only was he successful in the field of experimental physiology and clinical pharmacology but also in the field of climate and biorhythmic research. Full of admiration, Hans Erhard Block mentions the weekly lecture evenings in the Bornstein house in which prominent personalities, such as the Nobel Prize Laureate Hans Adolf Krebs participated. Griesbach attended these meetings regularly even after his withdrawal from the hospital[522].

The publications with K. Holm on the "Metabolism in one-sided and normal Nutrition" as well as the publications in which he participated together with F. Bertram on "Protein minimum" and on "Pharmacology of the entire metabolism" are among the relevant publications of Bornstein[523]. Additional works concerned Paralysis, the effects of Syphilis on physiological parameters and Changes in combination with mental diseases[524].

Griesbach met Bornstein in 1919 when he accepted a position as resident of the Directional Department in the General Hospital St. Georg under Theodor Deneke. Griesbach worked for Bornstein in the pharmacological institute alongside his clinical duties[525].

A hand-written note of Bornstein originating from 1919 describes how "a number of physicians, in particular residents from the hospital are engaged in scientific work in their free time due to his motivation and under [his] direction". He regarded this scientific work as "especially fruitful both for the young physicians and for research" and mentioned the researchers working under him, among others Griesbach[526].

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[519] Bornstein (1925), 343.
[520] The first Balneology Institute was founded in Wyk/Föhr in 1922; see van den Bussche (1989 b), 371.
[521] Hans Hermann Bennhold is named as a further significant student of Bornstein's; see Kallee and Bock (VC).
[522] Hans Eberhard Bock entered the GH St. Georg as a medical assistant in 1928, the last publication in which Griesbach participated in Germany was "Über die Erythrocytenmessung durch Halometrie", devised in collaboration with Bock; see Bock (VC).
[523] BLÄ II, 150.
[524] Braun (1989), 344.
[525] C.V. (E).
[526] The physicians mentioned correspond to the sequence of mention: Griesbach, Wolff, Niemeyer, Zuntz, Samson, Wilbrandt, Tebrich, Plaut and Lippmann, handwritten notices of Bornstein´s; StAH Akte Hochschulwesen II, Ai 6/1, reference file 12. 16-1, on Arthur Lippmann; see Andrae (1997).

In 1919 Griesbach became a "secondary physician"[527] and also operated a consultant's surgery from internal medicine from 1922[528]. However, he never desisted from his activities in the Bornstein's Institute during this whole period. From the 1st January 1922 he was a scientific assistant in the pharmacological institute[529] and was awarded the Venia legendi for pharmacology with the focus on metabolic pathology on the occasion of his habilitation[530]. Griesbach remained a private lecturer at the pharmacological institute after his resignation from the hospital in 1924[531]. He participated in the teaching as did the lecturers Fritz Rabe, Ernst Sieburg and Gustav Giemsa[532]. In 1926 he was appointed senior consultant in the GH St. Georg[533] and in 1930, senior lecturer for pharmacology[534].

Griesbach's publications, which were compiled during his research activities with Bornstein, concern not so much the specific special field of Bornstein, but must be seen predominantly as a continuation of the activities with Embden and Weintraud. These comprise the works: The metabolism of sugar, fatty acid and uric acid. Nevertheless, one sixth of Griesbach's publications in the years 1919 to 1933 were compiled in collaboration with Bornstein[535]. Further papers from Griesbach, compiled as clinical reports also originated from this period of time, likewise his papers on haematology[536]. Bornstein's influence on Griesbach may not be underestimated although the textual focus of the Griesbach's research area was certainly not coined by Bornstein but rather by Embden. As opposed to the teachers Embden and Weintraud, Bornstein was closer to Griesbach by virtue of age and their relationship was collegial rather than a relationship between student and teacher. Griesbach also spent his longest research period in Germany with Bornstein. In spite of the, in the past, differing focal themes in his own publications, Bornstein supported Griesbach's work and was decisively instrumental in the fact that Griesbach was conferred a professor title. An assessment of Griesbach from the pen of Bornstein who died suddenly in 1932 was regrettably not found in the estate[537].

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[527] C.V. (E).
[528] StAH: Akte Hochschulwesen; Dozenten- und Personalakten I 190.
[529] Deneke, 8.2.1926, certificate (E)
[530] C.V. (E).
[531] StAH: Akte Hochschulwesen: Dozenten- und Personalakten IV 319.
[532] Braun (1989), 344.
[533] Application documents (E).
[534] StAH: Akte Hochschulwesen: Dozenten- und Personalakten I 190.
[535] G. (1920 b-d), (1923 a), (1924 a, b).
[536] Special reference is made to the publication of the blood volume determination, the so-called Congo red method, and to the habilitation treatise "On the total blood volume", (1928 b).
[537] Braun (1989), 344: also Bock (VC).

3. Publications of the years 1910-1933

3.1. Research on metabolism

The greater part of Griesbach's publications compiled in Germany deals with the metabolic processes in the human body. The objects of his investigations were the metabolism of sugar, fatty acids and uric acid, whereby the sugar metabolism and namely the glycolysis[538] occupies a quantitative and qualitative projecting status. Only two of his publications concern fatty acids.

The focal theme of the following portrayal should therefore lie with the works on sugar metabolism. At the same time an attempt should be made to integrate the historical context in the portrayal.

3.1.1 Sugar metabolism

Griesbach's earliest publications concerned the research area Glycolysis[539], which can be traced back to his work in the Institute of Gustav Embden at that time[540.] Embden together with Otto Meyerhof and Otto Warburg did significant work on the complete elucidation of the metabolic pathway from glucose to lactate[541] in the muscles[542].

From the middle of the 19th century onwards the metabolism of glucose and related carbohydrates was regarded as one of the core problems of biochemistry, in particular in view of the clinical picture of diabetes mellitus. Proceeding from the widespread thesis of biological oxidation[543], Diabetes mellitus was thought to be caused by an incomplete burning

[538] The anaerobic degradation of carbohydrates to lactic acid was originally defined as glycolysis. Today, due to the equality in the aerobic and the anaerobic degradation of carbohydrates to pyruvate, glucose is now taken to mean the "degradation of glucose via fructose biphosphate and 3-phosphoglycerate to pyruvate". Pyruvate passes aerobically to the citrate cycle, the anaerobically generated lactic acid is reconverted to glucose in the liver via pyruvate, also defined as gluconeogenesis; see Karlson (1988), 226-230.

[539] The dissertation also covers this research field, G, (1913 b).

[540] David Nachmannsohn, co-worker of Meyerhof, described Embden as "one of the most brilliant and outstanding leaders in biochemistry during (that) period. His name is inseparably associated with the elucidation of the metabolic gateway of glycolysis, the scheme generally referred to as the Embden-Meyerhof gateway"; see Nachmannsohn (1979), 327.

[541] Syn: lactic acid.

[542] Fruton (1983), 29.

[543] Justus von Liebig had the idea that inhaled oxygen would be completed converted to carbon dioxide, He perceived the conversion as the cause of the generated heat; L.c. 26.

of glucose; H. Bence-Jones even defined diabetes as a disease of "sub-oxidation"[544]. Adolf von Bayer demonstrated in 1870 that the unstable linear 6-carbonic frame of glucose is split into two 3-carbon derivates and subsequently converted into lactic acid. The observation that these 3-carbonic derivates[545] occurred in the breath and urine of diabetics seemed to prove that the disease originated from an incomplete oxidation of glucose[546]. Shortly afterwards, it was possible to identify the 4-carbonic derivate acetoacetate and ß-hydroxyburtyrat in the urine of diabetics. The query to the origin of this ketone body led to further metabolic problems such as the glycolysis or the β-oxidation of fatty acids[547].

The investigation of the glycolytic pathway was a focal research theme in the twenties of the 20th century. At the end of the thirties, the glycolysis was portrayed almost completely[548], it was the first metabolic degradation pathway to be portrayed[549].Great significance must therefore by attributed to their investigations. The glycolysis was then investigated from two different aspects: from the alcoholic fermentation and the muscle glycolysis. The discovery of Hans and Eduard Buchner, that yeast extract is capable of alcoholic fermentation is "regarded as the birth of modern biochemistry"[550].

It was not recognised until 1925 that fermentation and muscular glycolysis are functional deviations from the same biochemical mechanism[551]. Numerous groups of researchers in Germany were engaged in the analysis of fermentation and glycolysis in muscles. Franz Hofmeister can be regarded as one of the pioneers of glycolytic research as he was one of the first to argue the enzyme theory of intercellular metabolism[552]. Together with Felix Hopp-Seyler, who also embraced ferments[553] inside cells, Franz Hofmeister[554] is regarded as one of the founders of the Enzyme theory[555].

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[544] Fruton (1983), 28.
[545] Acetone is meant here.
[546] Fruton (1983), 29.
[547] L.c.
[548] In the last year of his life, in 1932, Gustav Embden brought forward a complete glycolysis schema with his co-workers H. J. Deuticke, H. Host, G. Kraft and E. Lehnartz, before the entire extent of his discovery became generally known, After the death of Embden Otto Meyer and his colleagues verified the correctness of this schema during the following five years. They isolated the catalysing enzymes of the single reactions and presented them in the pure form; see Nachmannsohn (1979), 332.
[549] Florkin (1975), 91.
[550] Karlson (1977), 734.
[551] Florkin (1975), 15.
[552] Hoffmann´s relevant article originated in 1901, in which he expressed the thesis that the synthesis and the degradation of sugar are affected in various intermediate steps in the protoplasm. But this does not proceed via the same reaction but via a sequence of different chemical reaction; see Fruton (1983), 29.
[553] Older designation for "enzyme".
[554] Three of his students, J. K. Parnas, G, Embden and Carl Neuberg were leaders in this field, "Emblem's institute in Frankfurt/Maine contributed to the elucidation of glycolysis (also) due to the collaboration of several co-workers: S. Oppenheimer, H. Deuticke, M. Zimmermann, K. Baldes, E. Schmitz, G. Kraft, F. Kalberlah, H.

Griesbach's first publication from 1910 bears the title "Acetic acid in the liver of diabetic dogs"[556]. For this publication he repeated the tests conducted by Embden and A. Marx in 1908, according to which n-valerian acid possesses a toxic effect: n-valerian acid together with amino-n-capron acid and isobutyl acidic acid as substances which could inhibit the formation of acetic acid from fatty acids and amino acids[557]. Griesbach's investigations with doses increased by from two to six gram of n-valerian acid showed no indications of a liver toxicity.

In the following publication Griesbach tested different sugars for the conversion to lactic acid in collaboration with S. Oppenheimer[558]. Embden established in the course of several publications from 1905, 1906 and 1909 that "glucose, laevulose, glycerine and aniline would be degraded with the formation of natural d-lactic acid"[559]. Griesbach's co-author, S. Oppenheimer had observed as early as 1912 that 1-arabiboise and inositol do not form lactic acid as opposed to the hexoses[560]. In their co-publication, Griesbach and Oppenheimer came to the conclusion that arabinose does not increase the formation of lactic acid. Moreover, the formation of lactic acid from dextrose is more considerable than from galaxies, laevulose and mannose[561].

In 1912 Embden, K. Baldes and E. Schmitz demonstrated that, according to their findings, the degradation of glucose followed under the intermediate formation of two molecules of optically active glyceraldehyde. Griesbach also occupied himself with this question in his dissertation[562]. He accepted the opinion of Embden and his co-workers, according to which the non oxidative degradation of sugar disintegrates into at least two phases: the cleavage of glucose in two molecules of a triose and the conversion of the originated active glyceraldehyde into natural lactic acid. Griesbach therefore assumed two separate ferments

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Enger, W. Griesbach, H. Jost, H. Emde, W. Wassermeyer, E. Hirsch-Kaufmann, E. Lehnartz (and) T. Icker; see Florkin (1975), 15.

[555] Nachmannsohn (1979), 275 f.

[556] Acetic acid, synonymous acetic acetate (3-oxybutyrat) all belonged to the ketones together with their decay product acetone and the reduction product 3-hydroxybutyrat. Ketones are formed especially in the case of lipolysis; see Karlson (1988), 278.

[557] Embden and Wirth made this observation in 1919; see G. (1910).

[558] G. (1913a).

[559] L.c. 323f.

[560] Arabinose belongs to the pentoses. Inonsitol is a six valent cyclic alcohol which is active following esterification with phospatidic acid. Inositol phospatides are significant as cell membranes. Hexoses possess six carbon atoms; see Karlson (1988), 213 and 288.

[561] Glucose is also designated as dextrose, fructose as laevulose or fruit sugar. Mannose and galactose are aldohexoses; see Karlson (1988), 216 f.

[562] "Über Milchsäurebildung aus Kohlenhydrat im lackfarbenen Blute", G. (1913 b).

were responsible for these processes[563]. He tested this suspicion with the aid of haemolysed blood. The optical behaviour of the lactic acid created was the same as when cell-free blood serum was applied, so that a mixture of racemic and 1-lactic acid arose from d-l-glyceraldehyde in blood. Griesbach established the two main phases in the conversion from triose to lactic acid were bound with the intactness of the cells in varying degrees. Thus he came to the conclusion that the conversion from glucose to lactic acid occurred in cooperation with at least two different ferments[564], whereby the "glucose in the glyceraldehyde cleaving ferment" could easily be destroyed in the case of damage to the cell culture, whereas the second, the "ferment surrounding the glyceraldehydes in lactic acid" would remain unaffected by cell damage.

From today's point of view, two of Griesbach's sentences are interesting because they clarify the state of knowledge at the time. For example he described the Glycols as a very controversial field in which many attempts had been made to isolate the ferment from organs in cell-free juices. Furthermore, one has the impression that, apart from the blood, perhaps the liver (Adolf Magnus-Levy) and the musculature (O. Cohnheim) are also subject to a glycolytic effect"[565].

In a further publication compiled by Griesbach in collaboration with Embden, the two were engaged with the principle question as to whether the degradation of the sorbose molecule[566] in the artificially blood-perfused liver corresponded to its build-up.

Finally two additional sugars were tested for their glycolytic degradation path; d-Mannit[567] and Inositol. A considerable increase in glucose formation was defined on addition of d-sorbose to the fluid seeping through the liver of animals "poisoned with phloridzin"[568]. After perfusing with d-Sorbitol they were able to establish a rise in d-fructose as certain, meaning that the oxidative formation of laevulose in animal bodies could be proven for the first time[569]. Embden and Griesbach thought it probable that primary fructose was formed in the liver during the oxidation of the d-Sorbitol, which was then converted to d-glucose. However, "the

[563] Glucose is degraded via eight intermediate steps to lactic acid under anaerobic conditions; see Karlson 1988), 226-230.

[564] 564Alcoholdehydrogenase was described as the first glucose in 1909 by F. Batteli and L. Stern. In 1911 pyruvat-decarboxylase was defined by C. Neuberg and A. Hildesheimer and it was not until 1923 that hexokinase was identified as the first enzyme of glucolysis by O. Meyerhof; see Florkin (1975), 150.

[565] G. (1913 b).

[566] Sorbose belongs to the hexoses and is, in the form from of sorbit, the transitional product in the conversion of fructose to glucose and vice versa.

[567] Mannit is formed from mannose following reduction in the carbonyl group; see Karlson (1988), 288.

[568] The sugar is transported across membranes as symport. This can be inhibited by the "specific polyphenolglycosid phlorrhizin"; see Karlson (1988) 306 f.

[569] G. (1914 b).

test results of six value alcohols were still insufficient […] to allow the establishment of a constructional rule"[570].

The subsequent publications were papers by Griesbach on glycolysis which have been observed and cited the most frequently. In these papers Griesbach dealt with the existence of lactate acidogens"[571], which was described by Embden and his co-workers in 1912 for the first time and was seen as extremely controversial for a long time[572]. In their publication "On lactic acid and phosphorus acids in muscular extract"[573], Embden, Griesbach and Schmitz observed the occurrence of lactic acid in muscle extract after a short period of standing independent of glycogen and glucose content. They suspected a special type of precursor for lactic acid, the "Lactacidogen", the existence of which they wished to prove. In this case it was necessary to verify whether the formation of lactic acid in muscular extract was actually accompanied by a formation of phosphoric acid as had been observed by different authors. Embden, Griesbach and Schmitz saw the existence of the "Lactacidogen" as verified, as the result of their investigations, and suspected this included a carbohydrate compound which was closely affiliated with the degradation of carbohydrates in the muscles. They assumed that the "Lactacidogen" was a carbohydrate phosphoric acid[574]. The three experimenters then established that the biological significance of the lactacidogen could be debated according to the findings of several subsequent processing of stipulated materials. However, they had observed the "occurrence of lactacidogen exclusively in the musculature so far, (so that) the acceptance of a special significance […] for the muscular action seemed to be proven[575].

In the second project on "Lactacidogen" which Griesbach was working on, extracts from kidneys, testicles and spleens were tested for their capability to cleavage added hexophosphate and lactacidogenic solutions with the formation of lactic acid and phosphoric acid. In this case, Embden, Griesbach and Laquer were able to establish that considerable deposits of "Lactacidogen" occurred exclusively in the transverse musculature. The supposition that "Lactacidogen" was an intermediate product of the degradation of carbohydrate in the musculature was now proven for the authors[576].

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[570] L.c.

[571] The hypothesis of the existence of the "Lactacidogen" existed for over twenty years and arose due to the fact that an increased excretion of phosphate in urine during muscular activity had been observed. The chief origin of the phosphate, as is recognized today; is creatinine-phosphate. In 1931 Carl and Getty Cori demonstrated that the increase in inorganic phosphate was largely due to ATP, discovered in 1930 by K. Lohmann; see Florkin (1975), 87.

[572] L.c. 83.

[573] G. (1914 c).

[574] This proof was described as a "convincing presentation" by Florkin; see Florkin (1975), 83

[575] G. (1914 c).

[576] G. (1914 d).

The First World War interrupted the investigations in Embden´s institute[577]. The next publication created by Griesbach did not appear until 1923 in collaboration with Arthur Bornstein. It is the first of four additional works in which Griesbach concerned himself with the clinical aspect of sugar metabolism: Diabetes mellitus and the research of the hormonal substances which played a part in the processes[578].

In this case Griesbach and Embden investigated the effect of adrenaline[579] and pilocarpine[580] on the burning of sugar: the proof that the not inflammable adrenaline sugar was to be furnished with the aid of the blood perfusing method on dogs´ livers developed by Embden[581]. Furthermore it was to be investigated whether pilocarpine activated a hyperglycaemia, as several authors had already observed. Under the influence of the adrenaline the authors obtained a similar picture as was obtained for the diabetic liver and no mobilisation of glycogenic was established due to pilocarpine. Bornstein and Griesbach have proven the not inflammability of the sugar mobilised by adrenaline by means of two different biological methods; the perfusion test and the respiration test. Thus the two men delivered a "new contribution to the previous view of Bornstein, that although adrenaline encouraged the distribution of sugar in the liver, it also inhibited the burning thereof. This view is incompatible with the assumption that adrenaline is the physiological hormone of blood sugar regulation"[582].

Insulin has already been discovered when Bornstein and Griesbach brought out their next publication[583]. Their investigations, which were based on similar methods to the examinations

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[577] Gustav Embden resumed his experiments on "Lactacidogen" after the war. In connection with the formation of phosphoric acid and muscular activity became the focus of his interests in the following years. He discovered that muscular contraction was accom0anied by a reversible formation of phosphoric acid. He saw the task of the "Lactacidogen" as part of this process till the end; see Nachmannsohn (1979, 273 and 330. Otto Meyerhof began his research on chemical reactions during muscular activity after the First World War. The similarity with the research topics of Embden and Meyerhof led to some overlapping in the twenties. Meyerhof together with A. V. Hill was awarded the Nobel Prize in 1922 for his work, in which he had shown that the produced lactic acid volume is proportional to the stretching of the muscles and that glycogen is the origin of lactic acid; see Nachmansohn (1979), 273.

[578] Diabetes Mellitus is a disease which has been known since antiquity, receiving its name from Aretaios in the second century after Christ. It was observed at this time that polyuria with sweet-tasting urine occurred in conjunction with diabetes mellitus. Matthew Dobson established the sweet taste of the blood of diabetics in the 18th century. A chemical breakthrough came in 1908 when Stanley R. Benedict presented a method to determine sugar in urine; see Meyer-Steineg/Sudhoff (1965), 82 and Saffran (1992), 123f.

[579] Adrenaline leads to rapid glycolysis in the liver and muscles. These results in a decrease in the glycogen reserves and lipolysis see Karlson (1988), 415.

[580] Pilocarpine is used as parasympathomimetic to extend the Schlemm canals especially in the case of glaucoma.

[581] G. (1923 a).

[582] L.c. 40.

[583] Frederik G. Banting and Charles H. Best were able to isolate insulin 1921/22 with the help of the Duboscq colour meter, the physical basis of which can be attributed to Johan H, Lambert and Georg J. Beer; see Saffran (1992), 123 and 125.

involving adrenaline and pilocarpine, now concerned the interaction between insulin[584] and adrenaline[585]. Insulin does not cause a lowering of blood sugar even in a highly dosed form and therefore also no build-up of glycogen. In this surprising finding, both men refer to a good specialist on this question such as Fritz Laquer, who would accept without doubt that substances exist in our insulin preparations which have a conflictive effect on the insulin and thus increase the blood sugar. These substances have also been defined as anti-insulin[586] without being able to provide further details[587]. The effect of adrenaline which was considered to be rescindable by insulin in the surviving organ by Bornstein and Griesbach confirmed their opinion that insulin had an influence on the liver. Therefore we have been able to prove the antagonism adrenaline - insulin without doubt in our tests"[588].

A second publication from Bornstein and Griesbach "On the theory of the effect of insulin and pancreatic diabetes"[589] followed. After the discovery of pancreatic diabetes by Oskar Minkowski and Joseph von Mering in 1889, which they described following a pancreaectomy on a dog[590], as well as the illustration of insulin by Charles Best and Frederik Grant Banting more recently[591], Griesbach and Bronstein thought it necessary to process the field of carbohydrate metabolism from the aspect of insulin once again.

Bornstein and Griesbach observed that the sugar burning is unaffected by the level of blood sugar and that fructose is burnt more quickly than glucose. Therefore they assumed that it was not the common glucose but another "carbohydrate X" which was burning. For the investigations, they made use of glucose, fructose diphosphoric acid, glycogen or another carbohydrate and compiled a pattern of blood sugar regulation and the processes of carbohydrate degradation[592]. They saw the cause of the lack of carbohydrate burning in the diabetic organism in a lack of glycogen[593]. The primary effect of insulin was in the regulation of blood sugar according to their observations, whereas the secondary effect was the increased oxidation. They also confirmed the assumption that sugar was formed from fat in pancreatic

[584] Insulin lowers the blood sugar level, enhances the adsorption and degradation of glucose in the cells and inhibits lipolysis. This adrenaline and insulin have a contradictory effect; see Karlson (a988), 384.
[585] G. (1924 a).
[586] The antagonist of insulin in the liver and fatty tissue is glucagon. It stimulates Gluconeogenesis and therefore the degradation of the glycogen reserves and enhances lipolysis; see Karlson (1988), 414.
[587] G. (1924 a), 374 f.
[588] G. (1924 a), 375.
[589] G. (1924 b).
[590] Saffran (1992), 126 and 129.
[591] G. (1924 b).
[592] Glucose I glycogen → "carbohydrate X" → degradation of the carbohydrates.
[593] The glycogen as a storage carbohydrate in animal organisms is degraded first to glucose-1-phodsphate, then to glucose-6-phosphate. This is the final substance to the glycolysis degradation pathway. The degradation of the glycogen in the liver maintains the blood glucose concentration; see Karlson (1988), 248 f.

diabetes. They regarded insulin as a substance which deposited sugar as a type pf reserve material – supposedly to the glycogen.

In the twenties of this century Carl and Gerty Cori were able to elucidate this question on glycogen as they demonstrated a cyclic metabolic connection between muscular glycogen, blood sugar and blood lactic acid[594]. The opened a new chapter in Endocrinology when they demonstrated the hormonal control of cycle, which was thereafter named the Cori Cycle[595] after them in 1929.

Griesbach's last publication on sugar metabolism dealt with the question of the different behaviour in metabolic utilisation of different stereoisomer hexomers[596]. These kinds of tests had not been conducted on intact isolated muscles of endothermic muscles at that time.

3.1.2 Fat metabolism

Griesbach published only two papers on fat metabolism which appeared in 1928 and 1929. In both publications he dealt with the fat metabolism in the surviving dog muscle in accordance with the new methods described by Arthur Bornstein[597]. The first study dealt mainly with the location and degradation of fat acid and ketone bodies. The formation of the ketone bodies was of special interest at the beginning of this century. Around 1928 it became generally recognised that the formation of acetone[598] was an indicator of an intensive fat burning. Up to this time it was unclear where the ketone bodies were degraded. Griesbach's attention was caught by the musculature because several researchers have excluded the lung, the liver and the kidneys. He came to the conclusion that the formation of acetone and β-oxy-butyric acid and their reciprocal conversion in the liver was beyond all question. According to his observations, the musculature did not attack the fatty acids verifiably, but destroyed the degradation products acetic acid and oxy-butyric acid quickly and completely. "It can not be

[594] Fruton (1988), 29.
[595] Lactic acid diffuses from the musculature to the blood within the Cori-Cycle, whence it is transported to the liver and converted to glycogen. Glucose is formed from glycogen in the liver and then transported to the musculature as a source of energy; see Nachmannsohn (1979), 27.
[596] G. (1929 a).
[597] Bornstein developed a method to perfuse the "living-fresh extremities of the dog with blood from a foreign species in 1926; see (1928 a).
[598] Acetone was discovered in 1857 by W. Peters in the disease of the diabetic coma. G. Gerhardt found acetoacetate in the urine of diabetics and V. Arnold recognized in 1900 that this was the biological preliminary stage of acetone. As early as 1897, H. C. Geelmuyden expresses the view that the ketones were formed from fatty acids in the metabolism. Franz Koop formulated his hypothesis on β-oxidation of the fatty acids and indicated that an analogy to the excretion of β-oxybutyric acid would exist in diabetics; see Florkin (1975), 286 f.

stated how far this process can be considered for the energetic of the muscular work"[599] Griesbach remarked finally.

Griesbach´s second publication on fat metabolism attempted to find out how far a discrepancy in these results exists in electrically stimulated muscle[600]. However, this question resulted in no deviating findings as lower fatty acids do not form acetone even in the case of energetic activity.

3.1.3 Uric acid metabolism

Around 1829 so-called "skorish"[601] stimulation was accepted as the cause of gout[602]. A. B. Garrod described the deposit of uric salts in joints in 1859. The breakthrough in the research into uric acid metabolism came in 1903 when Emil Fischer elucidated the chemistry of the purine bodies. The designation "purine" also comes from him derived from "purum uricum"[603]. There was almost no interest in gout within specialist circles between 1914 and 1953, and W.H. Herrick and L. Tyson described in 1936 as the "forgotten illness"[604]. Salicylic acid was one of the first substances to which a diuretic effect was ascribed before A. Nicolaier and M. Dohrn discovered the uricosuric characteristics of the phenylchinoline-carbonic acid which was well received in the gout therapy under the name of "atophan"[605]. Wilhelm Weintraud played a significant part in the introduction of atophan as a remedy for gout[606]. At the same time his hypotheses according to which atophan had a primary electric effect on the uric acid degrading partial function of the kidneys,

Griesbach's publication on uric acid metabolism can be ascribed to the influence of his mentor Weintraud. Thus his initial research on purine metabolism was inspired in 1914 by Weintraud, had to be interrupted due to the war and could only appear in 1919 during his activity in Bornstein´s Institute[607]. Griesbach's publications on uric acid concentrated on two batteries of questions; the degrading path of uric acid and the effect of atophan.

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[599] G. (1928 a), 132.
[600] G. (1928 b).
[601] Scoria means slag.
[602] The uric acid level in the blood is increased in gout. This means that crystals of uric acid are deposited in the joints and kidney stones are formed. The cause of gout is an insufficient excretion of uric acid or an increased purine biosynthesis, See Karlson (1988), 109.
[603] Merz (1990), 35 and 40.
[604] L.c. 44.
[605] L.c. 46-48.
[606] Brandenburg (1920), 968.
[607] G. (1919 b).

The question whether uric acid was degraded via uricolysis was debated till 1920. Above all, it seemed questionable whether degradation and a new formation or the transition from a simple to a complex form was relevant[608]. Bornstein and Griesbach proved that a transition from bound to free uric acid and from higher nucleic bodies to bound uric acid was possible. They described this process as "uricopoesis"[609]. As opposed to the prevalent opinion they adhered to the uricolysis. The publication "on uric acid in the blood of humans"[610] was followed by several critical publications, for example one author saw gout alone as disturbance of the excretion of uric acid, another saw a restricted oxidation in the atophan effect and an increase in the kidney excretion.

In their first publication on uric acid metabolism, Griesbach and G. Samson went into Weintraud´s hypothesis on the kidney effect of atophan, which both proved as correct. However, they pinpointed the complex character of atophan: on one hand there was a stimulating effect on the function of kidneys in the excretion of uric acid, on the other hand a flushing of uric acid from physiological depots followed[611]. The question as to the mode of action of atophan had still not been clarified around 1933 as the Griesbach's last publication on uric acid in collaboration with B.C. Costopanagiotis appeared[612]. Weintraud´s hypothesis was generally accepted by then and Griesbach considered atophan as the ideal remedy in agreement with the earlier findings[613].

Griesbach dealt with allantoin for the first time in this publication[614]. He and Costopanagiotis were not able to establish an increase in the excretion of allantoin due to atophan and agreed that allantoin prevailing in human urine was due to food uptake[615].

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[608] L.c.
[609] G. (1929 d) and (1923 b).
[610] G. (1920 d).
[611] G. (1919 b).
[612] Atophan had to be withdrawn from the market at a later date due to considerable liver toxicity. The true history of medicinal products lowering uric acid began in 1948 as the effect of carinamide, the synthetic derivate is called probenecide, was discovered by W. Q. Wolfson, C. Cohn, R. Levine and B. Huddelstein, Probenecide was introduced two years later as the first the first uric-acid lowering substance in the gout therapy. The introduction of the uricostatic drug allopurinol followed in 1963, and within the last forty years the development of additional medicines such as phenylbutazone and indometacine occurred; see Merz (1990), 48-50.
[613] G. (1933 b).
[614] Xanthine is degraded to uric acid by xanthinoxidase. In humans uric cid is excreted in an unchanged state as an end product. Most mammals still convert uric acid to allantoin and allantoin-acid; see Karlson (1988), 109.
[615] G. (1933 b).

3.2. Haematological research topics

The three haematological studies occupy an outstanding position within the publications of Griesbach in Germany, especially the work relating to the "Congo red method"[616]. This publication was widely received and frequently cited in specialist literature. Griesbach's professorial dissertation "On the entire blood volume"[617] is his only publication in book from and was also frequently cited. The haematological research topics gain in significance in the existing study.

The methods to determine the blood volume were still very limited. Experiments were being made with carbon monoxide and an antitoxin before dilution was discussed as a feasible method. However, the trials could not assert themselves due to their intricateness or inaccuracy[618]. In relation to the question to a suitable method Griesbach came across a publication from 1915 soon after the war when foreign literature was accessible again. The research team Keith, L. Rowntree and Geragthy had colorimetrically measured the blood dilation of a dye[619] which has been injected in vivo and by means of dilution assessed the available blood volume. Till 1920 the "brilliant vital red method has been diversely applied in the USA and in Great Britain. Griesbach was unsuccessful in obtaining this dye for his own tests, so he was forced to use the non-toxic Congo red[620]. As a result of his findings, he considered the Congo red method as simple and reliable […] with which a great number of questions of a physiological and pathological nature could be answered[621].

Numerous research topics of other researchers[622] confirmed the new method as "good to use"[623] and "convenient"[624] as well as "useable and non hazardous"[625]. R. Seyderhelm and W. Lampe turned against the watery staining standard used by Griesbach in 1922/23, which. in their opinion supplied a blood volume value that was too low. Griesbach and W. Schmidt as well as E. Greppi and H.G. Schleck, however, found out concordantly that the difference in the findings of Griesbach and Seyderhelm could not be attributed to the watery standard[626].

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[616] "A clinically applicable method to determine the blood volume" (1921 b).
[617] G. (1928 b).
[618] G. (1921 b).
[619] They utilised brilliant vital red. This dye was also tested by G. H. Whipple in 1920; see G. (1928 b).
[620] The chemical designation is "sodium salt of the benzidine-diazo-bi-I-naphthyl-amin-4-suphonic acid which is an n anionic, rough dispersible dye; see G. (1921 b).
[621] L.c. 1291.
[622] Reference is also made to the work of Büttner (1923), Kronacker and Böttger (1928), Herzfeld, Mendershausen and Bohnen as well as Borrmann; see (1928 b).
[623] Anonymous: Therapeutisches aus Vereinen und Kongressen (1921), 270.
[624] Neubauer (1923), 520.
[625] Lacquer (1924).
[626] G. (1928 b), 679.

Griesbach observed further in the application of his Congo red method that the excretion curve of the staining ran differently in different diseases, an observation which would have further consequences. Griesbach assumed that ”in certain circumstances, abnormal Congo red curves give an important indicator of the endothelium constitution of the capillaries respectively to the function test of kidneys, investigations are carried out by my co-worker Bennhold”[627].

In his professorial dissertation, Griesbach committed himself to the Congo red method in detail and the follow-up investigations of Hans Hermann Bennhold[628] he had indicated. Therefore he examined the staining reduction in various diseases also in amyloidosis among others. By making grafts he discovered that some patients exhibited a macroscopic abnormal red staining of the spleen and liver. Bennhold was able to prove that Congo red leaves the blood stream by passing damaged capillary endothelia and entering a chemical combination with the contiguous amyloidal substance. In severe cases of amyloidosis, a rapid disappearance of the Congo red injected in vivo that Bennhold also defined as “dye combination reaction”[629].

In Griesbach’s professorial dissertation there appeared a summarised presentation of the direct and indirect blood volume determination as “the question of the normal blood volume still cannot be exclusively answered (and we) have not yet come to a final conclusion”[630]. Together with this presentation Griesbach described the blood volume under different pathological ratios whereby” our knowledge of pathological changes in the blood volume is still rather limited”[631].

In the third and last publication on haematology, which was completed in 1933 in collaboration with Hans E. Bock, Griesbach described the practical significance of halometry[632] for the clinic. Although the measuring of the mean erythrocyte diameter with the aid of halometry was extremely helpful especially for the disease of pernicious anaemia[633],

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[627] L.c. 1290.

[628] Hans Hermann Bennhold (1893-1976) came to the GH St. Georg hospital in Hamburg where Griesbach was working. He habilitated in 1932 under the supervision of Arthur Bornstein in the subject clinical pharmacology. his special field was the serum protein bodies; see Kallee (1993), 1336-1338; for further information on Bennhold and his position in National Socialism, see page 36 and Andrae (1997), 92-99.

[629] Bennhold 1923(1923), 32-34; ”free Congo red” was unknown at that time.

[630] G. (1928 b), 683.

[631] L.c. 688.

[632] Halometry is the determination of the mean corpuscular diameter by means of a so-called erythrocyte meter. This is a leading diagnostic instrument, in particular for pernicious anaemia, in which the mean corpuscular diameter is much heightened. The diagnosis of this disease is possible at a glance via halometry.

[633] Pernicious anaemia, also known as Morbus Biermer, is a megaloblastic anaemia with macroplanocytosis, i.e. the mean corpuscular diameter is increases. A vitamin B12 deficiency is the cause, based on a deficiency in an intrinsic factor. The lack of the intrinsic factor is attributed to an autoimmune reaction.

this method was not applied in Germany until 1933, Griesbach and Bock appealed against this[634].

[634] G. (1933 c).

3.3. Clinical reports and publications on methodology

Griesbach's publications on clinical questions will only be presented here marginally as they only contributed to a low portion of his publications. They also rank behind the publications on glycolysis and the haematological research in their significance[635].

Two printed lectures of Griesbach's[636] are worthy of mention, the first titles "On accessory nutritional substances "providing an overview on the status of the research on vitamins and the three vitamins recognised at that time and their significance.: the anti-rachitic vitamin A[637], the anti-neuritic vitamin B and the anti-scurvy vitamin C[638]. On the occasion of a training course for physicians about the "Symptomology, Diagnosis and Therapy of Poisoning" Griesbach gave the next published lecture in 1933[639]. Furthermore, two epicritic reports are published. The subject of one of the reports from 1931 was the "the only known case so far in which a severe leucopenic haemorrhage[640] caused by radiation could be healed by spleen extirpation[641]. Carl Hegler and Griesbach favourised this, at that time, controversial method as a possible therapy.

In other epicritic reports in collaboration with W. von Kapff, clinic director in Bad Kissingen, Griesbach portrayed the case of a female patient suffering from fits of ventricular flutter. This was successfully treated with atropine[642]. For reasons of entirety three further publications are mentioned here: a clinical report on medicine in India[643], a field report about a new medicine[644] and an overview of the contemporary standard of knowledge in the field of respiratory physiology[645].

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[635] An exception is presented in the following publication: Carl Hegler and Griesbach: "Case of roentgen-aleukia, cured by spleen extirpation", (1931 a); see below.

[636] G. (1921 a) and G. (1933 a).

[637] At this time eye and bone diseases and "perhaps rickets too" were thought to be induced by a vitamin A deficiency; see G. (1921 a), 37. Now is recognized that a vitamin D deficiency is responsible for rickets and osteomalacia in children and osteomalacia in adults.

[638] Between 1920 and 1949 the research into vitamins achieved a climax. Casimir Funk favoured the expression vitamin whereas other authors such as Abderhalden called the vitamins "nutramines" as well. Around 1920 research were aware of only three vitamins without having presented them or having determined their structure. For example vitamin B1, also known as aneurine or thiamine was displayed in the pure form first in 1926, an elucidation of the structure followed in 1931; see Karlson (1988), 723f.

[639] G. (1933 a).

[640] This disease, also known as pancytopenia, is a combination of anaemia, granulocytopenia and thrombocytopenia in mostly cell-deficient bone marrow.

[641] G. (1931 a), 79.

[642] G. (1931 b).

[643] Griesbach accompanied a rich patient as personal physician to the British and Dutch Indies from November 1929 to March 1930; see G. (1930).

[644] O. Nast and Griesbach expressed their opinion on an arsenic product called "arsamon" which was new on the market in this publication (1920 e).

[645] G. (1920 f).

Griesbach's publications on clinical methods of determination all appeared between 1913 and 1919. They did not reach the significance of the work on metabolism and haematology. For this reason they will only be mentioned briefly here.

Griesbach was engaged in two publications about the contemporary methods of blood sugar determination[646]. He dedicated a further publication to the testing and further development of the Abderhalden gestational reaction[647].

The fourth and final publication on clinical determination methods was followed by some reviews. Griesbach turned against the treatment of scarlet fever with human serum respectively convalescence serum. He pointed out the adverse effects which had been observed by other physicians[648].

[646] G. (1913 c) and (1917).
[647] G. (1914 a).
[648] G. (1919 a).

F. Research work in New Zealand

1. Institutions and co-workers

1.1. "Thyroid/Endocrinology Research Department" in Dunedin

The first medical courses of the Otago Medical School were established in 1875[649] after the opening of the University of Otago in Dunedin/ New Zealand in 1871[650]. Therewith the second medical school came into existence in the whole of Australasia after Melbourne (1864) and prior to Sydney (1883)[651].

Sir Charles Hercus stands for the emerging and development of medical research in New Zealand. As he returned to New Zealand following his service in the army, he notices a regional discrepancy in the occurrence of goitre[652] in school children[653]. So he began to investigate the iodine content in different soil samples in order to indicate the aetiology of endemic goitre[654]. Iodised salt was then introduced to New Zealand households due to the findings of Hercus[655] which lead to a containment of the disease[656].

In 1931 Hercus and H. Aitken began to examine the results of other researchers by means of laboratory tests and found that feeding rabbits with cabbage induced goitre[657]. This initial research work on the thyroid gland and especially on the goitrogenic dietetics was continued[658] from 1932 by Hercus and the chemist Herbert Dudley Purves[659]. The results they obtained from feeding cabbage were not satisfactory. Therefore they tested the goitrogenic effect induced by Brassica seeds, a species of cabbage, in rats[660]. At this point the stipends from the Ministry of Health to the Thyroid Research Department were waved due to cutbacks in the governmental expenses. The continuation of the research work was guaranteed by the

[649] Hercus (1955),120.
[650] Anonymous; Dunedin Hospital, 24.8.1926.
[651] Hercus (1955), 120.
[652] Goitre is endemic in New Zealand as it is in Switzerland.
[653] Carmalt-Jones (1945), 233.
[654] Purves: Endocrinology Research, Documents of the ERD.
[655] Hercus' research was financed from 1924 on by means of an annual grant from the NZ Ministry of Health. The goitre research received 350 pounds annually from the same source.
[656] Carmalt-Jones (1945), 234.
[657] Purves: Endocrinology Research, Documents of the ERD.
[658] Carmalt-Jones (1945), 234.
[659] Purves was inspired to study human medicine by Hercus (1935.41); see Hubbard: Obituary, Herbert Dudley Purves, unpublished; see the detailed presentation in the next chapter for further information.
[660] Purves: Endocrinology Research, Documents of the ERD.

university itself, if only with restricted means[661]. The year 1937 signified a turning point in the history of the "Thyroid Research Department"[662].

In February Hercus was appointed as the new Dean of the Medical University[663]. The wish to establish research in the medical faculty was a feature of his curatorship[664]. The limited financial means and the restricted space made it very difficult to win experts for the research work in Otago[665]. Hercus instigated extensions for research and preventive medicine at the beginning of his term of office as Dean which, however, could not be completed until 1948[666]. In 1956, after the most significant publications from Purves, Griesbach and Kennedy had already appeared, Purves noted that although the work in the department could well compete with the international standard; the performance was restricted by a lack of modern equipment[667].

A significant change for the research in New Zealand came about in 1937 as a result of the founding of the "Medical Research Council of New Zealand" in the scope of the "Health Act" from 1920. This new Medical Research Council[668] was constituted with eight members; two came from the medical faculty[669] and took over the existing research area "Goitre, Hydatid and Nutrition Research" immediately. The first chairman of the newly founded MRC was the Director General of health, Malcolm Watt. The greater part of the research department was located in the rooms of the medical faculty of Otago. The thyroid research department received 500 pound a year from the government as initial grant[670] Hercus´s significance in the founding of the MRC may not be underestimated. He was a very influential and highly

[661] L.c.

[662] Prior to 137 the University of Otago had to cope with an increasing disparity between student and lecturers as well as with the restricted means. As understanding was lacking in the "House of Representatives" in Wellington for these problems, the construction of a second medical university was refused. Thus the university saw the only solution in a restriction in the number of students to 60 each year- The increasing number of applications submitted by refugees from Nazi Germany worsened the existing situation; see Carmalt-Jones (1945), 239f. The difficult situation could explain the slight opportunities in the faculty to employ scientists in the Research Department; see the detailed description in Chapter D. 4.1.

[663] Carmalt-Jones (1945), 244.

[664] Monroe, S. (VC).

[665] The equipment of the research department was very limited both before and during the war so that for example only one binocular microscope was available. The sharpness of knives for the microtome was always a problem. It was difficult to obtain wax, slides and other material. Alcohol often had to be used more than once and diluted with water. When American scientists visited, they usually brought some good slides with them. Griesbach obtained extremely good slides from the States for the publications in collaboration with Berkeley. All in all, New Zealand was too isolated that the researchers only realised that one or more devices were lacking when they worked in other countries; see Hunter (VC).

[666] In 1948 the so-called south block was opened as the new building for the medical faculty of the University of Otago, the thyroid research department was located on the third floor. Prior to 1948 the medical research department and the physiological and anatomic departments were situated in Ferguson building; see Carmalt-Jones (1945), 245.

[667] Purves: Report on overseas travel 1960, Documents of the ERD.

[668] Abbreviated to MRC. The MRC was renamed Health Research Council; see Monroe C. (VC).

[669] They were Charles Hercus and Muriel bell; see Carmalt-Jones (1945), 246.

[670] Medical Research Council (1987).

esteemed personality and had especially good contacts to important politicians[671]. There was no institutionalised medical research in New Zealand until 1937. Prior to this era, research was conducted by professors or lecturers, in as far as interest and money was available. In 1941 Purves succeeded Hercus as principal research officer and director of the New Zealand Medical Council's Thyroid Research Department[672]. Griesbach was employed full time in the Thyroid Research Department first in 1941 after he had been employed in the physiological department part time[673]. The research department also received important impulses[674] from the researcher married couple Bielschowsky, who immigrated to New Zealand in 1947. Franz Bielschowsky became director of the Cancer Research Department in Dunedin, the New Zealand branch of the British Empire Cancer Campaign Committee. His focal topic in research lay in the investigation of the influence of hormones on carcinogenesis[675].

With the opening of the so-called South Block[676] in 1948 there were suitable rooms for research in the medical university after a long struggle. In the South Block[677], 47 researchers were now working under the umbrella organisation of the MRC, British Empire Cancer Campaign, Hugh Adam research Fund and Travis Trust[678]. Full of regret, Dean Hercus observed that among the academic researchers only three were graduates from the Medical University in Otago. Therefore it was a great concern for him to create a mutual relationship between teaching and research in Otago[679]. The fruitful work of the research department encouraged the interest and the achievement in the field of endocrinology in New Zealand. On

[671] Hercus was in the same party as the Prime Minister and also knew him personally; see Monroe C. (VC).
[672] Hubbard: Obituary: Herbert Dudley Purves, unpublished
[673] See the detailed description in Chapter D. 4.3.
[674] Bielschowsky came to New Zealand with his wife Marianne in 1947 after he had first emigrated to Amsterdam, then Madrid and Sheffield. Bielschowsky was born the son of the famous Berlin neurohistologist, Max Bielschowsky (Bielschowsky-staining for axons and dendrites) on 5.1.1902 in Berlin. He studied medicine in Berlin, Freiburg and Breslau and became a reader in Freiburg under the direction of S. J. Thannhauser. It is not known whether Bielschowsky and Griesbach had known each other in Germany; see Anonymous: Obituary, Franz David Bielschowsky.
[675] Hercus: Medical School Annual Report 1947, Hercus papers, Box 86, Historic Staff Room.
[676] The former South Block is now called Hercus Building after its founder.
[677] The pathology was located on the ground floor, bacteriology on the 2nd floor in which Leopold Kirchner worked. The 3rd and 4th floor contained the research departments for Thyroid, Cancer, Nutrition, Travis (TB research) and Virus research. 17 laboratories, workshop and stores, photographic room, micro-photo room, physical darkroom, media preparation room, glassblowing store (this room was known as the Griesbach room after 1959), balance room, hot room and office and staff rooms were located on the e3rd floor. The animals for the research departments were kept on the 4th floor; see Hospitals, Hercus Papers. Box 57-64, Historic Staff Room as well as Hunter (VC).
[678] Hercus (1955), 120.
[679] "Without this interaction, a university is but a technical school. For it is not the buildings, but rather the personalities of the teachers and students which create the character and tradition of an institution"; see Hercus (1955), 120.

17.5.1963 the New Zealand Society of Endocrinology was founded with Purves as president, R. L. W. Averill as secretary and Griesbach, Ibbertson and Kilpatrick as the committee[680]. Progressive insights into the field of thyroid research led to the name of the research department being renamed the Endocrinology Research Department in the course of time then renamed the Neuroendocrinology Department. This department closed on the retirement of Herbert D. Purves in 1937. Duncan D. Adams continued with the auto immunological research in his department, the Autoimmunity Research Unit, which however, no longer exists today[681].

[680] Minutes of the Inaugural Meeting, 17.5.1963; Documents of the ERD.
[681] Hunter (VC).

1.2. Research co-workers H. D. Purves, W. E. Griesbach and T. H. Kennedy

Charles Hercus was the initiator and patron of the research department of Herbert D. Purves, Griesbach and Thomas H. Kennedy. Initially engaged in the research himself, he was restricted by the time demanded by his office of Dean but he remained chairman of the Endocrinology Research Group and thus bound with their research. Hercus met with Purves, Griesbach and Kennedy every Saturday morning for a meeting, occasionally also for dinner in his home. Hercus was very influential and might have encouraged and admired Griesbach[682] on account of his medical capabilities. In any case the two men had great mutual respect[683], and Griesbach remarked that the Dean was rather different to the clinicians, "otherwise I could not have stood for it"[684].

Many of the names appearing as co-authors in Griesbach's papers such as, for example, W. H. Hall, N. Sirret, R. W. Hornabrook, NM. Bell or M. Livingston were members of other research departments in Dunedin, whose research topics occasionally overlapped with those of the endocrinological research group. Joint publications were made in order to save costs and to obtain as much information as possible from experiments with animals. In the following years there was active collaboration between Griesbach and researchers from Berkeley, such as I. L. Chaikoff[685], A. Taurog, E. Siperstein, E. S. Evans and R. C. Goldberg. The experimental work was undertaken in San Francisco and pituitary glands of rats were dissected, stained and evaluated in a type of double-blind test exclusively by Griesbach in Dunedin[686]. Griesbach counted the cell types, drew graphs and drew the conclusions from the conducted tests. It was always a great success when the findings were congruent[687]. Griesbach was in great demand in Berkeley as he was elsewhere due to the techniques he had developed in the area of histology of the pituitary gland[688].

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[682] Hunter (VC).
[683] Brook (WC).
[684] Letter from Griesbach to Lippmann of 4.8.1944; StAH, Familienarchiv Lippmann.
[685] About I. L. Chaikoff whom Griesbach met personally during his sojourn in Berkeley, Griesbach wrote to Purves, he had "apparently no other interest but his work, lives on the campus, is unmarried and talks biochemistry without interruption"; Letter from Griesbach to Purves, 6.7.1948, Documents of the ERD, the letter is a document annex, see Page. 202.
[686] Hunter (WC).
[687] L.c. (VC).
[688] The following excerpt from a letter from Griesbach to Purves of 6.7.1948 gives details on the beginning of collaboration: 'Though I found a nice welcome I felt the time that Chaikoff and his crowd did not really believe in the possibility of functional assay on he basis of pituitary histology. I could quite understand this when I saw their slides. They kept telling me that Koneff of Evans Department could do them better, but that they did not succeed and that his method was far too difficult and unreliable for routine mass examinations […] I saw

The most important scientific contacts during the time in Dunedin were his contacts with Purves and Kennedy. Although Griesbach discusses many problems and questions with Bielschowsky, only two joint publications appeared[689], which can be ascribed to the fact that their research area did not belong to the same umbrella organisation[690]. Bielschowsky and Griesbach used the histology room together meaning that they sometimes talked in German. This understandably led to problems

with co-workers. Although Griesbach and Bielschowsky were good colleagues, they were not bound by a close friendship[691]; Griesbach felt the presence of Bielschowsky as inspiring and was happy when he came to Dunedin instead of going to Sydney[692].

The effectiveness of the research department within the Thyroid Research Department in Dunedin is usually explained as being due to the collaboration of the complementary researchers Purves, Griesbach and Kennedy[693]. Although they were very different in temperament, the three scientists held a great deal of respect for each other and worked well together[694], each of the men had his own area of responsibility, for example, Griesbach was responsible for the pituitary gland sections and their staining and Kennedy was the chemist of the department. Nevertheless, all issues were discussed[695]. The men met regularly according to the state of the work.

On completion of a project, the results were often summarised in one article. Although Griesbach, Purves and Kennedy discussed the content of the article and findings at length, it was usually Purves who finally compiled the article. Griesbach, however, published an article of his own in German in the "Klinischen Wochenschrift"[696].

Koneff´s Kodochrome photo micrograms and they are really beautiful but nor better than our good ones. then showed then our slides (microscop.) and from that moment everything changed. Chaikoff admitted that he could see the total and part. Thyr. Extract (sic) the 12 and thyroxine effects easily and without doubt. It happened that they had just started histology a few weeks before and asked me to show their young chap the technique. When I left last week, the results were already perfect […]. So I got a formal note of thanks etc." Documents of the ERD, the letter is enclosed unabridged in the document annex, see Page 160.

[689] G. (1949 a); (1950).

[690] Hunter (VC).

[691] L.c.

[692] "Good that he couldn't come to Sydney, I mean for us", this was the comment written by Griesbach in a letter to Lippmann on 7.11.1948 about this topic; StAH Familienarchiv Lippmann; the reasons for Bielschowsky coming to Dunedin instead of Sydney are unknown.

[693] Adams (1968) described this as a "marriage of the systematic, morphological type of study of the old Austro-German school with the functional physiological approach characteristic of Anglo-American investigators".

[694] Adams (WC) remembers their gentlemanly discussions, as they analysed and planned experiments. Griesbach and Purves complemented each other.

[695] David Stewart, a former student and co-worker of Griesbach and Purves, today Dean of the University of Otago, described Purves and Griesbach as "exceptional people […] they had a big influence on each other"; Stewart (VC).

[696] The reason why Griesbach never wrote an English publication himself was his uncertainty in the use of the English language; Hunter (VC).

The important person in Griesbach`s immediate environment in the research department was Henry Dudley Purves. Purves was not very technically skilled and he would never have begun with the evaluation of the pituitary gland histology himself. His practical skills lay in the chemical, mechanical and electrical areas. He would not have been able to conduct micro-surgery on animals, as Griesbach was[697]. Although Purves was head of the research department, he was reserved, shy, and modest and tended to remain in the background. He could be very difficult and moody and often spoke to nobody for days[698]. When he was captivated by an idea, he could sit there for hours in contemplation and did not wish to be disturbed. At other times, inspired by the right question, it was impossible to stop him and lead him to the completion of his work[699]. As Purves had a mathematical line towards thinking and planning he was responsible for the statistical assessment of the tests. Griesbach, on the other hand, concerned himself with the works of other researchers and made comparisons[700].

The first meeting of Purves, Kennedy and Kennedy was in 1939. The research in the field of the pituitary gland and thyroid, in which Purves and Kennedy were already engaged, was offered to Griesbach after his arrival in Dunedin by Dean Hercus. At first, Griesbach worked autonomously and was given a room in the Anatomical Institute. The reason why Griesbach, Purves and Kennedy[701] knew nothing of each other at first remains unclear[702]. Griesbach investigated the differences in the pituitary gland in goitres both naturally induced and induced by Brassica seeds. The considerable increase in size and number of the basophile cells in the pituitary gland led him to assume an association of these cells to the secretion of the thyrotrophic hormone. This turned out to be a prelude to the further investigations on the relationship to cellular changes in the hypothesis and the relevant hormone secretion[703]. The inclusion of the pituitary gland histology in the experimental research can be ascribed to

[697] Hubbard: Obituary. Herbert Dudley Purves, unpublished.
[698] Hunter (VC).
[699] Hubbard: Obituary. Herbert Dudley Purves, unpublished.
[700] "Griesbach and Purves never made a mistake, they were precise enough compared with other research workers in this field. Griesbach had a big understanding for autoimmune diseases. Without him they would never have looked after the Graves´ disease"; Adams (VC).
[701] Thomas H. Kennedy was a chemist and was employed in the Thyroid research department shortly before Griesbach. First he was appointed with a study on iodine excretion in urine in the Pacific region. He later isolated the goitrogenic substances in Brassica seeds and then also the thiouracil derivates which are of decisive significance in the therapy for goitres. See Purves: Endocrinology research, October 1951, Documents of the ERD.
[702] This was possibly due to the absence of Hercus at this time, which was spending some months overseas; see the comprehensive details contained in Chapter D. 4.2.
[703] Purves: Endocrinology Research. October 1951, Documents of the ERD.

Griesbach[704]. This method set the basis of the subsequent success of the research department of Purves, Griesbach and Kennedy.

When the first preparations were produced with wax – the sections on the slide had to developing his be thinner – the problem was that no sharp knife was available. Griesbach demonstrated a lot of patience and staying power in the production of the sections, although only an old Leitz microtome[705] which had been discarded by the Anatomical department was available[706]. Griesbach was responsible for the cellular sections during this period in the research department; he modified the staining methods and photographed[707] his pituitary gland histological sections himself.

Griesbach and Purves were aware of their capabilities and held each other in esteem[708]. Although they could work well together[709], a private friendship did not develop between the two men[710]. But still it was a happy turn of fate which brought the two researchers together. By means of their complementary characteristics, they developed into an extremely effective team, attaining world fame in their field[711]. Purves was aware of what an able and experienced colleague he had found in Griesbach. He wrote, "Griesbach's personal attribution to pituitary gland cytology was very well known and the Unit would not have been able to make this contribution it had to the subject without Dr. Griesbach"[712].

Duncan D. Adams, a former younger co-worker in the research department describes the teamwork and the creative power of Purves and Griesbach aptly:

> "The sadness of his forced exile from Hamburg was outweighed by the good fortune of his research partnership with Dr, Purves. Together they solved pituitary gland cytology, identifying the cells which make the various anterior pituitary hormones. When they began, there were only three identified types of pituitary cells. Acidophil, basophile and chromophobe. When they finished there was an identifiable cell for all anterior pituitary gland hormones. They did it by using more than one technique,

[704] Purves (1974), 548-551.
[705] Even in later years Griesbach preferred this microtome to the newer versions; Hunter (VC).
[706] June A. Hunter reported that he frequently threw objects at her until she once retaliated. He then told her that he finally had respect for her because she would no longer put up with everything; (VC).
[707] Griesbach was a hobby photographer and took many photos in the department also developing his films. He was extremely precise in microphotography and took most of the photos himself; see Brooks (WC).
[708] Purves was his immediate boss. He (Purves) was a very capable and a good scientist, and Griesbach acknowledged that side of him, but I think that their relationship would not have been easy; see Brook (WC).
[709] During his research internship at Berkeley Griesbach wrote to Purves on 6.7.1948, "How much I had wished that you had been with me. I think you would enjoy this place"; Documents of the ERD. The letter can be found in unabridged form in the documentary annex, see Page 160.
[710] Hunter (VC).
[711] Adams (WC).
[712] Minutes of a meeting of the Endocrinology Research Committee, 9.4.1962, Documents of the ERD.

relating cytological appearance to hormone content as determined by bioassay, and to evidence of functional state, often modified by experimental procedure, such as administration of the inhibiting hormone. Griesbach was the originator of this work, showing Purves assays of precisely chosen and prepared sections of pituitary gland tissue. Purves was the brilliant analyst, who occasionally was the one who saw the explanation of complete observations, whereupon they both devised the further studies. I can still remember their gentlemanly discussions, as they analyses and planned experiments. Griesbach and Purves complemented each other"[713].

[713] Adams (WC).

2. Publications of the years 1941 – 1967

In his first publications in New Zealand, Griesbach was occupied with comparative studies on the structure and function of the thyroid and pituitary glands. The medical faculty in Dunedin was interested in the research into goitre due to the frequency of endemic goitre in New Zealand during the thirties. The initial research of Charles Hercus and Herbert D. Purves was mainly concerned with experiments involving the goitre-inducing "Brassica Seed Diet" with regard to a possible therapeutic procedure. Griesbach's first work in the "Thyroid Research Department" consisted of the implementation of a comparative test method between the experimentally produced goitrogenic conditions and the histological changes in the pituitary gland. These initial works developed increasingly into research concerning the discovery of the production sites of the corresponding anterior pituitary gland hormones, during the forties. The two research areas will be described in sections 2.1 and 2.3 were the focal topic for Griesbach during this period. Special attention should be paid to the publications on endocrine tumours.

Although Griesbach had already published some findings on tumours in the forties, most of the publications relating to endocrine tumours appeared during the sixties. The findings publicised by Purves, Griesbach and Kennedy at the end of the forties and in the fifties about the discovery of the production sites of all six anterior pituitary gland hormones present without doubt the most highly esteemed performances of this research team. Therefore the focal topic below will lie with the histological pituitary gland research, even if only the most significant publications will be mentioned. Apart from a relevant orientated presentation of previous or contemporary pituitary gland histology research in these areas at that time, reviews and a brief historic introduction will be included in the presentation.

2.1. Correlative studies on structure and function of thyroid and pituitary glands

The thyroid was well known in antiquity and was ranked among the salivary glands[714] he expression "glandes larynges" for the thyroid can be traced back to Bartholomeus Eustachius[715] which was first changed when Thomas Wharton designated the gland as a result of its anatomical proximity to the thyroid cartilage as "glandula thyroidea" in his famous document "Adenographia" from 1656[716] in the course of the 18th century, the knowledge became established that the thyroid was only one single gland and that the different known conditions[717] in which a characteristic swelling of the throat appeared, presented a pathological change of the gland. As early as 1827, the connection between the thyroid and the different bodily functions was discovered by means of experimental thyroidectomy[718.] The first comprehensive presentation of the symptoms of cretinism and myxedema[719] came in 1888 by William M. Ord. A description of the symptoms of the contrasting disease of hyperthyroidism was given by Caleb H. Parry in 1825, whereby he still described the swelling of the throat as "Bronchocele. The detailed detection of this disease was achieved by Robert J. Graves in 1835 and Carl A. von Basedow in 1840. Even today, the hyperthyroidism is known as Grave's disease in the Anglo-.American language and as Morbus Basedow in the rest of Europe[720].

The foundations for our current knowledge about the function of the thyroid reach back to early experiment tests. For example patients suffering from myxedema were injected with a glycerine extract from animal thyroid or were administered partially boiled sheep thyroid, which brought a successful alleviation of the hypothyroid symptoms. The connection between iodine administration and the functionality of the gland was discovered by E. Baumann, who established a high content of iodine in the gland, in 1896[721]. Twenty years later E. C. Kendall achieved the crystallisation of the first thyroid hormone, L-thyroxine (Tetra-iodo-thyronine;

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[714] Medvei (1982), 846.
[715] Up till the 19th century the swelling of the thyroid was defined as the so-called "Bronchocele" In the English-speaking area, the swelling was, and is, called goitre. The designation "Struma" means goitre and is attributed to Fabricius Hildanus; see Werner (1991), 3.
[716] He applied the plural form "glandulae thyroideae", as he erroneously assumed an independency of the thyroid lobes; see Schönwetter (1968), 35.
[717] Werner (1991), 3.
[718] L.c.
[719] Myxoedema is the complete disease of the primary thyroid hypofunction in the adult. Cretinism is the untreated complete picture of a congenital primary hyothyroidosis.
[720] Werner (1991), 4.
[721] L.c.

T_4). The chemical structure of thyroxine was clarified by R. Harington and G. Barger in 1926 and 1927[722]. The question of the thyroid hormone was asked again as J. Gross and R. Pitt-Rivers discovered a substance in the plasma and also in the gland containing three atoms of iodine, the 3,5,3 – Tri-iodo-thyronine (T_3). This hormone also proved to be physiologically more potent and rapid in its effect than the T_4. Today it is known that three thirds of the T_3 production occurs in the peripheral tissue from T_4 in healthy conditions[723].

The thirties brought about a considerable rise of knowledge in the field of pituitary gland research. This related especially to the hormones distributed by the pituitary gland sand the hormones from the associated peripheral endocrine organs. As a result of the research into hormones and their effects, the physiology was well ahead of histology at this time[724]. In their comparative studies Griesbach, Purves and Kennedy tried to find a connection between the physiology and histology[725] by creating pathological conditions of the thyroid and pituitary glands in an artificial manner and then making comparisons with the histological changes within these organs[726].

Griesbach's publications on the structure and function of the pituitary and thyroid dealt with the impacts of the goitrogenic[727] "Brassica Seed Diet"[728] and the effect of the thiourea[729]. He was also engaged in the structure and the efficiency of the thyroxine[730].

Prior to the introduction of iodine-added cooking salt, a diffuse thyroid hyperplasia was visible in the population in the form of goitre in many of the so-called goitrogenic areas of the world, i.e. in the areas with iodine deficiency. Follicular hypertrophy and hyperplasia together with the pathological picture of goitre and hypothyroidism was also induced in experimental investigations into thyroid deficient diet resulting involving specific goitrogenic ingredients. The goitrogenic substances include thiouracil, sulphonamides and also a range of progenies of

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[722] Cody (1991), 225.
[723] Werner (1991), 4.
[724] Romeis (1940), 76.
[725] "Griesbach has called attention to the value of quantitative cytological study of the adenohypophysis (anterior pituitary gland) for the estimation of thyroid function; see Goldberg and Chaikoff (1949), 64-70.
[726] "Griesbach looked at the pituitary glands of animals that had been given the Brassica seed diet which produced goitre and found what appeared to be a proliferation of basophil cells. Up to this time I had no interest in morphological studies per se. Changes in the apparent proportions of the three groups (acidophils, basophils, chromophobes) were useful as a measure of the intensity of change in physiological state to determine how much thyroxine was needed to reverse the changes produced by thyroidectomy without knowing the meaning of the changes themselves"; see Purves (1974), 548-551.
[727] Goitrogenic means that a multiplication of thyroid tissue (goitre) is generated. This always occurs when either a hypofunction of the thyroid is present or due to another cause – experimental or when a hyperfunction of the thyroid is fostered - proceeding from the body.
[728] G. (1941 b), (1943 b), (1946 c).
[729] G. (1944), (1945 a), (1949 a).
[730] G. (1947 b) and (1949 c); these two publications deal with the comparative efficiency of the isomers of thyroxine (d-T_4 and l-T_4) and needn't be mentioned in detail here.

the "Brassica" species[731]. These types of cabbage, especially, had been used by Griesbach, Purves and Kennedy to put the laboratory animals in an artificial state of iodine deficiency and Hypothyroidism[732]. This goitrogenic diet could possible inhibit the thyroid hormone synthesis in vivo in a dose which would have no effect on other organ systems[733].

As is known today, the most frequent kind of adaptation in rats on an iodine deficient diet, as conducted by Griesbach, is the displacement of formation of T_3 to T_4 in the thyroid. While T_3 is created from T_4 in the peripheral tissue under normal conditions, the majority of T_3 circulating originates directly from the thyroid in the case of iodine deficiency[734].

As a result of the experimental application of goitrogenic diet, Griesbach, Purves and Kennedy were able to observe that Brassica seeds were able to initiate a stimulating effect on the thyroid, in spite of thyroidectomy[735]. Neither was it possible to establish indications for a thyroid inhibitory activity following the administration[736] of desiccated thyroidea[737]. The administration of dried thyroid extract as well as thyroxine demonstrated the parallel between goitrogenic diet and thyroidectomy[738]. This was determined[739][741] both on the basis of the quantity of TSH[740] as well as the cellular changed in the pituitary gland[741]. These observations

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[731] Capen (1991), 25 f.

[732] J. H. Means writes in his publication on the diseases of the thyroid about "the significant work of Griesbach, Purves and Kennedy by feeding seeds of the Brassica". Similar findings were also observed by Sharpless and Hopson and Means is of the opinion that the findings are of "great scientific interest and may provide a new approach to the study of the pituitary-thyroid axis"; see Means (1942), 594-602.

[733] Green (1991), 322.

[734] Taurog (1991), 72.

[735] G. (1941 b); the control system between the hypothalamus, pituitary and thyroid is interrupted by hypophysectomy, which leads to an endogenous resistance in the form of increases TSH secretion.

[736] In this publication Griesbach and Purves investigated the opinion presented by J. Reforzo-Membrives in 1943, according to which an inhibition of thyroid by the pituitary of rats could be evoked when they had been fed with dried thyroid extract; see (1946 c).

[737] This corresponds to the administration of iodine; Brassica seeds, on the other hand, bring about an iodine deficiency, the reverse effect.

[738] The activity of the thyroid can be throttled by means of high external administration of iodine in the form of dried thyroid extract and thyroxine. Therefore deactivation of the thyroid is not only achieved by surgical methods, by thyroidectomy, but also by means of a high administration of thyroid hormones. This procedure is also known as "medicinal ablation" and is used in the treatment of thyroid carcinoma.

[739] G. (1941 a and 1943 a): alterations in the TSH secretion visibly influence the morphological structure of the thyrotropic cells in the anterior pituitary, leading to thyrotropic hyperplasia which can be nodular of diffuse. The area of the thyrotropic cells expands to include even other parts of the anterior pituitary; Kovacs, Horvath. Stefaneau (1991), 42.

[740] The thyroidea-stimulating hormone of the pituitary, also known as thyrotropin binds with the basilar side of the follicle cells and causes an accumulation of cAMP via the activation of the adenylate cyclase, whereupon biosynthesis and secretion of the thyroid hormones are triggered in the follicle cells. These functionally significant cells vary in size, according to the intensity of which they are triggered by pituitary TSH. Hence, the entire histological manifestation of the thyroid is clearly dependent on the TSH from the anterior pituitary circulating in the blood; see Capen (1991), 25.

[741] In his first publication (1941), Griesbach described the histological changes in the pituitary following a goitrogenic diet as an astonishingly high growth of the basophilic cells with hyalinisation, vacuolisation, and the formation of signet ring cells. The basophilic alteration was in an exact ratio to the loss of acidophilic cells, as Griesbach noted. Griesbach and Purves developed as new cell measuring method based on projection and reading of a celluloid scale; see (1943 a).

are illuminating from the contemporary standard of knowledge. It is known that goitrogenic substances induce a reduction of circulating thyroid hormones – whereby an increased secretion of TSH from the pituitary gland is excited – due to the negative reaction coupling in the feedback control between hypothalamus, pituitary gland and thyroid. The heightened stimulation of the thyroid by the TSH, on the other hand, results in hypertrophy and hyperplasia of the existing glandular tissue in the form of goitre. According to the extent of thyroid hormone reduction, which can of course be due to the exstirpation of the gland as well as to goitrogenic diet, can result in the pathological manifestation of secondary hypothyroidism as well as goitre[742].

Different goitrogenic substances, in medicinal form, hold a firm position in the therapy of hyperthyroidism. In the meantime medicines can be obtained which are able to inhibit each single step of the iodine metabolism in the thyroid[743]. The thionamide family prevent the functional assimilation of iodine, but not the iodine transport. The most effective group within the thionamides are the thiourea. Goitrin was the first thiourea to be isolated[744] from plants of the Brassica species (rutabaga, turnip, cabbage). After Purves, Griesbach and Kennedy has uses Brassica seeds as goitrogenic diet in almost all experiments during the initial years, it stood to reason to insolate the substances responsible for this effect. Kennedy, the chemist of the team, finally detected that this substance was thiourea[745]. The American Edward B. Astwood was a few weeks ahead of him in the isolation of thiourea[746].

Purves and Griesbach were not so much involved in research into the structure of thiourea as in the experimental application and functional verification of the newly isolated substance. They suspected that thiouracil possessed a toxic character and observed that acute toxicity could be prevented with potassium iodide[747]. Furthermore, they recognised that the goitrogenic activity of thiourea derivates was almost solely responsible for the repression of

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[742] Green (1991), 322.

[743] Examples of medicines, which have an inhibiting effect on the intrathyroidal iodine metabolism, are: halogen (iodine), pseudo halides (ClO4, thiocyanate), furthermore, thionamide (propylthiouracil, methimazole, carbimazole), sulphonamide, lithium salts and nitro tyrosine; see Green (1991), 323.

[744] Green (1991), 324.

[745] "Mr. Kennedy reports notable advances in the investigation of the chemical properties of the goitrogenic agent in rape seed and suggested that the substance might be a thiourea derivate. Nine thiourea derivates have been made and tested for biological activity. The results show that the thioureas are potent goitrogenic agents, allylthiourea being the most active compound so far investigated"; see Chairman's report, 2.4.1943, Documents of the ERD.

[746] Thiouracil was introduced by Edward Astwood in 1943 for the treatment of hyperthyroidism; see Cope (1952), 368-457.

[747] All the laboratory animals died of pulmonary oedema and pleural effusion after the administration of thiourea; (1944). Today we know that a (slight) danger of agranulocytosis always prevails when thionamide- antithyroid drugs are administered. Hence regular leukocyte controls are necessary. Nowadays, incomprehensively, carbimazole is most frequently used in treatment although it must be converted in the liver before it can react in the thyroid; Kallee (VC).

thyroxine synthesis[748], giving explanations for the known histological and function stages of thyroxine deficiency.

These observations from the forties conform with the contemporary biochemical knowledge concerning the inhibitory activity of thionamides. The oxidation and assimilation of iodine as well as the formation of iodothyrine in the thyroid is catalyzed by thyroidea-peroxidase. Thionamide medication blocks just this enzyme reaction[749]. This blockade is of fundamental significance as TPO is the functionally most important enzyme within the thyroid hormone synthesis. It not only oxidises the assimilated iodide ions to reactive iodine, it also causes the binding of mono-iodo-tyrosine and di-iodo-tyrosine to form T3 or the binding of two di-iodo-tyrosine residuals to from T4. Thus sulphurous anti-thyroid agents cause a suppression of the synthesis, not the distribution of thyroid hormones[750].

Although thiourea can be regarded as the preliminary substance for the other thionamides, it differs from propyl-thiouracile and others in many respects. For example, its ability to inhibit iodination does not consist of the inactivation of thyroidea-peroxidase but of the reduction of active iodine[751].

As well as his publications mentioned here Griesbach also conducted several add ional studies on thiouracil concerning a possible carcinogenic reaction which will therefore be discussed in the chapter, “Research on thyroid and pituitary tumours”.

Although the different diseases of the thyroid were already known in the19th century and the identification and characterisation of the hormones as well as a rough localisation of their sites of origin has been accomplished by the forties of the 20th century. Little was known about the hormonal feedback control that caused the physiological changes. This becomes obvious when one considers that G.W. Harris demonstrated the regulation of the anterior pituitary gland by the hypothalamus in 1948 for the first time[752.]

One of the latter publications from Griesbach and Purves on the comparative studies of thyroid and pituitary gland should be seen in this light. They investigated the cause of Morbus Basedow and the malignant exophthalmia observed in such cases[753]. The cause of thyreotoxicosis and exophthalmia continues to be unclear although extensive knowledge had been acquired with regard to the causes of hypo- and hyperthyroidic illnesses. Griesbach and Purves correctly recognised that thyreotoxicosis was not the result of TSH independent

[748] G. (1945 a).
[749] Green (1991), 325.
[750] Green (1991), 30.
[751] Capen (1991), 325.
[752] Melmed (1995), 3.
[753] G. (1949 b).

diseases, but that exophthalmia must be regarded as a TSH independent disease. In the course of their investigations Griesbach and Purves presumed the presence of a circulation abnormal thyroid stimulator[754] for the first time. The actual proof of existence and the presentation of this anti-TST-receptor were accomplished by Adams and Purves in Dunedin in 1956[755]. The antibody they described is an immunoglobuline G called LATS or long acting thyroid stimulator[756]. This discovery led to new routes in the research into Morbus Basedow as an autoimmune disease[757].

[754] G. (1949 b).
[755] Greer (1990), 452.
[756] "Because of Griesbach's influence, I spent 3 years with Purves developing a bioassay for thyrotrophin based on measurement of radioactive iodine levels in the blood of thyroid-hormone-treated baby guinea pigs. This resulted in the discovery of the "long-acting thyroid stimulator (LATS)", which proved to b e an autoantibody, demonstrating that von Basedow´s disease is an autoimmune disease. (…) Griesbach's telling me about the common search for evidence of autoimmune disease in Germany before WW 1. This happened when I was beginning to wonder if our "abnormal thyroid stimulator" was an autoantibody and encouraged the idea; see Adams (WC).
[757] Greer (1990), 452.

2.2. Research on thyroid and pituitary gland tumours

Since 1934 the question on whether thiouracil and radioactive iodine could result in the development of a thyroid tumour had been discussed intensively in the area of research. In 1941 Kennedy, Purves and Griesbach envisaged the origin of thyroid tumours[758] in rats that has been fed with Brassica seeds[759]. However, the first publication was in 1945 as the series of experiments was extremely time-consuming[760]. In their second publication Purves and Griesbach went into a possible tumour induction by thiouracil for the first time[761]. Four independent research groups, including Purves and Griesbach, were working at the potential carcinogenic properties of the thiouracil derivate[762] during this period. Shortly prior to the investigations, E. Astwood had introduced thiouracil in the treatment of hyperthyroidism in 1943. The findings of all the studies showed that the thyroid-stimulated hormone TSH of the pituitary gland was responsible for both benign and malignant tumour growth[763], and also that the malignant tumours exhibited autonomous growth in transplantation experiments[764]. Griesbach, Kennedy and Purves discovered, in the course of their investigations with Brassica seed, that a long-term application led to the formation of thyroid adenoma[765]. After they had examined especially the significance of thiourea for the formation of tumours, the suspicion intensified that TSH played a key roll in carcinogenesis as an excessive stimulant[766]. It was not only the prolonged stimulation of large quantities of TSH that brought about tumour

[758] An adenoma is a solitary, capsular lesion with a homogeneous structure which, however, differs substantially from normal thyroid tissue. The classical adenoma is cellular, fleshy and pale, as opposed to typical thyroid knots which appear translucent. The majority of adenomas or knots do not absorb radioactive iodine and are thus designated as "cold"; see LiVolsi (1996), 502-4.

[759] Minutes of meeting, 15.5.1941, Box MRC 1940-1945, Historic Staff Room.

[760] The tumours need twelve months to grow; see Chairman's report, Thyroid Research Committee, 2.4.1943, Documents of the ERD.

[761] G. (1946 b), "This paper has attracted widespread interest as judged by numerous requests for reprints received"; see Purves; Thyroid Research Committee – Report on Laboratory Research 1938", Box MRC 1948-1949, Historic Staff Room.

[762] Cope (1952), 368-457.

[763] G. (1945 b), (1946 b), (1947 c), (1950), (1951 c).

[764] Such autonomy is regarded as the biological proof of malignant growth in the human thyroid; see (1951 c).

[765] "Induction of these tumours was the result of long continued stimulation by excessive amounts of thyrotrophic hormone, not to any direct carcinogenic agent […] three different histological types of tumour appeared. One […] assumed more malignant characteristics. It was transplantable in rats with no thyroxine deficiency […] rapidity of growth and its lethal effect in many cases on the host […] The malignant variant however showed no selective iodine concentration"; see Hercus (1953), 531-537.

[766] The mechanism of the experimental production of tumours of the thyroid by goitrogens has been greatly clarified by the New Zealand team of workers (Purves, Griesbach and Kennedy, 1951). They have shown by a series of elegant experiments (1945 b), (1946 b), (1957 a), (1950), (1951 c) that, in the rat, a long continues stimulation of the gland by prolonged excessive secretion of thyrotrophic hormones by the anterior hypophysis plays an essential role in the induction and progressive growth of these tumours. This was acknowledged by the production of a chronic thyroxine deficiency with antithyroid drugs, since thyroxine deficiency however produced leads to increased thyrotrophine hormone production (Griesbach and Purves, 1943)", see Doniach (1953), 181.

growth, the inhibition of TSH also led to a retrogression of cells and colloidal retention of the thyroid tissue. Hence a reactive effect of adenoma on hormone fluctuation could be established[767].

It was not until his final publication that Griesbach worked on radioactive exposure as the cause of thyroid carcinoma. The majority of neoplasia in the thyroid is papillary carcinomas. Most malignant neoplasia in the thyroid is papillary carcinoma. This occurs with astonishing frequency in regions in which sufficient iodine is available. A correlation between radioactive exposure and the formation of papillary carcinoma, in particular, the effect of low-dosed radiation during childhood is unambiguously verified[768]. Papillary carcinoma grows infiltrative and frequently in combination with fibrosis. Metastases are occasionally observed[769]. The mean induction period from the formation of thyroid carcinoma following external radiation ducting childhood amounted to ten and a half years. A distinction should be made between external X radiation or gamma radiation and internal radiation such as radio-iodine. Beside the unique dose the complete dos also plays a part as it then comes to an increase in radiobiological effects[770]. The mixture of high-energy short-lived radio-iodine isotopes arising during an atomic accident caused a significant increase in benign and malignant thyroid tumours. Hence it is proven that short-lived, relatively high-energy iodine isotopes exercise a similar effect on the human thyroid as do external gamma rays[771]. Griesbach examined thyroids after X radiation[772] as well as pituitaries two years after internal and external radiation of the thyroid[773]. In the latter cases he was able to establish a significant increase in thyrotropin and gonadotropin pituitary gland adenoma. The question on the effects and hazards of internal iodine radiation was pursued from 1951, also in Dunedin, as radioactive isotopes could be applied in the medical school in Dunedin[774]. Radioactive iodine was employed in the treatment of thyroid toxicity at the end of the forties in the USA[775].

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[767] G. (1947 a).

[768] Almost all thyroid tumours following the Chernobyl Reactor Catastrophe are papillary carcinomas, see LiVolsi (1966), 505.

[769] L.c.

[770] Maxon and Saenger (1996), 342f.

[771] L.c. 344.

[772] G. (1966 b).

[773] G. (1967).

[774] "I was shown by Dr. Purves over the facilities at present provided by the Medical School for the use of radioactive isotopes"; see Roth 8.8.1951, "Hercus Papers", Box 86, Historic Staff Room.

[775] The University of Otago´s research on cancer of the thyroid was attracting particular attention in America, said Dr. Griesbach of Dunedin, who returned by air after a five weeks visit to America. He said he retuned with the impression that New Zealand was very well advanced in this particular branch of research. Similar research was being undertaken at the Berkeley and Stanford Universities in California. During his visit he had been particularly impressed by the use of radioactive iodine in the treatment of toxic goitre. This treatment, which required only one injection, was largely replacing that of an operation"; see "Evening Star", 23.7.1948, Dunedin Public Library.

Today it is known from experiments on rats that strong neoplastic growth can be attributed to radiation[776]. The iodine therapy possesses a protective effect against the development of benign knots. From the medical data relating to thyrotoxic patients, who had been treated with relatively high therapeutic doses of iodine, it is recognised that no definite increase in thyroid neoplasms occurs. However, it is still not definitely clear that iodine does not induce neoplasms[777].

Pituitary tumours can be formed from all types of cells. They are designated by homogeneous cellular layers which compress the surrounding tissue. The normal reticular network of the glands is interrupted by the adenoma. Malignant changes are extremely rare and in spite of a certain degree of local invasion, genuine metastases are seldom described. It is possible that almost all pituitary tumours produce active hormones. In some cases these are not secreted in sufficient amounts to be discernible in the level of substances in the circulating blood. For example, approximately forty percent of the inofficiously tumours consist of prolactin-secreting cells[778].

Griesbach's main interests were focussed on the basophilic pituitary adenoma, especially the TSH-producing adenoma. Thyrotropic adenoma can occur in humans but constitute the rarest anterior pituitary tumours. Thyrotrophic carcinoma is not described in the relevant literature[779]. The clinical phenotype of thyrotrophic adenoma is the hyperthyroidism with goitre and clinical thyrotoxicity. Additional phenotypes, which would correspond to the disease of Morbus Basedow, do not occur with the tumorous over-secretion of TSH[780]. These tumours used to be described as large, locally invasive and with high morbidity. Due to the key roll that TSH measurement has played in the thyroid diagnostics since 1990, many tumours can now be diagnosed as microadenomas, which is of prognostic relevance. Apart from the TSH secretion of TSH, an additional secretion of growth hormone (SH), prolactin (PRL) or follicle-stimulating hormone (FSH) can occur. In contrast, adenoma frequently present with a partial hypofunction of the pituitary gland, in particular, with loss of the gonadal function[781]. Ectopic TSH production corresponding to the ACTH in the case of parvicellular bronchial carcinoma has not yet been identified, so far. Although TSH tumours are usually benign, metastases in the central nervous system, in the liver and lungs have been

[776] Maxen and Saenger (1996), 345.
[777] L.c. 348f.
[778] Forsling and Grossmann (1986), 7f.
[779] Kovacs, Horvath, Stefaneau (19919, 45.
[780] Gesundheit (1996), 559.
[781] L.c.

detected[782]. The pathogenesis has not yet been elucidated; there are so far only hypotheses available: one possibility is the activation of pituitary-specific growth and differentiation factors, so-called protooncogens due to unknown factors. The second theory, according to which the loss of the normal negative feedback mechanism could be responsible, as happens in the case of primary hypothyroidism[783], is decisive[784], and was also upheld by Griesbach, Purves and Kennedy. Purves and Griesbach observed adenoma formation in the state of thyroxine deficiency[785] and a regression of TSH adenomas after thyroid substitution[786]. However, Griesbach, Purves and Kennedy conducted their experiments on rats meaning that a comparison with human conditions must always be considered with reservations. Although the essential features in the hypothalamus- pituitary- thyroid control system is identical in animals and humans, there still existing significant differences. For example a male possesses a higher circulating TSH level than the female rat and the plasma half life of the T4 is in rats considerably lower than in humans. In humans, apes and dogs, T3 is transported bound with TBG (thyroglobulin) and albumin, whereas in mice, rats and hens it is only bound to transthyretin and albumin. These differences especially in the half-time and the transport proteins of rats and mice can be considered to be cause of the fact that the thyroid of a rat develops hyperplastic or neoplastic nodules[787] while being chronically stimulated by TSH, as was also described by Griesbach[788].

Besides the thyrotrophic adenoma, Griesbach's interests also focussed on a second basophile pituitary adenoma: the adenoma of the gonadotrophic cells which constitute the most common pituitary adenomas. As this adenoma only secretes inefficient qualities of hormones and no clearly visible syndrome arises, it is usually recognized when it gives rise to neurological symptoms for reason of cerebral displacement[789]. Gonadotrophic adenomas synthesize and excrete gonadotropins, FSH, LH[790] and their subassemblies α- and β-FSH and β-LH[791]. Patients, in their initial perception of neurological symptoms, also describe symptoms of pituitary hormone deficiency. The most frequent hormone deficiency is that of the LH deficiency which arises as a result of compression of healthy gonadotrophic cells by the

[782] Gesundheit (1996), 560.
[783] Thyroid hormone resistance.
[784] Gesundheit (1996), 560.
[785] G. (1956 c).
[786] G. (1965).
[787] Capen (1991), 38.
[788] G. (1945 b), (1946 b), (1947 a), (1950), (1951 c).
[789] As is the case with other macroadenomas, these tumours can expand in any direction except in the direction of the sella turcica. This can lead to compression of the chiasma opticum, hypothalamus, the third ventricle as well as the cerebral nerve inverting the ocular muscles and liquor rhinorrhea; see Snyder (1955), 564.
[790] Follicle stimulating hormone or follitrophine and luteinising hormone or lutrophine.
[791] Snyder (1995), 559.

adenoma. In men this results in a subnormal testosterone level with a subsequent reduction in energy and libido. Pre-menopausal women complain especially about amenorrhoea. Occasionally, symptoms of TSH and ACTH deficiency are also described[792]. Griesbach also described a nodular hyperplasia of the adrenal cortex in gonadotrophic adenoma which arose after castration without being able to explain this phenotype[793].

The aetiology of the gonadotrophic adenoma, the focal topic of Griesbach's publications on this type of adenoma[794], is unclear even today. It is debateable whether the adenoma is induced by a neoplastic transformation in the pituitary gland or by excessive external stimulation. In more recent studies it is stated that many pituitary adenomas are monoclonal and thus a neoplastic transformation could be regarded as the probable cause. It appeared to be increasingly improbable that external hormone stimulation was the cause of gonadal adenoma. The possibility of stimulation of gonadotrophic cells due to a long prevailing primary hypogonadism was taken into consideration because patients with primary hypogonadism had occasionally developed an enlargement of the pituitary gland. Some patients with this adenoma are also pathologically hypogonadal[795]. Griesbach had observed a higher incidence of basophilic pituitary adenoma in male and female rats fifteen months after gonadectomy and assumed the time of gonadal deficiency as inducing factor to be decisive. Together with basophilic adenoma, however, prolactin-secreting acidophil tumours also occurred after gonadectomy[796]. Today it is assumed by virtue of the anamnestic, pathological and hormonal characteristics found in patients with gonadotrophic tumours that an affiliation with primary hypogonadism should be considered in a more differential manner[797]. In the pituitary enlargement, which originates from an untreated primary hypogonadism, the symptoms of hypogonadism do not appear until many years have lapsed. The patients then exhibit a pathological serious hypogonadal appearance. The opposite is the case, however, in gonadotrophic adenoma. In the case of primary hypergonadism, FSH as well as LH levels are elevated[798].

In general, Griesbach's oncologic publications on thyroid and anterior pituitary tumours – although they can not be described as irrelevant – do not play such a crucial role as does his research on anti-thyroid drugs or on the histology of the pituitary gland.

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[792] L.c. 567.
[793] G. (1956 c).
[794] G. (2956 c), (1960 a), (1967).
[795] Snyder (1995), 565.
[796] G. (1960 a).
[797] Snyder (1995), 566.
[798] L.c. 750.

2.3. Research on the histology of the pituitary gland

The first description of the diversity of the anterior pituitary gland cells can be ascribed to the year 1844[799]. With the aid of different procedures of staining, Max Flesch subdivided the anterior pituitary gland cells into parietal cells and chief cells forty years later, whereby this nomenclature referred to the supposedly similarity of the cells according to the stomach[800]. In 1866 two types of anterior pituitary gland cells were described, non-granular neutrophil chromophobic cells and granular chromophilic cells. A. Schönemann subdivided the chromophilic cells once again into acidophil and basophilic cells in 1892. As a result of the application of conventional haematoxylin-eosin the acidophil cells, eosinophilic and the basophilic cells, cyanophil appeared[801]. B. Romeis drew up the pattern which is customary today. Romeis described two groups of cells in 1940, namely chromophobic and chromophilic whereby the chromophilic cells were subdivided into eoisinophilic (acidophil) cells and cyanophilic (basophile) cells[802]. Furthermore, he developed his own nomenclature which he was, however unable to sustain. He wished to rename the known cells alpha, beta, gamma, delta and epsilon cells[803].

The acidophil and basophile cells comply with a fixed arrangement in the normal human pituitary gland which is of significance for application in the pituitary gland due to the localisation of microadenomas; It was a great progress in 1949 when A. G. Emerson Pearse recommended the histochemical periodic acid ship (PAS) method for the displaying of glycoproteins as it was now possible with PAS-staining methods to identify cells containing glycoproteins that are FSH, LH and TSH – producing. Adrenocorticotrophic hormone (ACTH) – producing cells also appeared as PAS positive which was initially surprising as it had not been regarded as a glycoprotein. Today it is known that sugar is anchored at the N-terminal fragment of the proopiomelancortin (POMC) which is secreted together with ACTH[804]. The staining testing methods have been modified many times in order to test the pituitary gland, according to which every hormone is secreted from a specific cell type. A number of secreting granules were identified with the aid of this technique but unfortunately a

[799] The HVL as well as the anterior pituitary are built as an epithelium and comprise all features of an endocrine gland. It consists of three sections, the pars infundibularis, the par intermedia and the pars distalis, which comprise the chief mass of the HLV and is situated completely in the sella turcica. The hormones of the pars distalis are polypeptides (prolactin or LTH), growth hormones or STH, adrenocorticotrope hormones or ACTH and melanocyte-stimulating hormones or MSH) and glycoproteins (TSH, LH and FSH), see Labhart (1978), 72f.
[800] L.c. 73.
[801] Forsling and Grossmann (1986), 5.
[802] Labhart (1978), 73.
[803] Romeis (1949), 76.
[804] Forsling and Grossmann (1986), 5.

standard nomenclature could not be determined. Later it was possible to determine the synthesis site of each single hormone with a certain degree of safety by means of the immunofluorescence and immunohistochemistry marking[805].

The largest acidophil cells are the somatotrophics which usually accumulate in groups along the sinusoids and which secrete the growth hormone (GH). Prolactin is secreted by the lactotrope cells found scattered in the entire pituitary gland. An increase in the number can be discerned during pregnancy. They are equipped with receptors for oestrogen, progesterone and also for dopamine[806].

Although they are assigned to the basophilic cells, the corticotropic cells have recently been allocated to the chromophobic category. These cells secrete ACTH and constitute ca. 16% of cells in the pituitary gland of rats. An enlargement of these cells can be seen after adrenalectomy. Gonadotrophic cells can be distinguished on the basis of their colouration, cell shape, cellular granules and their change following castration or FSH injection in FSH and LH cells. Although it is presumed that LH and FSH are synthesized by humans in the same cell, this has not yet been decisively proven[807].

TSH is secreted by the thyrotrophic cells, which constitute 2-4% of the parenchymal cells of the anterior pituitary gland (HVL). The number and histology of the cells is not greatly influenced by TSH. On the contrary, changes in the circulating concentration of thyroid hormones bring about distinct changes in the number and staining characteristic of the cells[808].

The connection between the thyroid and the pituitary gland has been known for a long time now. But the cell type in the anterior pituitary gland, which produces TSH, has been identified morphologically for no longer than forty years. The American researcher, Nicholas S. Halmi as well as the team Purves and Griesbach – independently from each other, identified the TSH- producing cell. They had neither immunohistochemical methods[809] nor the electron microscopy to help with the identification. Their sole aids were different staining markers, above all periodic acid Schiff (PAS), aldehyde fuchsine (AF) and aldehyde thionin (AT)[810].

There was a lot of controversy about where even the best known hormones, STH, TSH and GTH were produced before Griesbach, Purves and Kennedy discovered the sites of production.

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[805] L.c.
[806] L.c.
[807] L.c.
[808] L.c.
[809] L. A Sternberger (1974), K. Kovacs, E. Horvath, N. Ryan (1981) are associated with this method. The relevant investigations with the electron microscopy are attributed to J. F. Rinehart and G. Farquhar (1953) as well as E, Horvath and K. Korvacs (1988); see Melmed 81995), 4.
[810] Kovacs, Horvath and Stefaneau (1991), 40.

All examinations proceeded from the supposition that granulates were the indicators for the investigated hormones. The majority of the authors were in agreement that the acidophil cells were the production sites for STH, especially because of the fact that findings in relation to the disease of acromegalia[811] had been available for a long period. The production of GTH in the basophilic cells was clarified but there were contradictory opinions on the site of production of TSH, LTH and CTH[812].

One must imagine in this context that the identification, isolation and characterisation of the HVL hormones were first attained in the early twentieth century; the growth hormone was the first hormone to be isolated in 1921 thanks to H. M. Evans and C. W. Long. The adrenalotropic and parathyrotropic substance was isolated in 1933/1934 by K, J. Anselm, L. Herold and F. Hoffmann as the last hormone[813].

Still in the first twenty years of our century researchers such as H, Cushing and M. Simmonds contributed to the fact that the endocrine function of the pituitary gland could be elucidated. E. and B. Scharrer presented their assumption of neurosecretion in 1940. In 1948 G. W. Harris proved that HVL was regulated by the pituitary gland with the help of so-called releasing hormones[814]. The isolation and description of the encelophines, the endorphins as well as the clarification of the constitution of the beta-lipotrin and prolactin are further examples of the endocrinology development in the post-Griesbach era[815].

The experiments separating the anterior (HVL) from the posterior pituitary gland (HHL) with extracts was still difficult until the beginning of the thirties. It was also unclear whether the extracts corresponded to the intra vitem of the hormones delivered. The experiments in extirpation had not led to satisfactory findings up till then due to the difficulty of the methods used. Hence the research into the mode of action of single parts of the pituitary gland had always had to be restricted to two procedures: the observation of the deficiency after extirpation and the observation of the effects of the extracts[816].

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[811] Acromegalia was elucidated for the first time in 1886 by Pierre Marie and was the result of a somatotrophic adenoma of the HVL with hyper production of growth hormone (GH of STH). This can be presented by pathological gigantism, acromegalia or viscero-megaly. O. Minkowski established the connection between acromegalia and a pituitary tumour; see Melmed (1995), 3.

[812] Romeis (1949), 197-202.

[813] Labhart (1978), 71.

[814] Melmed (1995), 3.

[815] Labhart (1978), 71.

[816] Hegler (1939), 229.

2.3.1 Cellular changes correlated with changes in the thyroid gland. Search for the place of production for TSH.

Before Griesbach commenced his research on the histology of the pituitary gland three methods were essentially known for the stimulation of pituitary gland histological changes: thyroidectomy, a goitrogenic diet and experimentally induced thyroxine deficiency – if the thyroid was taken as the starting point. Rogowitsch described histological changes in the pituitary gland following thyroidectomy for the first time in 1889. During the following period, there were many contradictory descriptions which focussed on the enlargement and the weight gain of the pituitary gland. In 1924 B. Romeis found so-called "goitre cells" as a reaction of the thyroidectomy, S. A. Satwornitzkaya so-called "thyroidectomy cells", Severinghaus et al. as well as Zeckwer et al. a deregulation of the acidophils and an enlargement of the basophils to "thyroidectomy cells". D. Marine, S. H. Rosen and C. Spark, on the contrary, saw the acidophils as responsible for the thyroid stimulation and its granules as the TST production site[817].

Griesbach began in 1941 with the investigation of the pituitary glands of animals, which had developed goitres for reason of the Brassica seed diet"[818]. He noticed for the first time the proliferation of basophil cells. The recognition of the character of a cell is based on its granules. If these are lost the cell will become chromophobe. An absolute deficiency in thyroxine therefore leads to an increasing loss in the granules of acidophil cells, until they can no longer be recognized as such. Hence the counting of the cell types of all three categories (acidophil, basophil and chromophobe) has no fundamental significance here, and it seems to be more helpful to observe the changed proportions. The fact that both acidophil and basophil cells basically change after thyroidectomy leads to confusion on the identity of the cell, which produced TSH[819].

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[817] G. (1941 a), (1943 a), (1945 a).

[818] Griesbach worked – at least in later years - with a Leitz Ortholox Microscope and a Leica camera; see Griesbach to Rosenthal, 4.7.1956, Documents of the ERD.

[819] "The study of the change in the pituitary which accompany the action of the goitrogenic agent, commenced by Dr. Griesbach last year, has been extended to include assays of the thyrotropic hormone concentration, In a most intensive investigation, using over 200 rats and 150 guinea pigs, the changed in hormone content of the pituitaries have been correlated with the histological changes. The results show that the effect of thyroidectomy is to cause a great reduction in the amount of stored thyrotropin and a simultaneous degranulation of the acidophil cells. The changes produced by the goitrogenic diet were of the same nature as those produced by thyroidectomy, though of a lesser degree. The correlation between thyrotropin content and acidophils indicates that the acidophil granules represent stored thyrotropin and that the degranulation of the acidophils after thyroidectomy or on a rape seed diet represents a depletion of these stores by rapid secretion", see Chairman's Report, Thyroid research Committee (TRC), 21.4.1942, Box MRC 1949-1945, Historic Staff Room.

Griesbach and Purves noticed that the effect of the thyroidectomy could be traced back to the former feeding of the animals. If the fodder contained meat parts as opposed to meatless fare, which presumably contained some thyroid hormone, the cells would retain their granules[820]. This behaviour correlated with the growth of the animals. Small doses of thyroxine, administered daily, allowed the acidophils to swell and also induced bodily growth[821]. Hence Griesbach and Purves came to the conclusion that the changes in the basophil cells were associated with the production of TSH[822] and the acidophil changes with the secretion of growth hormones. If merely one cell changed its form and only one hormonal change was evident, it seemed very probable that exactly this cell type produced the equivalent hormone. This logic however had to be abandoned if several changes in the hormone production or cell change became evident[823]. Griesbach and Purves observed that excessive quantities of thyroxine lowered the TSH content of the pituitary gland to undetectable amounts, whereas basophil cells remained to an almost normal extent. Conversely, the treatment with estrogens causes a reduction of the gonadotrophic potency of the pituitary gland, without causing a change in the number of basophil cells. The reflexion led them to suppose that there were two kinds of basophil cells in the pituitary gland[824]. However, there seemed to be no way to prove this point in 1946[825].

[820] G. (1943 b).
[821] G. (1945 a).
[822] The findings of Griesbach, Purves and Kennedy, which were no longer questioned in the fifties, gave rise to criticism as a result of their new extraordinary results, such as for example, from H. R. Donald: "Griesbach and Purves (1945) of Dunedin, by giving fractional doses of thyroxine to thyroidectomised and thiourea treated rats, have studied in detail the pituitary changes brought about by the fact that the very earliest histological change in the pituitary is the increase in number of the basophil cells, from which they deduce that these are responsible for thyrotropic secretion […] I would make many comments on Griesbach and Purves´ conclusions: 1. that they make no attempt to explain or to correlate the precisely simple changes in the basophil cells which follow thyroid feeding. 2. that experienced histologists such as Severinghaus have reached exactly opposite conclusions from very similar evidence (Severinghaus, 1937). 3. that out knowledge of pituitary histology id not yet sufficiently developed to justify any but the most elementary inferences"; see Donald (1949), 534-539.
[823] Purves (1974), 548-551.
[824] "Dr. Griesbach's studies into the function of the basophil cells of the pituitary have led to the unexpected result that the basophils produced by castration are not the site of the increased gonadotrophin secretion which follows castration. The basophils produced by thyroid disturbance could therefore have the same function as the basophils produced by castration. In neither case can it be assumed that their function is known"; see Chairman's Report, TRC, 2.4.1943, Documents of the ERD.
[825] Purves (1974); 548-551.

2.3.2 Discovery of the sites of production of all anterior pituitary hormones

The methods for the experimentally induced thyrotrophic cell alterations were carried out in later years with regard to the gonadotrophic hormone by means of gonadectomy and testosterone injections equally. Fisher carried out the first gonadectomy in 1905 and observed an enlargement and increase of basophils. Investigations by Desclin, Ellison and Wolfe, A. E. Severinghaus and B. Romeis followed in the thirties who, on the contrary observed an increase in basophils. New fundamental findings on the hormone cell allocation where the discoveries of Griesbach and Purves are based on were only obtained by two significant inventions: the PAS (positive periodic acid ship reaction) dye method from J. F. A. McManus in 1946 and the aldehydfuchsine dye method from G. Gomori in 1950. The PAS colouration permits the display of glycoprotein, the AF staining the display of elastic fibres. In 1949 Purves met H. R. Catchpole in Chicago. Catchpole had successfully applied the McManus PAS colouration method for the staining of pituitary gland sections. As the PAS colouration caused a red colour in saccharated proteins and it was already known that FSH was a saccharated protein, Catchpole's tests demonstrated the hormone content of the glands. This hormone content was considerably different from the display of the granules derived from the Mallory staining method[826]. Griesbach and Purves also pursued different questions with the new colourations and were thus able to describe two types of basophil cells in 1951; the gonadtrope (caudal and cranial in HLV) and the thyrotropic cells (in the central region of the HLV)[827].

During the fifties, Griesbach and Purves experienced their greatest success. As a result of differentiated sections due to improved cell sectioning Griesbach succeeded in the distinction of the basophils by virtue of their cell form. The thyrotropes presented themselves as angular with PAS colouration, the gonadotropes round[828]. Thus the evidence was furnished that the basophil cells of the HVL consisted of thyrotropic and gonadotrophic cells[829] S. Halmi was able to publish his findings on the pituitary gland colouration with aldehydfuchsine

[826] L.c.
[827] G. (1951 a).
[828] L.c.
[829] "The identification of the two cell types which secrete the gonadotrophic and thyrotrophic hormones represent the successful conclusion of a line that has been followed since the pituitaries of rats on the Brassica seed diet were first investigated"; see Endocrinology research, Chairman's Report, 25.4.1951, Box MRC 1951, Historic Staff Room.

colouration at the same time[830]. The aldehydfuchsine colouration stains the thyrotropic basophil in a specific wax according to Gomori[831]. With thyroxine substitution stages, the proof could be furnished that the granules of the thyrotropes displayed a TSH storage pool[832]. The findings of Griesbach and Purves with reference to the thyrotropic cells of the pituitary gland were agreed upon by the majority of researchers who were dealing with the same theme, such as A. G. Emerson Pearse[833], N .B. Myant[834], E. E. Pochin, M .L. Rosenheim and N. S. Halmi[835].

The further measures taken by Griesbach and Purves were to completely eliminate the content of a hormone and then to determine the type of cell granules, which had disappeared at the same time. For example, R. O. Greep, I. Chester and Jones had shown in 1950 that the female rat exhibited a pituitary gland which contained only FSH and no trace of LH after treatment with androgens[836]. Purves and Griesbach were able to prove the existence of a FSH and a LSH cell based on the cell form by means of this experimental setup and with the help of PAS staining[837]. The findings which they obtained in the gonadtrope cells were also recognized internationally as can be followed from the letters of M. G. Farquhar[838], and J. F. Rinehart, E. Rennels, M. Herlant[839], M. Alanson[840], E. B. Astwood[841] and V. Trikojus[842].

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[830] Purves (1974), 548-551.
[831] G. (1951 b).
[832] G. (1951 d).
[833] "Certainly I agree with you (…) disagree with Halmi in his assertion that the beta and delta cells belong to distinct species"; see Pearse, 23.10.1951, Documents of the ERD.
[834] "May I say how mush I enjoyed hearing of the work done by you and your colleagues?"; see Myant, 1.2.1952, Documents of the ERD.
[835] "Purves and Griesbach expressed their belief that the bet cells are identical with their "thyrotrophs" and the delta cells with their gonadotrophs". […] to point out the excellent agreement between our findings and those of the New Zealand investigators"; see Halmi (1952), 140-142.
[836] Purves (1974), 548-551.
[837] G. (1954 b).
[838] "We have been working in an area similar to yours except that we have been applying the electron microscope […] we arrive at conclusions which are quite similar to those you have presented "; see Farquhar, 20.4.1955, Documents of the ERD, and also Farquhar and Rhinehart (1954), 516-541.
[839] "Nos observations sur l´hypophyse de la femelle due Murin conferment intégralement cette opinion. [...] Tout récemment, l´existence d´une troisième cellule basophil a été signalée chez le Rat (Siperstein, Nichold. Griesbach et Chaikoff, 1954 ; Purves et Griesbach, 1954, 1955 ; Farquhar et Rinehardt, 1954 ; Ladmann et Barnett, 1955), son identification a toutefois exigé des artifices expérimentaux ou même l´aide du microscope électonique (Farquhar et Rinehardt). Or, chez le Murin, la présence d´une troisième cellule basophil bien distincte des autre frappe les yeux"; see Herlant (1956), 89-185.
[840] "I tried all techniques I could find on distinguishing the classes of gonadotrophs but found your morphological and topographic work the only reliable guides to follow"; see Allanson, 1962, Documents of the ERD.
[841] "Professor Astwood considered some of the best work in the world in that field was done here"; see Otago Daily Times, 30.6.1954, Hocken Library, Leigh Street.
[842] "Some great work is being varied out by a first class group of men in this field, and an opportunity to further the exchange of information about such research should not be missed"; see "Evening Star", 10.8.1954, Hocken Library, Leigh Street.

In collaboration with E. Siperstein, CW. Nichols and I. L. Chaikoff from Berkeley, it was possible for Griesbach to assign five hormones to the corresponding sites of production. Accordingly the gonadtrope hormones FSH and LH as well as the thyrotrophic hormone TSH originate from the basophil cells, whereas STH and LTH originate from the acidophil cells of the HVL[843].

The two remaining cell types, the granules of which possess only protein and no carbohydrate and the origin of which was not yet completely proven, were identified in 1957[844] by Griesbach and Purves as somatotropic and lactotropic hormone producing cells[845].

Throughout his entire creative period in New Zealand, a close exchange bound Griesbach with the research team in Berkeley. But there had also been active cooperation since the fifties with S. Rose[846] in Melbourne, D.S. Farner in Washington and A.G. Emerson Pearse[847] in London. This illustrates the international esteem in which Griesbach, Purves and Kennedy were held[848].

In September 1963 the International Council for Nomenclature of the anterior pituitary gland met to establish a universally valid nomenclature for HVL histology[849] and to limit the number of standardised colouration techniques[850].

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[843] G. (1954 a).
[844] G. (1957 c).
[845] Purves (1974 c).
[846] "Dr. Purves and I have decided to cut and stain a few of your pituitary grafts if you send them over to us […] it would be an impossible load for me to cut all the glands of your experiment, which I would have to do if we were to get good results. […] for fixation we use 90 parts of concentrated (5 %) mercury sublimate solution with 10 parts of 40 % formalin. Fixation: six to twelve hours. Dehydration: half to one hour in the ascending alcohols. Clearing: in cedar wood oil"; see Griesbach to S. Rose, 12.5.1956. Documents of the ERD.
[847] "We gathered from it that you have not been successful in staining human pituitary with aldehyde-fuchsine. In our experience the human pituitary is much more readily stained by the aldehyde-fuchsine method than is the rat pituitary. Our troubles have been with the preparation of the aldehyde-fuchsine […]. Dr. Griesbach prefers to use the original aldehyde-fuchsine as used by Halmi but the use of a stable powder would have the advantage of consistency if it could be used successfully. Dr. Griesbach has been staining sections of human pituitary which are referred to him by the Pathology Department […] We have not so far had any useful results with the Wilson methyl blue stain, applied to rat pituitaries"; see Purves to Pearse 25.7.1955, Documents of the ERD.
[848] This was also well documented by the negative replies given to international researchers who would have liked to come to Dunedin for a study visit: "regretful to answer your application in the negative for the reason that not only is all the working space in the Department already occupied but there is a waiting list of applicants from overseas for the future"; see Griesbach to Gosh, 28.10.1957, Documents of the ERD.
[849] The majority of members preferred the suffix –tropic to the (etymologically incorrect) suffix – trophic. The functional names of cell types were also established; see van Oordt (1965), 131-134.
[850] Periodic acid >Schiff (PAS) – orange G method, aldehyde-fuchsine - methods (Halmi 1952, Gabe 1953), Herlant´s Alcian blue at low pH PAS-orange G, Herlant´s tetrachrome methods (Herlant 1960), Ezrin´s aldehyde thionine method (Ezrin, Murray 1963), L.c.

2.3.3 Supplementary studies

After 1955 Griesbach verified the pituitary gland histological findings in six additional publications. Hence two publications were concerned with the so-called thyroidectomy cells and two papers dealt with the differences in the histology in dogs and in other vertebrates. One publication was concerned with HLV alterations in vitamin E deficiencies and the other dealt with the contentious question of the acidophil regranulation via iodide.

M. Kojima described thyroidectomy cells[851] for the first time in 1917. During the following years various contrasting opinions prevailed about these cells with regard to their origin, the vacuolization and the comparison with castration cells. Encouraged by the research of Scharf and Foerster[852], Griesbach and Purves also examined these cells. They also examined a paper of Bailiff's in which it as claimed, that hypothermia produces a hyperplasia of the basophils. Griesbach and Purves were able to establish a granulation of the thyroidectomy cells which could not be compared with normal TSH basophils in 1956. In this case they did not accept a correlation between thyroidectomy cells and TSH produced cells[853]. They confirmed the increase in basophils in the case of hypothermia and saw a changed TSH secretion as the cause[854].

Animated by the investigations of Goldberg and Chaikoff in 1952 in which they distinguished two types of basophil cells and a zeta cell, Griesbach and Purves examined the pituitary gland of the dog, though with the Crossman-Mallory colouration. They obtained the same cellular division (without zeta cells) as has been described by Griesbach in 1951 in collaboration with Berkeley. The pituitary gland of the dog did not differ from the pituitary glands of the other animals examined so far[855].

On the initiative of R. Ortmann, who had determines the deviation in cell colour in frogs; the investigation was continued together with Griesbach with the wallaby, a small kangaroo. These findings yielded four types of acidophil and three types of basophil cells. A peculiar carmine red stained cell was described which, although acidophil, could also be stained with

[851] These cells appearing after thyroidectomy were large, swollen and possessed a strongly vacuolated cytoplasm. The intrafollicular colloid exhibited an increase and the pars intermedia was thickened, see Romeis (1940), 536.
[852] Scharf and Foerster expressed the view in 1956, after observation of the decline in basophils following thyroidectomy that thyroidectomy cells must originate from another type of cell as the basophiles; see Griesbach (1956 a).
[853] L.c.
[854] G. 1956 b).
[855] G. (1957 a).

PAS and AF, which was in itself a contradiction. Ortmann and Griesbach were unable to find an explanation for this phenomena[856].

In 1926 and 1933 K. E. Mason depicted the destruction of the epithelium of the tubules seminiferi in the case of vitamin E deficiency. This corresponds with the condition of a partial castration in which no signet ring shapes the so-called castration cells resulted[857]. After the accurate differentiation and localisation of the gonadotrophic cells by Siperstein, Griesbach and co-workers[858] a re-examination of the vitamin E deficiency by means of new colouration techniques was an obvious choice. On this occasion, cell alterations corresponding to the changes following castration thus an increase in FSH cells and almost no LH cells were defined[859].

The final publication, in the context of the pituitary gland histological research, dealt with a clarification of a controversy between Griesbach and Purves as well as E. S. Evans with co-workers. In 1946 Griesbach and Purves determined a 50% remainder of granules following an administration of iodide after thyroidectomy, against which Evans was able to observe an acidophil regranulation. For the clarification of the differences Griesbach, Evans and Chaikoff assessed the regranulation of acidophils up to the 14th day with a subsequent total decline in a joint project. It was also possible to observe weight and skeleton growth parallel to the cell changes, which could be explained by the acidophil character of the STH[860].

The question on the site of production of the HVL hormones seemed to be proven by the pituitary gland histological findings of Griesbach and Purves as well as Halmi and additionally by the electro microscopic as also the immunohistochemical corroboration for decades. But even earlier the opinion that a hormone could be assigned to a cell from which it originated was not always regarded uncritically[861].

Some years ago, though, it has been possible to observe the transition from somatotrophic to thyrotrophic cells in the pituitary gland s of rats which had been treated with propylthiouracil. This discovery supported the assumption that the different cell types of the anterior pituitary gland could not always be distinguished as a transformation of the cells in each other in

[856] G. (1958).
[857] 1925 von Wagenen, 1933 d Nelson.
[858] G. (1954 a).
[859] G. (1957 b).
[860] G. (1963).
[861] Bielschowsky (1958), 106-115, wrote "Some authors are of the opinion that a particular identifiable cell can secrete a variety of pituitary hormones (Russfeld, 1955); others often believe in the existence of specialized, monofunctional cell types (Purves & Griesbach), 1951, 1954; Herlant, 1956). In our opinion undifferentiated nonfunctional cells exist in the anterior lobe but, once differentiation has taken place, the resulting mature cell types are committed to manufacture one specific product. All chromophilic elements belong to this class".

certain situations. Hence the thesis “one cell, one hormone” could no longer be valid with the five different cell types and the corresponding six anterior pituitary gland hormones[862].

[862] Kovacs, Horvath, Asa, Stefaneau and Sano (1989), 95.

G. Appraisal

Walter Edwin Griesbach was born in 1888 in New York as the second child of German parents. Coming from a bourgeois Jewish home, he was influenced by Morris Simmonds, professor of pathology, after the early loss of his father. Already during his medical studies, he gained experience in research by working in Simmonds' Institute which gave him important basic knowledge of science and research, which was of assistance for his further career.

Griesbach's career started during the 1920s at some of the most famous research institutions of Germany, such as the laboratories of Gustav Embden or of Arthur Bornstein. His work in these institutions, which led to early publications of his work, allowed him to meet famous people as Paul Ehrlich, Franz Knoop or Hans A. Krebs.

Gustav Embden thought of Griesbach as of one of his best pupils, with an exceptional personality, and he valued especially Griesbach's eagerness, his mature judgement, organisational talent and exceptional medical knowledge, which is associated with a special gift for medicine. Therefore, it is not astonishing that Griesbach achieved leading positions in medicine at an early stage and that for instance Embden predicted a magnificent scientific future for him. Despite this success Griesbach remained modest, open, gently aloof, high-principled, but naturally not without faults. From the start of his studies he had tried to live up to the highest expectations of a physician and scientist. Although he realised his abilities, his actions were never stamped by arrogance. He had talents far beyond medicine – especially in music – and was skilled in an exceptionally broad classical knowledge. Privately, Griesbach was quite a modern man. This is demonstrated by his interests as well as his marriage to a notably vanguard woman. His character was empathic, loving, open and assiduous, but he could nevertheless also be moody and demanding. Supervisors were not exempt from his critique, and he expected criticism where necessary from his subordinates. Knowing his own qualities, he could sometimes be sarcastic, angry and abrasive towards low-brow people.

Griesbach's exceptional human as well as medical abilities might have led him to highest positions in science. Indeed, until 1933, he was already a highly esteemed specialist in Internal Medicine, researcher with many publications, and senior lecturer at the University of Hamburg. Without the historical influence he would have probably, as predicted by his academic teachers, reached the highest positions at the university and certainly achieved some scientific awards.

Thanks to the realism of his wife, her family bonds to New Zealand and last but not least the efforts of his brother, he was able to set out for New Zealand at the end of 1938. Little is known about Griesbach's thoughts about everything he experienced during the National Socialism period and the emigration to New Zealand. It is not surprising, that he was hesitant in his decision to emigrate, as this must have seemed to him as the collapse of his former life and work. Where others bent opportunistically to the claims of the immigration country and others served a repetition of their medical studies, he refused this, being aware of his abilities. He was fortunate enough that research opportunities were made accessible for him. Frustrations, sorrows and a certain amount of bitterness are mingled within the first years of the emigration. Mixed within the thankfulness for the affiliation and the research position were rather ambivalent feelings. From his letters during war time to his friend and colleague Arthur Lippmann, who emigrated from Hamburg to Sydney, a high level of sarcasm, loneliness, depression and escape into physical impairment can be revealed.

Although the research work in New Zealand began modestly, under difficult circumstances, with increasing physical impairment and financial limits, these problems gave way with time. Several publications of the New Zealand team of researchers of Herbert D. Purves, Walter E. Griesbach and Thomas H. Kennedy led to international recognition and collaborations. This research work began to play more and more a central role within Griesbach's life. This new purpose satisfied him until the end of his life and also finally led to the successful conclusion of his scientific career.

Although he was never honoured with big awards and high positions for his complete career, a personality like Griesbach's, who never aimed to acquire superficial things, was reconciled with destiny in respect of his achievements in life. Not only in this respect does Walter Edwin Griesbach impress as the German ideal of science and education in the late 19th century, which today, in view of specialisation, is hardly in evidence: the great scholar in the classical sense.

H. Summary of results

This analysis examined the life and work of the endocrinologist and metabolic pathologist Walter Edwin Griesbach who was born in 1988 in New York and passed away in 1968 in Dunedin/New Zealand. Apart from short notices in biographical reference books, an obituary and a passage in one thesis, there was no analysis available which gave information about Griesbach's life and work. Therefore, this analysis is the first description of his life and appreciation of his contribution to medical science.

The different sources, which were used for this analysis, were of very heterogeneous nature and had to be sorted and made accessible at locations far apart, as for instance in Hamburg/Germany and different locations in New Zealand. Further very valuable information could be obtained through oral and written interviews of contemporary witnesses in Germany, U.S.A., Italy, New Zealand and Australia. This is also the first time that the estate of Griesbach could be seen and used for this analysis. The evaluation, establishment and characterization of the sources which gave insight into Griesbach's life and work, was performed for the first time during this analysis.

The first main part of this analysis, Chapter C, is of introductory character and gives a historic overview of Endocrinology until the year of 1940. This chapter is supposed to demonstrate the knowledge of endocrinological research in the areas of pituitary and thyroid glands, therefore grading Griesbach's research within the historical context.

In Chapter D, Griesbach's life, which was until then only known by some dates and circumstances, is specified. His medical life could be investigated, demonstrated and proven quite exactly, sometimes in great detail. Unfortunately, about Griesbach's private life, his opinions and feelings only few references could be found. The main effort of the demonstration of Griesbach's life, however, was to testify in an exemplary manner the circumstances of life of a German-Jewish physician during the National Socialist Regime in Germany and to demonstrate the conditions these doctors had to face when immigrating to a country of the Commonwealth.

The analysis of Griesbach's research work was performed in Chapters E and F separated by time and content for the different parts in Germany and New Zealand. The issue of the interaction between the content of Griesbach's research work and the institutes he was working in are addressed in Chapters E.2. and F.1. Therefore, the institutes and research focuses of Gustav Embden, Wilhelm Weintraud, Arthur Bornstein and Herbert D. Purves, are also illustrated. One main focus of this analysis was to explain, integrate and assess

Griesbach's scientific research in the field of biochemistry, haematology and the pituitary gland work done in New Zealand. The bases for this evaluation were apart from his publications especially reviews, letters, reports, conclusions, surveys and other sorts of records. In this respect, the best conditions could be found for the endocrinological research Griesbach did in New Zealand, so that in this example it was possible to describe very exactly, how Griesbach approached scientific questions in his experimental work, mostly even with limited resources.

Griesbach's publications about the intermediate products of glycolysis as well as his development of the "Congo-Red-Method", which was a widely honoured and used a method to determine the in vivo-blood volume, are of exceptional interest for medicine. The discovery of the goitre-producing compound within Brassica seeds led the research team of Herbert D. Purves, Walter E. Griesbach and Thomas H. Kennedy to the development of 'Thiouracil', a medication still used for the treatment of thyroid diseases. The most important development of the team of Purves, Griesbach and Kennedy was the identification and linkage of all cells of the pituitary gland to the hormones controlled by them. The basic principle for this discovery was to combine histological analyses of the pituitary gland to situations in vivo, where hormone excess or deficiency was artificially created. The introduction of this method into the thyroid research was without doubt Griesbach's merit.

The unfortunate lack of scientific or personal appreciation of Walter Edwin Griesbach could be corrected with this analysis. Nevertheless, the words of Duncan D. Adams in the New Zealand obituary are embarrassing: "This classical work on pituitary gland cytology will constitute a permanent memorial to Dr. Griesbach. All New Zealanders can be proud that it was performed in their country".

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J. Index of sources and literature

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1.2. Documents of the "Endocrinology Research Department" in the basement of the "Pathology Institute", Otago Medical School, Dunedin, N. Z.

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1.3. "Historic Staff Room", of the Medical Library of the University of Otago, Dunedin, N. Z.

Box MRC 1940-1945.
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K. Appendix

In the appendix a hand-written letter of Walter Edwin Griesbach to his New Zealand colleague Herbert D. Purves from 6.7.1948 can be found. This letter was written during Griesbach's first research visit to Berkeley. It documents the circumstances Griesbach faced during this first meeting with research workers in Berkeley and also demonstrates the struggle for international recognition of the new and unknown research group around Purves, Griesbach and T. H. Kennedy. This letter further offers an insight into the collegial atmosphere between Griesbach and Purves and the content of their research at this time. It was made available through the Documents of the ERD in Dunedin.
Beside this letter three photographs are attached, which show Griesbach's colleagues Charles Hercus, Herbert D. Purves, Thomas H. Kennedy and I. L. Chaikoff.

1. Letter from Griesbach to Herbert D. Purves, 6.7.1948

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6. 7. 48.

Dear Dr. Purves,

I trust you have received Dr. Ch.'s letter and that I'll find your answer to it on my return to Berkeley next week. Though I found a nice welcome I felt all the time that Ch. and his crowd did not really believe in the possibility of functional assay on the basis of pituitary histology. I could quite understand this when I saw their slides. They kept telling me that Koneff of Evans' Dept. could do them better, but that they did not succeed and that his method was far too difficult and unreliable for routine mass examinations. (Celloidin mod. Kan) I saw Koneff's Kodochrome photo micrograms and they are really beautiful, but not better than our good ones. Then I showed them our slides (microscop.) and from that moment on everything changed. Ch. admitted that he could see the total and part. thyr. ect. the I_2 and thyroxine effects easily and without doubt. It happened that they had just started histology a few weeks before and asked me to show their young chap the staining. When I left last week, the results

were already perfect except that the sections did not stick to the glass because albumin was not applied. So I got a formal note of thanks like ps I wrote to Sir Charles Leonhartz (Board man) showed me three hypophysectomies, I took photos of the arrangement and bring P.'s technique along hoping that it can be copied in d. I think that we shall get 100% success also with P.'s technique. Konopka had tables on his wall on the effect on rats, thyroidectomy during the first 4 days, of growth hormone growth horm. + thyroxe. and thyroxine alone. I did not like to copy them but as far I remember the growth rates were 1) untreated - nil 2) Growth horm. +33 g 3) G.H + Thyroxin+67 g 4) Thyroxine+63 g 5) decapitated rat+24 g. Acidophils he not only counted but took their size in a Camera lucida drawing (100 in each pit.) it went parallel to the growth. K. did not understand me, when I hinted that Thyr. might be in his type G.H. "you mean in the thyroxin hormone"? So I gave up. But Chaikoff did understand it. I think we should come out with the story as soon as possible. Leb. says his Chemical thyroxine method (Chanley)

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is so good now (as ~~confirmed~~ judged by parallel estimations radioact. T_3 method) that he can estimate Thyroxine in pooled serum without injecting I^{131}. But he thinks a lot of whatever plans you might suggest.

Yanney, the chemist of the show, had just finished a paper on the organic plasma Iodine, ~~etc~~ in which he proves (by both methods) that at least 80% is thyroxine, the rest containing D.I.T. and perhaps 5% trio-T_3. He showed me the paper in Hebrew and also the Lehaney method (Cer-As decolorisation by T_2, estimated in a electrocolorimeter.) I shall photograph the destillation apparatus etc. next week. He Yanney, is a very good man. By the way, he got a thyroxine di (or tri) peptide out of thyroid and showed by the carrier method that at least this peptide is not present in plasma.

The whole Dept. was busy over the Iodide "inhibition" action. A paper of Wolff and Chaikoff has just come

out (J. biol. Chem. 134) showing the mechanism of plasma Iodine ~~Thyroxine, D.T and acety. T~~ and thyroid Dr. D.T. and T2 under the influence of increasing doses of KJ (J 131). It is believed that here again is a homeostatic mechanism with an optimal dose somewhere about 50-100 micrograms (I forgot the exact figure) and inhibition of thyroxine formation by doses 200, 500, 1000 γ. I'll try to get a reprint on a copy of the manuscript. Tehaikapps trouble is, that he does not get thyr. enlargements (the epithel. in these rats is normally high) and the few pit. I saw did not show the thyr. ech. changes with the 1000 γ doses. Ch. asked my advice for tackling the problem. To show him our results on para. thyr.-ect. + KJ and thiourea + KJ. But I told him to take suboptimal thiourea doses (perhaps 0.05% or less in the drinking water) + 1 mg T2 and see what he gets. He thought that good hint suggested that we should do it ourselves, as we knew more about the histology. He now takes hypophysect. rats, injects 5 γ and 1000 γ J 131 (to different rats) and assays Dijodthyro-

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in the thyroids, which he expects should not be there or decreased until the higher dose (1000γ). If this is inhibition I was also interested by Vanny's separation of very small amounts of th. and D.T. by chromatography on filter paper.
There is a specialist for paralysis in Evans' Dept, van Dyke and it possible I want to see him doing the operation. Evans I saw but did not meet, as everybody warned me and they say he is quite inaccessible. (He looks it, Do.) Pencharts did not really believe the malignant nature of our thyr. carcinomas as long as they have not shown growth on transplantation. Ch. has prophylthiouracil rats going for 9 mths. but I could not feel any tumors yet, of course. He wants to see what I 131 does and what the Colloid contains after the I 131 injection in the adenomas.
How much I had wished that you had been with me. I think you would enjoy this place

In many respects the working space is inferior to ours, but in ~~other~~ many others it is of course superior. I do not know how many Peiping Comm lines are busy all the time, at least 4 I saw and a girl sitting and regulating them, as far as they are not automatic. Ch. has just proved the synthesis of cholesterol from acetic acid, and works at the breakdown of fatty acids with C Biotope. That man has apparently no other interest but his work, lives on the campus, is unmarried and talks biochemistry without interruption. Do you can imagine that a 5 p.m. I was driven home completely useless to my family. Now I am for a fortnight on this beautiful spot on Monterey Peninsula and have a good rest.

I hope to be back in D. on the 26th July.

I do hope that little Robert is better.

Kind regards to Jay, your family, Tom, Hall and Buckminsky

Yours truly K Eppenbach

P.S. I think, under the circumstances we should not omit to publish the part. Hux cut + K3 remarks

2. Photographs

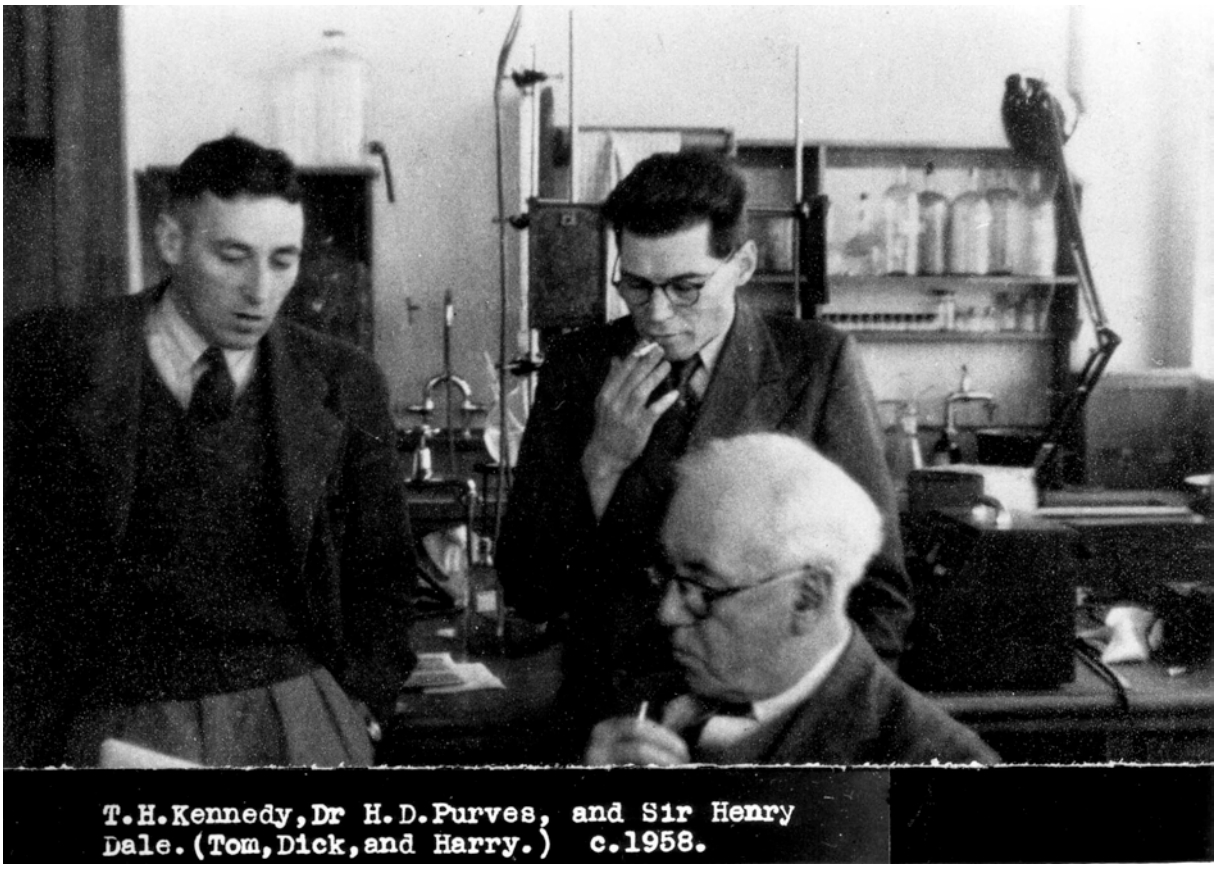

Fig 1: Document of the Otago Medical School, Historic collection of Prof. Dr. John Borrie, Dunedin, N. Z.

Fig. 2: Walter E. Griesbach; Charles Hercus, Dean of the Otago Medical School; Leopold Kirschner, Microbiologist and also “refugee doctor” as Griesbach. Photography taken around 1960 within the research department of the Otago Medical School; kindly made available by W. Lassally, Auckland, N. Z.

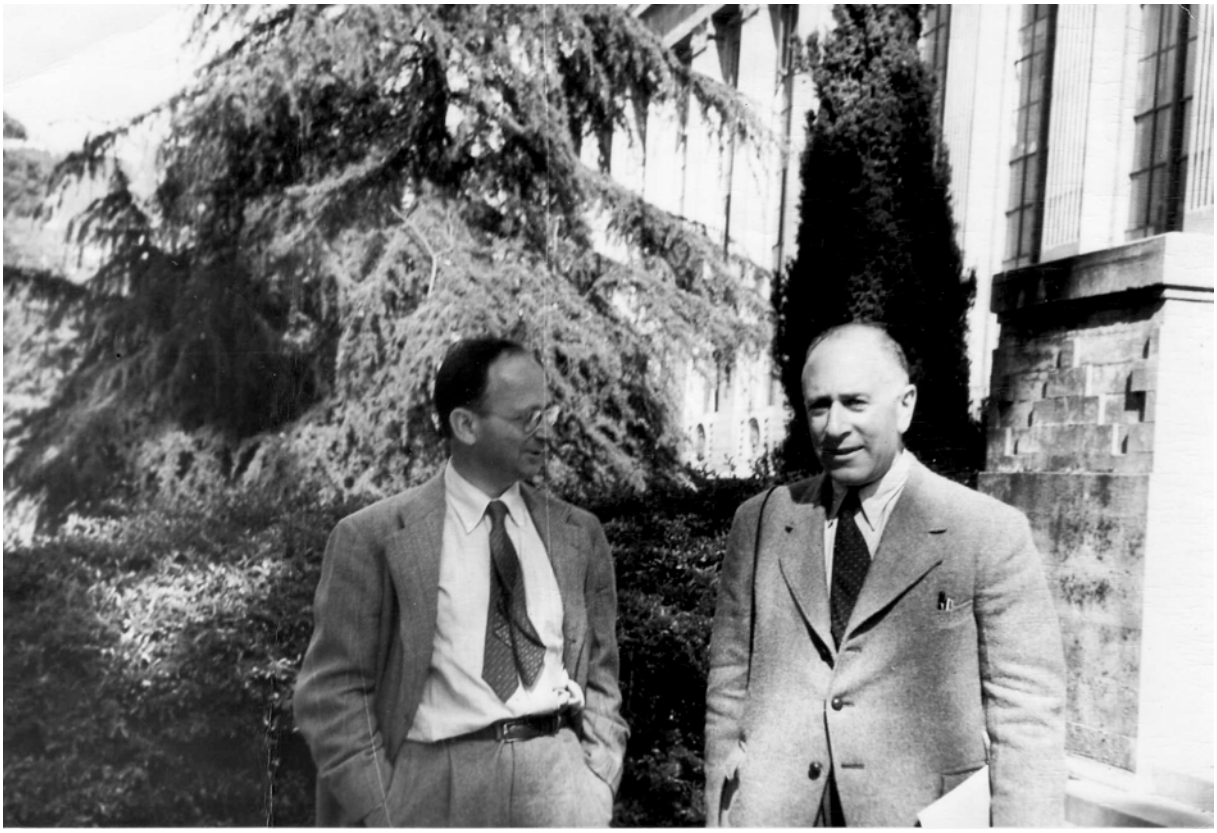

Fig. 3: I.L. Chaikoff and W. E. Griesbach in Berkeley in front of the “Life Science Building” on the Berkeley University Campus, U. S. A. (E). Descriptions about people and localisation by Prof. Dr. Howard A. Bern, Berkeley, U. S. A.

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The biggest help in Dunedin was without doubt Miss June A. Hunter. It is due to her inexhaustible willingness to report on the research work in the institute, the private life and environment of the Griesbachs, that many details of Griesbach's work and life could be reconstructed.

According to the biggest discovery in Dunedin, the un-archived documents of the research department of Purves, Griesbach and Kennedy (ERD), now archived in the Hocken Archives, Dunedin, my thanks belong to Professor Dr. G. and P. Petersen and Mrs. M. Turner. Apart from the people I have already mentioned who helped me in Dunedin, I would like to especially thank Mrs. J. Howard, Dr. J. Presland, Dame Daphne Purves and the families Friedlander, Malcolm and Monroe. Further, the Professors of the University of Otago, Dr. F. Fastier, Dr. E. Herd (†), Dr. J. Hubbard(†), Dr. G. Satchell, Dr. D. Taylor and Dr. W. Trotter. A special thank you belongs to the Dean of the University of Otago, Professor Dr. D. Stewart.

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Back of book:

This thesis aims to describe for the first time the life and work of Walter E. Griesbach and to honour his contribution for medical science. An introductory chapter gives a historic overview of endocrinology until the year of 1940, grading Griesbach's research within the historical context. In the first main half of this thesis, the main taste was to demonstrate the life of a German-Jewish physician during the National Socialist Regime in Germany and the conditions in an immigration country of the Commonwealth. The second main half of this thesis aims to explain, integrate and assess Griesbach's scientific work: the identification of glycolytic intermediate products, the development of the "Congo-Red Method" and his most important scientific achievement, the identification of all cells of the anterior pituitary gland in their connection to different hormones.

Viola A. Schwarz was born in 1969 in Kirchheim/Teck, Germany. From 1988 on study of law at the Universities of Erlangen and Tubingen, and from 1990 on medicine at the University of Tubingen. Internships abroad in Dunedin/New Zealand, London and Zurich. Medical career since 1998 in the University Hospital of Zurich, Department of Gynaecology and Obstetrics. This thesis was honoured by the "Henry E. Siegerist"-Award of 1999 from the "Swiss Society for Medical History". From 2002 till 2004 for two years on a research sabbatical with a Scholarship from the "Swiss National Foundation" doing ovarian cancer research at the Garvan Institute of Medical Research, Cancer Research Program, Sydney, Australia. Married since 2002 to Matthias Heinzelmann, one child. Currently back in Zurich working 50% as a Consultant in Clinics and 50% heading as a group leader the Translational Research Group of the Research Department, Clinic for Gynecology, University Hospital Zurich.