Development of Pediatric Pulmonology in the United Kingdom, Europe, and Australasia

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ABSTRACT

The organization of medicine in Europe, the UK and the Commonwealth countries was always much less formal than in the USA for many years and pediatricians interested in pediatric lung disease and asthma often started off as adult internists or specialists in adult pulmonary medicine. The early leaders in developing a special interest in the breathing of children during the 1940s and 1950s were predominantly physiologists and clinicians who began to apply physiological techniques to the study lung function in healthy and sick infants and children. A major contribution to our understanding of the epidemiology of wheezing in children was the early establishment of a cohort study in Australia which is still yielding important information. It was during the early 1970s that pediatric pulmonary "politics" began to emerge in the UK when pediatricians interested in lung diseases began to arrange an informal society and meet regularly under the auspices of the British Paediatric Association. In fairly

characteristic fashion, pulmonology in Europe was represented for a while by several different societies but due to the efforts of some dedicated enthusiasts there finally emerged the Paediatric Assembly of the European Respiratory Society (ERS) and its first Head, Max Zach, went to become President of the ERS itself. Despite some early doubts about the future for pediatric pulmonology as a specialty in Europe and Australasia it is clearly flourishing as shown by the rising membership of the professional societies and the constant stream of high quality basic science and clinical publications. (*Pediatr Res* 55: 521–527, 2004)

Abbreviations

BPA, British Pediatric Association
EPRS, European Pediatric Respiratory Society
ERS, European Respiratory Society
LRPC, Long-Range Planning Committee

In many ways, the organization of medicine in Europe, the United Kingdom, and the commonwealth countries has always been much less formal than in the United States, especially in relation to specialty practice. Although some might regard this state of affairs as harmful to the practice of specialist medicine, it did allow for the relative ease with which physicians in training could move between subspecialties. This was especially true for pediatricians who were interested in pediatric lung disease and asthma, many of whom started as adult internists or specialists in adult pulmonary medicine. In this way, it was possible for the application of techniques borrowed from adult medicine, such as the measurement of lung function and bronchoscopy, to be introduced into pediatric practice with appropriate modifications. In Australia and New Zealand, pediatric pulmonology evolved, in some ways, as a hub between disciplines and between continents, very likely as a result of geographic isolation. There has been considerable movement

of those training in pediatric pulmonology between Australia, Europe, and North America. Collaborative studies with neonatologists, radiologists, immunologists, intensivists, and thoracic surgeons have led to valuable reports on the physiologic and clinical features of neonatal lung disease with analysis of long-term sequelae. The collaborations have enabled documentation, through epidemiologic studies, of the wide range of features associated with childhood lung diseases. In Europe and Australasia, the specialty of pediatric pulmonology evolved mainly over the second half of the 20th century, slowly at first but with increasing professionalism and organization as time went by. The development of subspecialization in pediatrics needs to be seen in light of the fact that it was only some 30 y ago that pediatrics itself was recognized as distinct from internal medicine as far as the specialty examinations of the Royal Colleges of Physicians (board equivalents) were concerned.

It is interesting to speculate what drove academically minded pediatricians to specialize in pulmonology. Was it the advances in technology that enabled those with a physiologic bent to study lung function in children? Was it the ability to

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diagnose and treat cystic fibrosis? Or was it the awareness of the rapid increase in the incidence of asthma? Remember, the flexible fiber-optic bronchoscope and computed tomographic scanning came much later. Some may think that it was the development of safe and effective drugs for treating asthma with the large-scale funding available from the drug companies to finance research that provided the impetus, given that asthma and wheezing are such common problems in children.

THE 1930s–1940s

Where did it all start? Pediatricians and other physicians who treated children in the United Kingdom and elsewhere were chiefly involved in the management of infectious diseases, especially tuberculosis, until well into the 20th century. Apart from anecdotal reports of various lung diseases in children, it was only in approximately the 1930s that attention was focused in any scientific manner on the physiology and diseases of breathing in children—the forerunner of pediatric pulmonology. The fifth volume of the *Archives of Diseases in Childhood*, published in 1930, carries a wonderful account of asthma in children by Bray (1) with clinical and epidemiologic data, much of which could have been written today. Of children attending a special asthma clinic at the Hospital for Sick Children, London, 22% began to wheeze under 1 y of age and 40.5% under 2 y—pretty close to what we know now from epidemiologic studies especially in Australia. However, there was almost nothing in this paper about the treatment of asthma other than the advice that “intermarriage between asthmatics should be discouraged.”

Nothing really important developed in the field of pediatric pulmonology during the war years and immediate post-war period. On the whole, children were treated for lung problems by general pediatricians, and the pediatric journals carried only sporadic reports of pulmonary interest. Nevertheless, in the 1940 issue of the *Archives of Disease in Childhood*, there is an excellent account by Asherson (2) of the importance of bronchoscopy in the recognition and removal of nonopaque foreign bodies in children. Ten years later, there was still only a general interest in lung disease, and it is a chilling reminder to us today that in 1950 there was a 37% mortality from pneumonia in children younger than 6 mo, despite the use of sulfonamides or penicillin (3).

THE 1950s–1960s: THE “FOUNDING FATHERS” EMERGE

A more specific interest in pediatric pulmonology started in the late 1940s and early 1950s, largely because of the increasing interest in the physiology of breathing in infants and children. One of the driving forces at this time was Kenneth Cross, who began studying the mechanics of breathing and chemical and control in the newborn infant using a “head out” plethysmograph that he developed (4–6). This was a wondrous device in which the infant was enclosed within a rigid box and its face peeped out through a soft inflatable “tire” that formed the seal. As long as the infant did not wriggle too much, respiration could be recorded from changes in pressure of the chamber. Across the world in Australia, Kate Campbell, a

pediatrician interested in neonatology, made an outstanding contribution by noting objectively that it was oxygen that was responsible for causing retrolental fibroplasias in the premature infant (7). This she did by the simple expediency of noting a much lower incidence of retrolental fibroplasia in infants from a private nursery, where parents had to pay for the oxygen, as compared with the public nursery, where it was free and hence used much more liberally. In London, Leonard Strang was applying the then new technique of spirometry to normal children and reporting normal values of lung function for children aged between 7 and 18 y (8). In the late 1950s and early 1960s, Cross and others continued to expand the knowledge of neonatal and pediatric pulmonary physiology (9) while Strang was conducting a therapeutic trial in children with asthma using lung function as an outcome measure (10). In 1962, Dick Jones, a pediatrician at the Alder Hey Children’s Hospital in Liverpool, reported a then totally novel observation that changed thinking about asthma forever (11). He showed that exercise lasting 8–12 min produced a fall in forced expiratory volume in 1 s, which reached a minimum 1–5 min after exercise and then rapidly rose toward the resting level. The level of exercise determined the degree to which these changes were evoked. He also noted that the fall in forced expiratory volume in 1 s could be minimized or abolished by the inhalation of isoprenaline (isoproterenol). This was apparently the first demonstration of bronchial hyperreactivity in asthma using objective measurement to document the changes, although exercise-induced asthma had clearly been described almost 300 y earlier by Sir John Floyer (12). Jones and his colleagues went on to conduct a series of studies related to asthma severity and bronchial reactivity in children, and, in fact, using very simple techniques, they established many of the facts as we know them today about exercise-induced asthma (13, 14). Across the channel in continental Europe, pediatric pulmonology was also on the move with important clinical studies, especially of tuberculosis in children, by Jan Rudnik in Poland and Alf Backman in Finland while Alois Zapletal from then Czechoslovakia published his monumental work on lung function and forced expiratory flows in children (15), which is as valid and useful today as it was in 1969.

Toward the end of the 1950s, Howard Williams was appointed the first full-time director of research at the Royal Children’s Hospital research foundation in Melbourne. He not only contributed to knowledge in pediatric pulmonology directly but also led the way as a mentor for the next generation of physicians in this specialty. His own reports included accurate descriptions of the clinical presentations and natural history of tuberculosis in childhood, analysis of the effects of the aspiration of milk on the lungs, and documentation of structural abnormalities of the airways leading to bronchomalacia (16). He was a pioneer of physician endoscopy, although at the time, this was restricted to rigid bronchoscopy. He reported the natural history of wheezing illnesses after bronchiolitis. A major contribution was the establishment, together with McNicol, of a cohort study of asthma in 7-y-old children (17). This was initially designed to define the features of wheezing illnesses in 60,000 second-grade children in Melbourne, Australia. He showed a pattern of illness that indicated that most

was due to asthma leading to a marked reduction in the inappropriate use of antibiotics for wheezing bronchitis in children. Subsequently, the patterns of wheezing illnesses in young people have been more refined, but these studies provided the first new approach to understanding this complex problem. This cohort has subsequently been followed up and now, in the 21st century, is having its 42-y assessment. As in the United Kingdom, there was also an active interest in lung function in infants and children in Australia, with Eric Burnard reporting important information in neonatal pulmonology with his studies on infant lung physiology, ventilatory response to challenges, and chest wall mechanics (18). David Henderson-Smith subsequently continued these important studies in Sydney. In Melbourne, Peter Phelan, who trained with Howard Williams, began making his own special contribution to documenting lung function in children (19).

THE 1970s–1980s: THE NEXT GENERATION

During the 1970s, The Hospital for Sick Children in London became a hotbed for producing a whole generation of pediatric pulmonologists stimulated by Archie Norman and David Hull. This group included Tony Milner, John Price, Peter Weller, David Heath, and Jeremy Cogswell—some of the first British pediatricians who made a full-time career of pulmonology. It is interesting how often the same personalities appeared in published reports from different institutions and different topics. Milner alone and in collaboration with Cogswell, Lenney, Hiller, and others was producing a whole string of papers on techniques for measuring lung function in infants and young children and what were then original studies of the efficacy of bronchodilators in wheezy infants and toddlers (20–23). John Warner, who was to play such an important role in pediatric pulmonology, showed early on that our specialty not only related to chronic lung diseases such as adenoviral-induced lung damage (24) but also overlapped with pediatric allergy and immunology (25). Always there, stimulating whole generations of others to be interested in the epidemiology and management of pediatric lung diseases, was Hamish Simpson. At the same time, Simon Godfrey and his group at the (now Royal) Brompton Hospital in London were very active in studying the best ways to assess and treat asthma, studies related to exercise-induced asthma and studies of exercise physiology in healthy and sick children (26–34). From the Brompton group emerged a number of very successful pediatric pulmonologists, and without any intention of belittling the contribution of the others, Michael Silverman and Sandra Anderson deserve special mention. Michael went on to become one of the leaders of pediatric pulmonology and professor of pediatrics in Leicester with a remarkable talent for sorting out the wood from the trees and bringing common sense and refined judgment to bear on pulmonary issues. Sandra Anderson joined the group as a laboratory technician and went on to obtain her doctoral degree for research on exercise physiology in children. After a very successful period in the United Kingdom, she returned to her native Australia to work with Ann Woolcock and became, literally, the worldwide authority of exercise-induced asthma research.

After transplanting from the Brompton to the Hammersmith Hospital, Godfrey's group became very involved in the investigation of lung function in infancy and the effect of premature birth and its management on subsequent lung function (35–38). At that time, a young nurse with a bachelor of science degree in nursing and a desire to become a district midwife was persuaded by a lot of arm twisting to join the group. She was, of course, Janet Stocks, who went on to obtain her doctoral degree and become the undisputed “Queen” of infant lung function testing, holding court in the Institute of Child Health at the Great Ormond Street complex. During the 1980s, the same pediatric pulmonologists with a few new recruits were active in the field of lung function testing, especially in infancy, but now with more serious attention to the elucidation of clinical problems (39, 40). Several important epidemiologic studies were undertaken to investigate the nature and the prognosis of wheezing in infancy, notably by Mok and Simpson (41, 42), and an outstanding study, which is just as valid today, 20 y later, was undertaken by Pullan and Hey (43). In a beautifully designed and executed prospective study, they showed that respiratory syncytial viral bronchiolitis in infancy was associated with transient wheezing over the early years but not with overt asthma in late childhood. The group also began to influence thinking about pulmonary problems in children at a national level and together with some eminent contributors from abroad, John Warner and Michael Silverman, organized the first meeting to establish guidelines for the management of asthma in children (44).

The new generation within continental Europe also began making advances, especially in various aspects of pediatric pulmonary function. Jan Bjure from Sweden was investigating various aspects of exercise physiology and lung function in children and, more recently, in the investigation of cerebral blood flow. Kjell Aas and Svein Oseid in Norway were documenting allergic aspects of childhood asthma (45), while in the Netherlands, Karel Kerrebijn was setting up epidemiologic studies of childhood asthma that produced much important data (46) and are still doing so today. In France, Claude Gaultier has been one of the pioneers in pediatric lung physiology. She has worked with a variety of topics, including describing function in premature infants (47) and their subsequent changes with growth (48), as well as studies of the control of breathing. Roberto Ronchetti in Italy was developing the use of isotopic inert gases to investigate lung function in young children alone and in collaboration with the group in Hammersmith (35, 49). During the 1980s, a number of new pediatric pulmonologists began making contributions in Europe. Max Zach from Austria, whose early study of the relationship between recurrent croup, allergy, and bronchial reactivity (50), was followed by many more clinical and physiologic studies, in addition to which Zach was to play such an important role in the development of the specialty in Europe. In Italy, Attilio Boner established a residential home for children with asthma high in the Alps, where he and his colleagues have undertaken interesting studies of the effect of environment on childhood asthma (51). Francois Marchal from France was beginning a series of important fundamental studies of lung function in children with special emphasis on the use of forced oscillation (52). In the

Netherlands, Jorrit Gerritsen, the present head of the Pediatric Assembly of the European Respiratory Society, was continuing the tradition of epidemiologic studies of childhood asthma (53).

In Australia, a similar situation was developing with a new generation emerging to expand knowledge in clinical and physiologic aspects of pediatric pulmonology. A number of these pediatricians also traveled abroad to expand their interests and returned to Australia to become driving forces in advancing the specialty. These included Phelan, who went to Boston to work with Jere Mead and colleagues, and Lou Landau, who trained initially with Phelan and then went for a period to Montreal, where he worked with Peter Macklem and Pierre Beaudry and began a long-term collaboration with Lynn Taussig. After returning to Australia, these investigators and their colleagues published a number of important studies that included an evaluation of tests such as oscillation and multiple-breath nitrogen washout for measuring small airway function in children (54), a continuation of the asthma cohort follow-up analysis with James Martin (55, 56) as well as numerous studies on the management of asthma and cystic fibrosis with particular focus on treatment and prognosis (57, 58). Studies have been continued by Tony Olinsky, Colin Robertson, and Phil Robinson. At the same time in Sydney, the remarkable adult pulmonologist Ann Woolcock, who passed away recently, began to study lung function in children. Her epidemiologic studies with Craig Mellis and Jenny Peat have provided valuable information on the patterns of bronchial reactivity in childhood and further contributed to understanding the evolution of wheezing illnesses through childhood into adult life (59). Others from the group in Sydney included Peter Van Asperen, John Morton, Penny Field, Richard Henry, and Gus Cooper. In New Zealand, Malcolm Sears, another adult pulmonologist, began to study various aspects of the clinical manifestations and epidemiology of childhood asthma (60) and has continued to contribute up to the present time after moving to Canada.

In 1977, Simon Godfrey moved again, this time not just across Hyde Park but from London to take up the chair of pediatrics at the Hadassah University Hospital in Jerusalem. Not only was he able to gather together a local group of budding pediatric pulmonologists, but he also was able to play host to a number of outstanding visitors, among whom were Lou Landau and Lynn Taussig. During a very "mini" sabbatical period of study leave in Jerusalem (and many beers), the rapid thoracic compression technique was developed for the measurement of forced expiratory flows in infants (61). Caroline Beardsmore also spent some time in Jerusalem and made important contributions, which included the development of computer techniques that made it possible to measure airway resistance continuously during tidal breathing in infants (62). Others were also on the move, Lou Landau moved across the continent from Melbourne to Perth and established a major center for pediatric pulmonology. Peter Sly and Peter Le Souef set up in Perth and made important contributions to our understanding of pediatric pulmonary physiology.

It was during the early 1970s that pediatric pulmonary "politics" began to emerge in the United Kingdom. Pediatricians

who were interested in lung diseases began to arrange an informal society that was named the British Pediatric Respiratory Group and that met chiefly at the annual general meeting of the British Pediatric Association (BPA). This was a very useful and friendly setting at which members were able to pick each other's brains over technology and clinical matters. At first, the group was regarded somewhat with distaste by the BPA members, who were against subspecialty groups that they thought would draw people away from the general pediatric meetings. However, as time went by, the various subspecialty groups' meetings became an established part of the annual BPA meeting. In the late 1980s, the Australian Pediatric Respiratory Group was established. This collaboration between all pediatric pulmonologists in Australia and New Zealand has continued and with input from pediatric pulmonologists in all Australian states and New Zealand have produced important guidelines for understanding and treatment of childhood lung diseases.

During the 1980s, pediatric pulmonology really began to get organized in Europe. Until that time and in fairly characteristic fashion, pulmonology in Europe was represented by several societies. There were two for pulmonology in general—the *Societas Europea Pneumologia*, which had no interest in pediatrics, and the *Societas Europea Physiologiae Clinicae Respiratoriae*, which did have a pediatric working group. In addition, there was the independent European Pediatric Respiratory Society (EPRS) as well as pediatric allergy and cystic fibrosis associations and East European pediatric respiratory group (63). Ultimately, a "marriage" was arranged between the *Societas Europea Pneumologia* and the *Societas Europea Physiologiae Clinicae Respiratoriae*, the offspring of which was the creation of the European Respiratory Society (ERS). Archie Norman from United Kingdom was one of the early pioneers. John O. Warner and John F. Price were secretary and treasurer in this society. The EPRS continued to run meetings in different parts of Europe, but by 1990, the ERS had also developed its own Pediatric Assembly, and in January 1993, the eighth meeting of the EPRS was organized in Oslo by Kai-Håkon Carlsen as a joint meeting with the Pediatric Assembly of the ERS. At this meeting, in which there were 650 participants, common sense finally prevailed and it was decided that the EPRS should cease as a society and join with the Pediatric Assembly of the European Respiratory Society. This was effected at the last meeting of the EPRS as an independent society in Rotterdam in 1995.

THE 1990s–2000+: CONSOLIDATION

During the past 12 y, pediatric pulmonology in the United Kingdom finally reached maturity and even attained formal recognition as a subspecialty of pediatrics. After much debate and heart searching, the good old BPA finally emerged from infancy and childhood as the mature and fully fledged Royal College of Paediatrics and Child Health. Along with this change, the very informal British Pediatric Respiratory Group became the somewhat more formal British Pediatric Respiratory Society attached to the Royal College, and even more recently, a syllabus for the training of pediatric pulmonologists

has been established with formal certification on satisfactory completion of the training. Much of this change has been brought about through the hard work of John Price, Michael Silverman, John Warner, and Andy Bush, among others. The U.K. training program also includes training for a pediatrician who has special interest in respiratory medicine and is intended to run a specialist service within a district general hospital rather than a teaching hospital. In the research field, both Janet Stocks and Caroline Beardsmore have been busily applying infant lung function testing to the elucidation of clinical problems (64, 65), while Andy Bush and other clinicians have worked hard on developing novel approaches to diagnosis and treatment of lung diseases in childhood (66–68). The Jerusalem group continued to research pediatric pulmonary problems and, in particular, undertook studies into the nature of bronchial hyperreactivity in childhood lung diseases and developed the “PC_{wheeze}” technique for measuring bronchial reactivity in preschool children (69–72).

The Perth group has been very active in developing and applying new techniques for measuring lung function in infants and very young children, including the application of forced oscillations to measure impedance (73). Le Souef and his colleagues have further refined the forced expiratory rapid thoracic compression technique with measurements from raised lung volumes (74), and he has also contributed to knowledge in aerosol mechanics and treatment as well as the genetic basis of lung diseases. In association with Patrick Holt, they continue to contribute to the understanding of the immunologic and physiologic evolution of asthma in early childhood. In Melbourne, the studies in clinical aspects of lung disease have been continued by Tony Olinsky and in the epidemiology of childhood asthma by Colin Robertson. Stephen Stick began working with the Perth group and subsequently developed a program that measured the transmission of pressures in the rapid thoracic compression technique and reported studies of ventilatory control, including better understanding of sleep physiology in childhood. In New Zealand, Innes Asher and Pattemore and their colleagues undertook international comparisons of clinical and physiologic aspects of childhood asthma (75), and Asher has taken on the role of Australasian coordinator of the International Study of Asthma and Allergy in Children Studies. In Europe, the group of academic pediatric pulmonologists continued to expand with, among others, the Danish investigators Hans Bisgaard, working on asthma therapy in children, especially in relation to inhaled corticosteroids (76), and Søren Pedersen and Agertoft and their colleagues working chiefly on the side effects of treatment (77). Johannes de Jongste from the Netherlands was working on measuring airway responsiveness (78) and later on exhaled nitric oxide in children, while Kai-Hakon Carlsen of Norway was undertaking a number of studies, including bronchial provocation in young children and the efficacy of inhaled adrenaline (epinephrine) in bronchiolitis (79). Last but by no means least of this group was Erica von Mutius from Germany, whose studies of the differences in asthma incidence in children between the former East and West Germany started the whole concept of the “dirty environment” hypothesis about the prevention of asthma (80, 81).

With the winding up of the EPRS in 1993 and its incorporation into the ERS as its Pediatric Assembly, Max Zach was appointed as the first head of the assembly and later went on to become president of the ERS itself. Zach was succeeded by John Warner as head and then from 1997 by Kai-Håkon Carlsen. At the present, Jorrit Gerritsen from Groningen in the Netherlands is the head of the Pediatric Assembly, which is presently the second largest assembly of the ERS. Within the Pediatric Assembly are seven groups that represent all aspects of pediatric pulmonology and neonatology. In addition, specific problems related to pediatric pulmonology may be addressed by *ad hoc* task forces that are often initiated by the scientific groups. Presently, the Pediatric Assembly has two active task forces. One is the joint task force of ERS and American Thoracic Society on infant lung function tests, headed by Janet Stocks. Historians should note that this important and very fruitful idea was originated by Michael Silverman, Bob Castile, and a few friends in the bar of a hotel in Cincinnati. The second task force, headed by Jacques de Blic, concerns pediatric bronchoalveolar lavage.

Early on, the Pediatric Assembly formed its Long-Range Planning Committee (LRPC), which was initially headed by John Price and now by Felix Sennhauser. With the approval of the executive committee of ERS, the LRPC of the Pediatric Assembly arranged joint meetings with other societies, including the Pediatric Week (Rotterdam 1994), the European Society for Pediatric Allergy and Immunology held in Odense (1996), and again at a special meeting organized by Elif Dagli from Istanbul (Berlin 1999). During the past few years, the European Society for Pediatric Allergy and Immunology has become the Pediatric Section of European Academy of Asthma and Clinical Immunology, and a joint meeting of the Pediatric Assembly, the ERS, and the Pediatric Section of European Academy of Asthma and Clinical Immunology took place in Valencia in Spain in November 2002. The LRPC has also been active in the development of rules for specialization throughout Europe. Max Zach and Attilio Boner have represented LRPC and the Pediatric Assembly and reached agreement within Confederation of European Specialty Pediatrics for a European subspecialty of pediatric respiratory medicine. The European School of Respiratory Medicine was created in 1992 and was responsible for postgraduate courses at the annual congresses of the ERS. It has now developed into the European Respiratory Society School and is organizing postgraduate courses at the annual congress, ERS School Courses on different locations in Europe, and has its own learning resources on the web. Kai-Håkon Carlsen from Oslo is the present head of the ERS school.

WHERE ARE WE NOW?

Despite some early anxiety that pediatric pulmonology might get swallowed up by the neonatologists and allergists or simply become the realm of the family practitioner or pediatrician (63), this is clearly not the case and the specialty seems to be thriving if one looks at the membership of the professional societies and the constant stream of high-quality publications. Perhaps it was the pediatric fiberoptic bronchoscope

more than anything else that spurred on the specialty because the pediatric pulmonologist has become the undisputed master of this investigative technique and the clinical information that it elucidates. Lung function testing, especially of infants, has also contributed to a much more evidence-based approach to pediatric respiratory problems as has the intelligent use of computed tomography. Cohort studies are clearly elucidating the perinatal and childhood origins of adult lung disease. The neonatologists and intensivists have gone their own way, albeit with very healthy cooperation, in the management of specific problems. It now looks as though pediatric pulmonologists are here to stay and are recognized by the pediatric profession as the correct address to which to refer children with all but the most straightforward respiratory problems.

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