Endemic Cretinism

John Dennison
Charles Oxnard
Peter Obendorf
Editors

Springer

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Authors
John Dennison, M.Sc., B.A.
Department of Anatomy
Otago School of Medical Sciences
Dunedin, New Zealand
john.dennison@stonebow.otago.ac.nz

Peter Obendorf, B.Sc (Hons), Ph.D., M.Litt.
RMIT University
School of Applied Sciences
Melbourne, VIC, Australia
peter.obendorf@rmit.edu.au

Charles Oxnard, MBChB, Ph.D., D.Sc.
University of Western Australia
School of Anatomy and Human Biology
and in the Forensic Science Centre
Crawley, WA, Australia
charles.oxnard@uwa.edu.au

ISBN 978-1-4614-0280-0 e-ISBN 978-1-4614-0281-7
DOI 10.1007/978-1-4614-0281-7
Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2011933836

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Foreword

I am honoured to contribute this update as recognition of the pioneering work of Professors F. De Quervain and C. Wegelin in their classic book on endemic cretinism published in 1936. Their book, which provides a remarkable coverage of the literature on cretinism over hundreds of years, is now available for the first time in English.

We are indebted to John Dennison of Otago University, New Zealand for this expert translation from the original German Text.

I include also reference to the current status of the problem, its scientific understanding and the significant activities which have developed over the past 25 years to control what has been a substantial global scourge. Iodine deficiency is now recognised by the World Health Organization as the most common preventable cause of brain damage in the world today.

The Appendix is based on a longer paper entitled 'Cretinism Revisited' by my colleague Professor Chen Zu Pei (Tianjin Medical University, China) and myself and published in *Best Practice & Research Clinical Endocrinology & Metabolism* 24: (2010) 39–50.

Basil Hetzel A.C., M.D., F.R.A.C.P.
Former Executive Director and then Chairman of the International Council
for Control of Iodine Deficiency Disorders (ICCIDD)
Michell Building
Women's & Children's Hospital
72 King William Road
North Adelaide SA 5006
Australia

Preface

On 26 September 1936 the *British Medical Journal* reported: "The house of J. Springer, Berlin, notable for its scientific publications, issues the seventh volume of a series of monographs on topics of special interest to clinicians and pathologists… This little book is a valuable compendium of the latest views on a difficult subject."

On 3 October 1936 *The Journal of the American Medical Association* wrote: "Professor de Quervain is chief of the surgical clinic at the University of Bern, Switzerland, and received his early training under Professor Kocher. Prof. Carl Wegelin is director of the institute of pathologic anatomy of the University of Bern. Both de Quervain and Wegelin have been intensely interested in the goiter problem, situated as they are in Bern near the center of the endemic goiter belt of Switzerland, where unfortunately a large proportion of the population is affected by a "goiter noxia" which results in cretinism. This monograph summarizes their lifelong study of the problem and presents in an authoritative manner the various clinical types of cretinism, the pathologic anatomy and histology, the pathologic physiology, the pathogenesis and the accepted methods of prophylaxis and treatment."

Those quotations may set the scene for a "nice little historical read". However, in the World Health Organization/UNICEF Report (2007) *Iodine deficiency in Europe: A continuing public health problem*, this work of de Quervain and Wegelin is still cited for its value, among 217 references. In 1993 Steven Boyages and Jean-Pierre Halpern, writing in *Thyroid*, described this work as "their classic monograph", while a two-page 1936 review that was republished online in *The Journal of Pathology and Bacteriology* (2005 DOI/10.1002/path.1700430224/pdf) concluded: "Since cretinism is unknown in the sites of endemic goitre in Britain this monograph should be welcome to British pathologists interested in endocrine disturbances."

All these comments describe a text that has, to our knowledge, never been published in English!

As an anatomist at the University of Otago, Dunedin, New Zealand, and a published translator of similar books, I was contacted and invited to undertake this translation by Dr. Peter Obendorf (School of Applied Sciences, RMIT University, Melbourne, Victoria, Australia), and Prof. Charles Oxnard (School of Anatomy and

Human Biology and Forensic Science Centre, University of Western Australia, Crawley, Western Australia), who point out that there is so little detailed knowledge or numerical data on cretinism available in the English-speaking world.

Professor Basil S. Hetzel, recently-retired WHO Chairman of the International Council for Control of Iodine Deficiency Disorders, suggested that Springer-Verlag, as publisher of the 1936 book, would be the appropriate publisher of "this valuable work", especially given the current re-emergence of iodine deficiency around the world. Basil Hetzel has recently published (end 2009) with Dr. Chen Zu-pei on the resurgence of iodine deficiency in China. Charles Oxnard has this year been invited by the Government agency to participate in an iodine survey of Timor Leste where 26% of school-age children are iodine-deficient (Ministry of Health National Nutrition Strategy, 2004). Australia has now made it mandatory for most bread to contain iodized salt in place of ordinary salt.

The aim of this project, therefore, is to make this much-cited work, "... which remains the most authoritative and comprehensive account of this condition" (*British Medical Bulletin*, 1960) available to English-speaking researchers.

My wife, Ann, spent many long hours correcting, and rechecking my initial draft. I am most grateful for her meaningful discussions.

Professor Oxnard and Dr. Obendorf have joined with me, the translator, to edit this work.

Dunedin, New Zealand Kenneth John Dennison

Contents

Introduction

Monographs on cretinism have appeared from time to time over the last 150 years. These sometimes included a discussion of endemic goitre; at other times they gave a presentation on hypothyroid conditions, congenital myxoedema, and acquired myxoedema. In reviewing these studies, we become aware that quite varied reflections have awakened interest in the characteristic clinical picture of cretinous degeneration. At the forefront, for the whole of the last century, were the humanitarian and economic aspects of the problem. People felt the urgency for a remedy, and, in a systematic manner, sought out the causes of this assault on public health. Anthropology, epidemiology, and pathological anatomy were all taken into consideration to solve the dual puzzle of the origin of goitre and the relationship between cretinism and goitre. There was a fair share of natural philosophical speculation alongside detailed scientific observation. However, from a merely cursory glance, the importance of an investigation into cretinism as a scientific problem gained full recognition only when the physiology of the thyroid gland became understood. In anticipation of this, in 1830 Troxler, in Berne, expressed the idea that the function of the thyroid gland could be clarified only by studying cretinism. However, another 50 years passed before this idea took shape through the investigations of Horsley, Kocher, Bruns, and others. Nevertheless, it should not be thought that the purely human and economic side of the question had receded into the background. Scientific interest supervened, raising cretinism from a series of disease processes of purely local interest to one of general physiological enquiry. We have dedicated several years of particular interest in this aspect of the problem, continuing the fundamental research of our teachers and predecessors in office, Theodor Kocher and Theodor Langhans, which would likewise guide our further analyses. We have also been able to rely on the constant support of physiologists like Asher and Abelin. Our study was further assisted by the availability of a large observational sample. The almshouses of Berne canton, especially those of Riggisberg, Frienisberg, Utzigen, Worben, and Langnau, which through the courtesy of their medical and administrative leadership had always been forthcoming, care for some several hundred cretins of every type, from puberty right through to old age. We were always able to observe any typical case or any specially noteworthy case from among these people, in a clinical setting. We found younger cretins, from school-age onward, in institutions for the feeble-minded and for deaf-mutes, and we were also able to observe them in

the clinic when necessary. We thus had access to a sample that probably had never been so localised. One of us acquired extremely grateful, devoted patients from among the numerous cretins who became free from severe goitre in the clinic, and was given ample opportunity of examining their physical and mental behaviour. The only regret is that up till now it has not been possible to undertake an autopsy of those cretins who had died in institutions. Up until now the administration has not granted permission for this. Accordingly our anatomical material is relatively small, being restricted to those individuals who had died in the *Inselspital* [the Berne University Hospital] and in asylums for the insane.

We hesitated to undertake the present exposition, already long-overdue, after Eggenberger (1927) in the *Handbuch der inneren Sekretion*, and Gamper and Scharfetter (1932) in the *Handbuch der Geisteskrankheiten* had compiled the current wisdom and their own observations into first-class presentations. However, once we had resolved, at the behest of the publisher, to set down these pages, it was not done with the intention of reaffirming what has been known for a long time, but from a perceived, over-arching need to bring to light the problem of cretinism, from our own study and observations, as being not only an epidemiological problem but also a pathological-anatomical and pathological-physiological problem. It is in the nature of things that we will come into constant contact with the pathology and the clinical aspect of endemic goitre. Cretinism and goitre behave like two circles with a common centre – the inner circle has dropped out to a greater or lesser extent depending on the demarcation of cretinism. A sharp boundary occurs just as rarely as in most other natural processes, and the dividing line between the man who appears normal apart from his goitre, and the cretinous goitre-sufferer, is, to some extent, hidden by subjective experiences. Nevertheless it cannot be our mission to bring forth a definitive presentation on the problem of endemic goitre. We must simply be satisfied with pointing out the tip of the iceberg, whose surfaces become blurred whenever we are able to introduce a comparison from a country where goitre is at a low level.

Chapter 1
Etymology of the Word 'Cretin'

Until quite recently a kind of uncertainty has predominated as to the origin and original meaning of the word 'cretin'. It is acknowledged that it emerged only in the eighteenth century, and was mentioned for the first time in the French encyclopaedia of 1754. The word belongs among the dialects of south-eastern France.

By far the most likely derivation is from 'Christianus', from which the word 'Cretin' has evolved via 'Crestin'. Salvioni states that 50 years earlier at Lake Maggiore the word 'Christian' was used to designate a cretin. The relationship with the word *Chrétien* is therefore at hand. The change in meaning has perhaps been brought about in such a way that the cretin was, to begin with, labelled as *pauvre chrétien* out of sympathy. According to another explanation, said to have come from Fodéré, the cretin, because of his limited intellect and harmlessness, might have appeared as *bon chrétien*, which would agree with the fact that in certain areas of the French Alps the cretins were also called *beats* or *innocents*. However, as Virchow has already pointed out, such references cannot be found in the original text of Fodéré's work.

Tracing the word 'cretin' back to 'cretira' (*cretura*) is highly unlikely. Ackermann states that around Ilanz in the canton of Graubünden the designation *cretira*, which belongs in the Rhæto-Romanic language, is used for 'wretched creature, rascal' and that is how the expression 'cretin' arose.

The derivation from *creta* (chalk) is equally unsatisfactory. It is based on Rösch's comment that young cretins are said to have a chalky-white appearance, which is certainly not always accurate and has already been refuted by the brown skin tone of many cretins having led to their being called 'marrons'. Also, as my colleague Prof. Jaberg, Professor of Romance Philology in Berne, has assured me, the word 'cretin' could not have been derived etymologically from *creta*.

Finally, Finkbeiner believes that he has found the explanation in the Swiss dialect word *Krätti*, which means 'pannier', and is used for both the carrier of the basket and for hunch-backed and misshapen. 'Cretin' might then be nothing other than the French dialect form of the Swiss-German *Krätti*. This deduction however appears totally erroneous since cretins due to their physical weakness usually do not carry

J. Dennison et al., *Endemic Cretinism*,
DOI 10.1007/978-1-4614-0281-7_1, © Springer Science+Business Media, LLC 2011

panniers, nor do they suffer kyphosis, nor can it be assumed that the Swiss-German dialectic word would have penetrated as far as Piemont and Savoie.[1]

It is certain that the term ‘cretin’, which has found entry today not only into the medical nomenclature but also into the common language of every country, had been limited originally to quite a small region, and was used only in Savoie, the Aosta Valley, and the French portion of Valais. Other countries had their own names – actually, in the German language a whole heap of labels has been coined for cretins according to local region, for example *Fexe* in Salzburg, *Trottel* in Steiermark, *Gauche* in German Wallis. Today all these names have only historical and folkloristic value. Therefore we refer here to the older works of Rösch and Iphofen, which introduce the expressions occurring in the various dialects. They give a looking-glass picture of cretinism in the whole richness of its shades and nuances. It should also be mentioned that in certain areas of France it was customary to use the word *Cagots*.

[1]I express my deepest gratitude to Professor Jaberg, who most willingly advised me on these etymological questions.

Chapter 2
Definition

More far-reaching than the label question is the problem of *defining* cretinism. Setting aside all theories for the time being, when we simply ask ourselves which physical and intellectual defects have been designated by the name 'Cretinism' over the course of time, we come to the conclusion that it is a localised physical and intellectual limitation of development and an inferiority that is distinguished in popular perception from forms of feeble-mindedness and dementia common to all countries and all peoples. A second statement from time immemorial is that cretinism is found only where endemic goitre also occurs to a pronounced degree. We must acknowledge these two 'historical' attributes if we do not want to lose ourselves in the infinity of universal intellectual and physical insufficiency – the so-called international imbecility and nonsense.

Research, as we shall see, has so far indicated the justification for such a demarcation, both in terms of localization and in relationship with endemic goitre. Comparative geographical-pathological investigation reveals more and more that there is actually a condition of physical and intellectual retardation of development that is not influenced by 'race', and occurs in all parts of the world where endemic goitre is deeply entrenched, i.e., the centre of endemic zones, and is bound to these zones. We combined these statements in the definition of cretinism that we proposed in 1923.

> Cretinism is an endemic complex of somatic and mental disorders occurring in centres of severe, endemic goitre, appearing mainly on the skeleton, skin, and nervous system, in which retardation of developmental processes and vital functions play a principal role, and which cannot be traced back to either some other congenital or acquired cerebral illness (encephalitis etc.), or to a well-defined skeletal disease that is independent of endemic goitre, such as rachitis, chondrodystrophy etc.

When we utter this sentence we must immediately identify two groups of cases that have often caused confusion in the literature by obscuring and preventing a clear recognition of the picture of cretinism.

The first of these, occurring in every country independently of any endemic goitre, are cases of teratological errors of the thyroid gland – *thyroaplasia*. This is purely a malformation, with the thyroid gland absent or limited to a rudiment in the tongue region (Thomas' 'dystopic hypoplasia'), while the parathyroid glands are

J. Dennison et al., *Endemic Cretinism*,
DOI 10.1007/978-1-4614-0281-7_2, © Springer Science+Business Media, LLC 2011

still present. This malformation, which can present widely variable clinical degrees of hypothyroidism depending on the level of function of the tongue–thyroid gland rudiment, has nothing to do with endemic thyropathy and, as Pineles emphasised back in 1902, it causes only confusion when Gull's original diagnosis of 'sporadic cretinism' continues to be used for such cases. Whether in individual cases thyroid gland failure can be traced back to an intrauterine inflammatory lesion as Siegert surmises, rather than a teratological process, must be left unresolved. As yet, there is no anatomical evidence for this. On the other hand, the distinction between teratological-, congenital-, and early-childhood-acquired myxœdema among the following group is blurred in that the congenital thyroaplasia is often incomplete so that its clinical *sequelae* do not begin to be expressed immediately after birth but only after infancy.

The second world-wide group of thyroid gland disorders causing confusion is *acquired, infantile myxœdema*. This is based on a lesion of the thyroid gland (acute infectious disease), probably almost always inflammatory, acquired postnatally and leading to a cretin-like appearance while not being aetiologically related to endemic cretinism. These cases too would earn the term 'sporadic cretinism'. Their only common feature with genuine cretinism is thyroid malignancy, but this is not the cause. In 1923 Wieland did splendid work on this topic both historically and clinically, in particular pointing out the importance of radiology for all thyrogenic disorders. Progress in defining the *underlying clinical picture* can be brought about only through careful pathological investigation of cases of illness accurately observed in a clinical setting. We undertook this monitoring during therapeutic implantations in several cases that could be clarified only in this manner.[1]

In addition to the thyroid disorders not attributable to endemic cretinism, in the endemic arena, just as anywhere else, we find the most varied forms of congenital and acquired primary mental deficiency. We also find growth disorders and systemic diseases of the skeleton which have nothing to do with the thyroid gland, such as hereditary dwarfism, chondrodystrophy, osteogenesis imperfecta, etc. All of these pathologies have been preferentially ascribed to the thyroid gland by physicians inexperienced in this field, especially when the patient is somewhat goitrous. Given the current state of our knowledge, to throw every chance-event in the endemic arena into a big pot together with endemic cretinism is no longer justifiable as a means of circumventing certain diagnostic difficulties and easing the attainment of a solution to pathogenetic problems. We will make an advancement in our knowledge of individual forms of physical and mental developmental errors only when we try to trace them back to their *origins* and clearly differentiate the various possible causes. By using blurred concepts we drop back a whole century. The discussion on pathogenesis will give us the opportunity of returning to this argument.

A particular difficulty in the definition of cretinism is the *multi-faceted nature of the clinical picture*, both from a somatic and a psychological point of view.

[1] It is noted here that the case introduced in Wydler's series as No.111 is not to be regarded as a full cretin, but as a case of thyroaplasia. In error, it was not excluded.

Finally, the dissociation of cretinism from the normal state is made more difficult by our having to deal with *fleeting transitions*. We find certain psychological *stigmata* of cretinism suggested also among individuals who earn their living well or poorly, keep up their civil duties and perhaps even serve in a minor post. You could even say that endemic thyropathy puts its stamp on the entire population of certain regions. Extensive personal observation of a great amount of material is obligatory in order to review all these demarcation problems. This cannot be substituted by studying books. It alone gives an overview and critique, and offers a safeguard against hasty conclusions.

Maffei, who devoted his 1813 dissertation to cretinism, stated in 1844 when he was working again in that field that the subject became steadily clearer and more understandable to him during the first 15 years, but in the subsequent years it seemed to diminish in clarity once more because, with greater experience, that which had seemed positive and correct steadily collapsed in on itself. He is not the only one to have experienced this.

Chapter 3
Historical

In spite of cretinism's very probably having been indigenous to certain countries over many centuries, we have had scientific information of its occurrence only for a relatively short time. That it is not mentioned anywhere by the physicians of ancient times is all the more remarkable, since even non-medical writers of Roman times (Pliny, Vitruvius, Juvenal, Ulpian) have drawn attention to goitre endemic to the Alps. For the first definite account of the occurrence of cretinism we are indebted to Paracelsus (1493–1531) who, as an outstanding observer, recognised immediately the connection between goitre and cretinism. I shall quote several examples demonstrating this in all its clarity (cited in part from Damerow):

> "The lunatics that the animal spirits have given birth to, are ill-bred through weakness; belong among reasonable cattle; probably carry a misgrowth, an outgrowth such as goitre and the like on their body, and even though this is not *proprium stultorum* [the stuff of fools] but is something else, this applies most often." According to Paracelsus the origin lies in that "not only is reason shredded, but the body also."

Further accounts came from Felix Platter (d. 1614), working in Basel University and describing the cretins in his homeland of Wallis; and the historian Josias Simmler (1574) in Zurich. In addition, the Dutch physician Peter Foreest (d. 1597) observed many cretins in Veltlin. Then almost total silence fell until the second half of the eighteenth century, when the natural scientist H. de Saussure of Geneva studied the problem of cretinism during his travels in the Alps and connected it with sea level and air quality. Surprisingly, cretinism is mentioned only very briefly by Albrecht von Haller who, as director of the Bex saltworks in the lower Rhone Valley (1758–1764), probably had ample opportunity for personal research. He describes cretins as 'only half humans', who are totally unfit for all business of human life, have enormous goitres and often even die because the excrement in the colon has grown to an unbelievable size. Haller is of the opinion that the heat of the sun's rays has perhaps contributed to influencing the brains of cretins to their detriment.

Then from 1780 lively interest was awakened in the scientific investigation of cretinism, with not only travellers reporting its extent and its presumed causes, but attempts being made also on the medical front to penetrate more deeply into its essence. In 1788, for the first time, Malacarne in Turin included a description of

J. Dennison et al., *Endemic Cretinism*,
DOI 10.1007/978-1-4614-0281-7_3, © Springer Science+Business Media, LLC 2011

three cretin skulls in his letters to Peter Frank in Pavia. Two skulls had undergone a detailed examination in Pavia by Ackermann. As a result, that investigator from Mainz sought out the cretins in their homes, and in 1790 set down his impressions in a little book, *Über die Kretinen, eine besondere Menschenabart in den Alpen*. According to the book, cretinism was nothing other than the highest grade of rickets.

Then came a flood of literary preoccupation with cretinism, through the work of Fodéré that appeared for the first time in 1792 in Turin and later in Paris, with a German translation published in Berlin in 1796. It referred especially to the situation in Savoie and in the Aosta Valley. The book is still worth reading today because of its abundance of outstanding observations and opinions. In his anatomical investigations culminating with the assumption of an extraordinary hardness of the brain and spinal cord, Fodéré admittedly travelled down a wrong path. This earned him criticism by Joseph and Carl Wenzel in Vienna, who in 1802 gave a good description of the cranial base, whose alteration gave rise to disorders in brain development. They rejected rickets as the cause of cretinism.

Noted in passing, the cretinous degeneration of the Wallesian population evidently made such a strong impression on Napoleon I, during his military campaigns that took him through Wallis into Italy, that he charged his Prefects with producing an official, topographical-statistical inquiry into cretinism in the Simplon Département (*cit.* Köstl).

In the first half of the nineteenth century we encounter an astonishingly copious literature on cretinism. A detailed monograph by Iphofen (1817) followed the works of Troxler, Demme, Thieme, Stahl, plus the extensive report on cretinism by the *Sardinian Commission*, that had been ordered by King Karl Albert. At the instigation of Troxler and Guggenbühl the Swiss Natural Scientific Society engaged themselves with the question of cretinism firstly in 1830 and then on repeated occasions. In 1834 Autenrieth raised the same question with the Assembly of German Natural Scientists and Physicians. Prime interest was in the geographical extent and the presumed causes of this evil, sought mainly in climatological-atmospheric influences. Associated with this was the question as to the curability of cretinism that was put forward by Guggenbühl and answered by his opening of the first psychiatric hospital for young cretins in 1841 on the Abendberg at Interlaken. His undertaking initially met with approval and gained moral support throughout Europe and America. However it did not achieve the success hoped for, and became a miserable failure after about 20 years. From the Noric Alps and Württemberg, Maffei and Rösch (1844) published studies that belonged among the best written at that time.

The anatomical investigation of cretinism received a massive boost through the outstanding work of B. Nièpce who in 1851 produced detailed reports of several autopsies, and through the important work of Virchow (1856–62) in following up the Lower Franconian endemia from Wurzburg. He devoted his attention particularly to the physical proportions of the cretin skull, and came to the conclusion that the skull deformities often had an autonomous character and, for their part, determined the development of the brain. He was responsible for the doctrine of premature synostosis of cranial bones, to which he ascribed a major role in the origin of

cretinism. As the pathogen of goitre and cretinism, Virchow proposed a miasma whose lesser effect presented goitre and the greater effect: cretinism.

At the instigation of the Swiss Natural Scientific Society the epidemiology of cretinism in Switzerland underwent a detailed exposition by Meyer-Ahrens (1854). In France Nièpce (1851), Fabre (1857), Morel (1863), St Lager (1867) and Baillarger (1873) studied not only the geographical extent of goitre and cretinism but also the aetiology in great detail, admittedly without coming to any definite conclusions on the latter. The internal connection between goitre and cretinism throughout the world is accentuated in these works. H. Bircher (1883) and Allara (1892) dealt with endemic cretinism and the *sequelae* of total thyroidectomy in a similar manner, but with the addition of clinical pathology. Bircher traced mainly the Swiss epidemiology, Allara the Italian.

The work of Th. Kocher (1892) brought a completely new point of view of the pathogenesis of cretinism. Starting from the major discovery of *Cachexia thyreopriva*, he drew a parallel between cretinism and the outcome of total thyroidectomy, explaining the former as precocious suppression or severe disturbance of thyroid function. For the first time, a severe, endemically occurring disorder in the development of the entire organism was traced back to an endocrine gland. From this point on, in the eyes of many researchers, endemic cretinism was nothing other than an internal secretory disorder – hypothyroidism.

In his first publication in 1883 Kocher attempted to explain the clinical picture of *Cachexia strumipriva* through anaemia, deducing the latter from an atrophy of the trachea as a result of vascular repression. The first reference to the 'breakdown in physiological function of the thyroid gland' as a cause of cachexia was by Rud. Grundler in 1885. The author came to this conclusion during a study supervised by P. Bruns, when he observed three cases of total extirpation in Brun's clinic, and witnessed the trials by Schiff and Wagner. He writes, 'Analysis of all the symptoms makes it likely that with *Cachexia strumipriva* we are dealing with a disorder of the central nervous system that can happen only when the presumed activity of the thyroid gland, viz. its metabolic involvement, is diminished'. Cretinism was automatically included in the problem and threw the question of the nature of thyroid function into the centre of the debate. The exchange of ideas between Kocher and Horsley, and the research by Hofmeister, Ewald, Leichtenstern and Murray brought progress. Around 1890–1893 the proponents and *Assistents* of Kocher and Langhans considered the basic question as settled – cretinism in its various stages is a deficit in endocrine function.

Subsequently, Kocher's point of view found partial agreement, and was supported in both the anatomical and clinical aspects by new investigations (Langhans, Beyon, Weygandt, Wagner von Jauregg, Cerletti, de Quervain, Wydler and Eggenberger). In some quarters it also came up against quite strong resistance (H. and E. Bircher, Dieterle, Scholz and, in part, Ewald), with changes in the cretin's body being perceived as a direct consequence of noxious goitre. Admittedly, in recent times opposition to Kocher's opinion has steadily quietened down.

Not completely however—in 1923 Finkbeiner attempted to resolve the problem of endemic cretinism from an anthropological point of view by perceiving cretins as