

Theodor Escherich: The First Pediatric Infectious Diseases Physician?

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The career of Theodor Escherich (1857–1911) qualifies him as the first pediatric infectious diseases physician. His landmark bacteriologic studies identified the common colon bacillus (now known as *Escherichia coli*), and he was very committed to pediatrics, serving as chairman of several prominent departments of pediatrics, including the Department of Pediatrics at the University of Vienna and St. Anna's Children's Hospital in Vienna, Austria, arguably Europe's most prestigious pediatric position.

Until at least the 20th Century, the history of pediatric infectious diseases closely paralleled the history of its parent specialty, pediatrics, because infectious disorders comprised the major causes of childhood morbidity and mortality, as they do in the developing world today [1]. Thus, many early descriptions of childhood illnesses by the ancient Greeks and Romans and by the Arabic physicians of the 10th and 11th centuries were of tuberculosis, acute exanthems, ear infections, diphtheria, and helminthic infestations [1–3].

Therefore, it may be somewhat arbitrary to identify a specific individual to be considered to be the first bona fide pediatric infectious diseases physician. In this article, we define applicable criteria and argue that such an individual can be identified—the Austrian pediatrician Theodor Escherich.

Criteria. We propose that an early pediatric infectious diseases physician should have been specifically trained in and devoted to pediatrics and, therefore, a physician whose clinical

practice was essentially limited to the health and illnesses of children. In addition, specific training in a scientific discipline, such as microbiology, bacteriology, immunology, infectious diseases, and/or epidemiology, is a reasonable criterion. Additional criteria should probably include an enduring commitment to the training of pediatricians with interest in infectious diseases of children and significant scientific contributions that improved the understanding, therapy, and/or prevention of infectious diseases of childhood.

Theodor Escherich (1857–1911). Theodor Escherich (figure 1) was born on 29 November 1857 in Ansbach, Germany, to Dr. Ferdinand Escherich (1810–1880), the district medical officer of health and a noted medical statistician, and his third wife, Maria Sophie Frieder, daughter of a Bavarian army colonel. Dr. F. Escherich was concerned about high neonatal mortality rates, as well as health care for the poor, about which Theodor also became concerned. Theodor's mother died when he was 5 years of age, and the family moved to Würzburg, Germany. It is said that Theodor was a prankster and, thus, was sent to the Jesuit school “Stella Matutina” in Feldkirch, Austria [4]. After completing his basic education and a 6-month

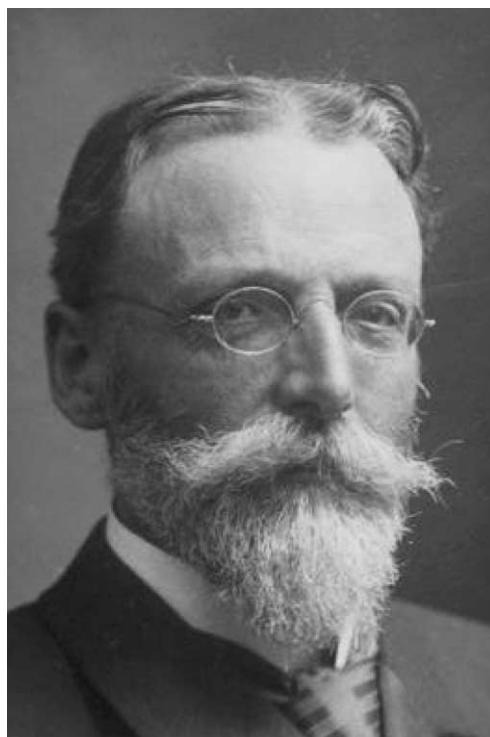


Figure 1. Theodor Escherich (1857–1911)

Received 13 March 2007; accepted 7 July 2007; electronically published 10 September 2007.

Presented in part: The Historical Perspectives Poster Symposium, Pediatric Academic Societies, San Francisco, California, May 2006 (abstract 2195.5).

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Clinical Infectious Diseases 2007;45:1025–9

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1058-4838/2007/4508-0015\$15.00

DOI: 10.1086/521946

military service in Strasbourg, Austria, Escherich began his medical studies in Würzburg in 1876 and then (as was the German custom) continued his studies in several medical centers, including in Strasbourg, Austria, and Berlin, Munich, and Kiel, Germany. In 1881, Escherich qualified to practice medicine with top grades. After 6 months in the military at the garrison hospital in Munich-Oberwiesenfeld, Germany, Escherich became first assistant to Professor Karl C. A. J. Gerhardt (1833–1902) in the Department of Internal Medicine at Julius hospital in Würzburg in July 1882. Although he was trained as an internist, Gerhardt was very interested in pediatric medicine, serving as editor of the first German *Handbook of Pediatrics*, a 16-volume work published during the period 1877–1893. Under Gerhardt's influence, Escherich developed a great interest in pediatrics and, in October 1882, wrote a doctoral thesis, "Marantic Thrombosinosis in Cholera Infantum," under Gerhardt's supervision; this was Escherich's first publication. In 1883, Escherich published 6 articles on clinical (non-pediatric) topics. During October–November 1884, Gerhardt facilitated Escherich's interest in both pediatrics and the emerging science of bacteriology by selecting him to travel for 2 weeks as a scientific assistant to study the large cholera epidemic in Naples, Italy, with Rudolf Emmerich from Munich. Apparently, Escherich quickly became adept with bacteriologic techniques and readily observed *Vibrio cholerae* in fecal samples from affected individuals—more readily, in fact, than the more senior Emmerich. Escherich gave a presentation on cholera in Naples on 3 December 1884 in Munich, and the report was published the same year [5].

Because pediatrics was not yet fully developed in Germany, in 1884, Escherich studied for a semester in Vienna, Austria, at the well-respected St. Anna Children's Hospital and attended the popular lectures of Hermann von Widerhofer (1832–1901). von Widerhofer was the first Chair of Pediatrics at the University of Vienna and a highly renowned pediatrician who was considered to be the first Professor "Ordinarius" of the Diseases of Childhood. St. Anna Children's Hospital, founded in 1837, was the third oldest children's hospital, behind the hospitals in Paris, France, and St. Petersburg, Russia. Escherich's experiences in Vienna convinced him to devote his career to pediatric medicine, and he also began bacteriologic studies of the flora of mother's milk and of intestinal microflora at the Vienna Pathological Institute, where Heinrich von Bamberger was director. After the period he spent in Vienna, Escherich attended lectures by Jean Charcot (1825–1893) at the Salpêtrière in Paris.

Munich, Germany (1884–1890). After moving to Munich in August 1884 to obtain his Habilitation (a postdoctoral qualification required to lecture at a German university), Escherich focused his research on 3 related issues: defining the normal bacterial flora of the infant intestinal tract and its changes immediately after birth, assessing the role of bacteria in the phys-

iology of digestion, and characterizing the relation of these findings to pathologic conditions in infants.

In Munich, Escherich had access to Max von Pettenkofer's (1818–1901) hygienic institute, Otto von Bollinger's (1843–1909) bacteriology laboratory, Karl von Voit's (1831–1908) physiological institute, and Franz von Soxhlet's (1848–1926) dairy facilities. Escherich learned the very new basic techniques of pure culture and bacterial characterization from Wilhelm Frobenius, a physician who had learned bacteriology from Robert Koch during 3 short visits to Koch's laboratory in Berlin. Frobenius made no other contributions to science, and in 1888, he became a medical missionary in the East Indies and German East Asian colonies [6]. Escherich knew of only 1 study involving microbiologic examination of infant fecal samples (by Julius Uffelmann in 1881 [7]) and very few such studies involving attempts to cultivate bacteria from fecal samples from adults using Koch's new methods. Escherich demonstrated that meconium was sterile and that bacterial intestinal colonization is attributable to the infant's environment (including milk) within 3–24 h after birth, with a variety of bacteria present by 24 h (although not as diverse as in adults). Although Uffelmann observed only 2 different bacteria in infant stool samples microscopically, Escherich isolated 19 different bacteria, including bacilli and cocci. These included campylobacter and enterococci, as well as, probably, *Bacillus subtilis* and pseudomonas [6, 8–10]. Escherich used Christian Gram's new staining technique and was among several investigators, including Hans Buchner, who developed anaerobic culture methods. In these studies (which were performed over 15 months), Escherich described in detail *Bacterium coli commune* (the common colon bacillus now known as *Escherichia coli*) and *Bacterium lactis aërogenes* (now known as *Klebsiella pneumoniae*). He demonstrated their fermentation characteristics and the nature of the gas produced during fermentation, and he showed that, under anaerobic conditions, growth was totally dependent on carbohydrate fermentation. Breaking with dogma, Escherich concluded that any role of the intestinal flora in nutrition was minor at best.

On 17 December 1884, the 27-year-old Escherich lectured in Munich to the Society for Morphology and Physiology about his bacteriologic methods [11], and on 14 July 1885, he presented his findings on *B. coli commune* to the same society in Munich. In 1886, Escherich published his 177-page postdoctoral thesis as a monograph entitled, "The Intestinal Bacteria of the Infant and Their Relation to the Physiology of Digestion" [12]. He acknowledged his clinical training under Karl Gerhardt by noting on the title page that he was former assistant doctor at the Medical Clinic in Würzburg. This work was also published in *Fortschritte der Medizin* [13] and was reprinted in English in *Reviews of Infectious Diseases* in 1988 and 1989 [14,

15]. These studies clearly established Escherich as the foremost expert on bacteriology in pediatrics.

By March 1886, Escherich resumed his clinical work and became a clinical assistant in Munich at the Children's Polyclinic of the Reisingerianum and the Hauner Children's Hospital under Heinrich von Ranke (1830–1909). The following year, he became Lecturer in Pediatrics at the Ludwig-Maximilian University in Munich. Clearly, Escherich was able to balance his scientific studies and his clinical work. Ballabriga [16] pointed out that the bacterial era of the study of nutritional disturbances was initiated by Escherich, who recognized that the anatomic doctrine was insufficient to explain many digestive tract disturbances.

In Munich, Escherich continued studies of infant nutrition, identified the hazard of the high sodium content of cow's milk, emphasized the value of breast-feeding, and developed the volumetric system of infant feeding that involved the weighing of infants before and after nursing.

Graz, Austria (1890–1902). Escherich's most prominent work on infant fecal flora was performed before his 30th birthday. He continued his work in Munich until 1890, and at 33 years of age, he was selected by the Austrian Ministry of Education to succeed Rudolf von Jaksch (1855–1947) as Professor Extraordinaire (nontenured Professor) of Pediatrics and Director of the St. Anna Children's Hospital founded in 1843 in Graz. His years in Graz have been described as his happiest. In 1892, he married Margarete von Pfaundler, daughter of a renowned physicist, and their children Leo and Charlotte-Sonja were born in 1893 and 1895, respectively. Escherich's student and brother-in-law Meinhard von Pfaundler later became Chair of Pediatrics in Graz and, then, Professor of Children's Diseases and Director of the Children's Clinic at the University of Munich. He coedited a multivolume text, *Handbuch der Kinderheilkunde* (1906) [17]. In 1894, Escherich was appointed Professor (Chair) and Examiner at Graz after he declined the professorship in Leipzig, Germany. In this role, Escherich demonstrated remarkable organizational and administrative ability; the Children's Hospital was renovated and modernized, incubator rooms were created, and laboratories and a lecture theater were built—changes that led to massive increases in inpatients and outpatients [4].

Escherich was also involved in several important research activities during this time, including investigations of the etiology and pathogenesis of diphtheria. By 1893, Escherich and Rudolf Klemensiewicz had demonstrated the presence of diphtheria antitoxin in serum samples from children convalescing from diphtheria. Despite considerable opposition, in 1894, Escherich helped to establish the role of Emil von Behring's diphtheria antitoxin for the treatment of children with diphtheria, and in 1895, he wrote a book on diphtheria and serum therapy. In addition, Escherich described the clinical signs of idiopathic

infantile tetany (in 1890), including what has been termed Escherich's reflex. This is pouting of the lips after stimulating the labial mucosa by tapping the lips—often called the snout reflex [18, 19]. Escherich concluded that hypoparathyroidism played a role in tetany, and in 1909, he wrote a monograph on the subject. Continuing his interest in intestinal bacteria, Escherich found that coliforms were associated with acute, contagious intestinal infections in infants, and he described "colicystitis," noting the frequency of isolation of *B. coli commune* from urine samples from symptomatic young girls, thus recognizing the significance of urinary tract infections. He also studied the cutaneous reaction to tuberculin. Shortly after Wilhelm Roentgen's discovery of X-rays, Escherich obtained funds to purchase an X-ray apparatus.

Escherich's fame as an outstanding teacher, clinician, and researcher attracted several young, brilliant students to pediatrics. Both Clemens von Pirquet (1874–1929), who studied serum sickness and founded and named the field of allergy, and Bela Schick (1877–1967), who developed the Schick test to assess immunity to diphtheria, made outstanding contributions to pediatrics. Both von Pirquet and Schick came to America, the former as Chair of Pediatrics at Johns Hopkins Hospital in Baltimore, Maryland, and the latter as Professor of Pediatrics at Mt. Sinai Medical Center in New York.

Vienna, Austria (1902–1911). In 1902, Escherich's brilliant success in leading the pediatric department at Graz to prominence led him to be nominated unanimously as Chair of Pediatrics at the University of Vienna and Director of the St. Anna Children's Hospital in Vienna, succeeding Hermann von Widerhofer. This was the institution where Escherich studied 20 years earlier, and the position was one of the most prestigious in Europe. In these new roles, Escherich again demonstrated outstanding leadership and administrative abilities, modernizing the hospital and clinics, building laboratories, establishing a school for training nurses in infant care and to provide nursing care for children with tuberculosis, founding an infant welfare society (*Säuglingsschutz*), cofounding the Austrian Society for Children's Research, establishing the Association of Pediatricians in Vienna, and organizing a pediatric advisory service for the obstetrical clinics of Vienna. Escherich pioneered the use of X-rays as a diagnostic tool in children. He was a master clinician and teacher; he championed the importance of prevention in pediatrics and played an active, supportive role in the research of his pupils and faculty, including both von Pirquet and Schick, who moved with him from Graz. Another well-known student was Ernst Moro (1874–1951), who described the neonatal reflex, studied cutaneous tuberculin reactions, and discovered "bacillus acidophilus." Escherich's academic interests in Vienna included scarlet fever, tuberculosis, dysentery, and allergy, and he remained the leading pediatric bacteriologist. In 1904, Escherich was the only European pe-

diatrician invited to address the International Congress of Arts and Sciences (19–25 September) at the St. Louis World's Fair; his presentation was entitled "The Foundations and Aims of Modern Pediatrics" [20]. In 1906, Escherich was named Court Counselor (Hofrat) by Emperor Franz Joseph, and he and his wife were invited to dinner at court several times. He crusaded to increase awareness of the unacceptably high infant mortality rate in Vienna, and in 1908 (Emperor Franz Joseph's 60th jubilee year), he again drew attention to this issue. Escherich's efforts led to the construction of the Imperial Institute for Maternal and Infant Care. He was far ahead of his time in his interest in the social welfare of children, and he was highly successful in persuading many socialites to support his important endeavors.

Just a few days before the opening of the new Children's Hospital in Vienna that he had helped to design, Theodor Escherich developed a headache and began to speak in several languages during a visit to the wards; he died the next day (15 February 1911) of an apparent cerebrovascular accident at 53 years of age [21]. The Boston Medical and Surgical Journal obituary of Theodor Escherich included the following:

He was a contributor to numerous medical periodicals, a member of many learned societies, and was known as a pediatric consultant throughout Europe. His professional reputation was international. His energy for work was tremendous, and his disposition strenuous and masterful. He is described as impulsive, uncommonly strict, strong-willed, faithful, severe with himself but kindly towards others. That the children, his patients, loved him, is evidence that he loved them and, therefore, had a good heart. His career is an admirable example of the life of the German university physician, scientist, and professor [22, pp. 474–5].

He had published 3 books (*The Bacteria of the Intestines of the Infant*, *Diphtheria and Serotherapeutics*, and *Tetany*) and ~160 articles. He was the most renowned pediatric pioneer of his era and the preeminent pediatric bacteriologist.

In 1919, Castellani and Chalmers proposed the designation *Escherichia coli* [23]. This name was not officially sanctioned as the name of the common colon bacillus discovered by Escherich until 1958 [24].

Another possible candidate for the first pediatric infectious diseases physician. Many early pediatricians demonstrated their interest in infectious diseases, because they comprised the most prevalent and important diseases of children. It is reasonable to consider whether any of these pediatricians had credentials to challenge our proposal that Escherich was the first bona fide pediatric infectious diseases physician. The fact that the beginning of Escherich's career occurred at the inception of the science of bacteriology and his acknowledgement as the premier bacteriologist among pediatricians of his period provide him with a nearly unique set of qualifications.

Another reasonable candidate is Jacques-Joseph Grancher (1843–1907), who is considered one of the founders (with Antoine Bernard-Jean Marfan) of modern French pediatrics (figure 2). Grancher studied medicine in Paris and was well known for his dissertation on the unitarian theory of tuberculosis (1873). After studying histology, he was named Director of the Laboratory of Pathological Anatomy and joined the staff at l'Hôpital Necker and l'Hôpital des Enfants Malades in Paris. Grancher wrote extensively about pulmonary tuberculosis (1872–1890) and received the Lacaze Prize of the French Academy of Medicine in 1880 for that work. From 1881–1886, Arnold Netter and Grancher introduced a method to obtain blood samples aseptically from patients suspected to have endocarditis for culture of the blood samples [25]. Grancher also wrote a series of reports on isolation and antisepsis (infection control) in l'Hôpital des Enfants Malades (1889–1890), where he, in fact, housed infectious patients with a latticed folding screen around the bed and introduced surgical gowns and handwashing for staff [26]. In 1885, Grancher was chosen to succeed Marie-Jules Parrot as the Chair of the Children's Clinic at l'Hôpital des Enfants Malades, and he also presented lectures on bacteriology from 1885 through 1907.

Grancher became a very close collaborator of Louis Pasteur. In 1885, Grancher assumed medical responsibility for administering Pasteur's experimental rabies vaccine, and Pasteur appointed him to direct the vaccination center that was near the Institut Pasteur. Grancher vaccinated Joseph Meister, the first patient saved by the vaccine, over 10 days beginning on 4 July



Figure 2. Jacques-Joseph Grancher (1843–1907)

1885. He even received the rabies vaccine series himself after an accidental exposure [27]. On 11 January 1887, Grancher successfully orchestrated the defense of Pasteur's antirabies method before the French Academy of Medicine when the safety and efficacy of the method were challenged [28]. He served as the Secretary of the Board of Directors of the Institut Pasteur from 1887 through 1900 and joined the editorial board of the *Annals de l'Institut Pasteur* in 1888. Grancher presented his research studies (with H. Martin) on the immunization of animals against tuberculosis in 1891. Grancher collaborated with Marfan and Jules Comby to publish the massive *Traité des Maladies de l'Enfance* in 5 volumes in 1897, with several later editions. In 1900, Grancher was elected Vice Chairman and, from 1905 through 1907, was Chairman of the Board of Directors of Institut Pasteur.

A strong case can be made on behalf of Jacques-Joseph Grancher for the designation as the first pediatric infectious diseases physician upon review of his accomplishments in pediatrics and bacteriology. However, by comparison, we believe that Theodor Escherich's superb administrative leadership of several very prominent departments of pediatrics (including the Chair in Vienna, arguably Europe's most prestigious), his fame as both pediatrician and bacteriologist, his interest in and studies of a wide variety of infectious disorders over several decades, and the prominent ongoing association of his name with one of the most common of all bacteria persuade us that he warrants the designation as the first pediatric infectious diseases physician.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

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