Review Article

Medical Progress

PEDIATRIC SURGERY

First of Two Parts

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THE scope of pediatric surgery is broad, encompassing the care of patients from before birth through the adolescent years and addressing a wide range of conditions, including congenital malformations, cancer, trauma, and disorders requiring transplantation. The roots of pediatric surgery can be traced to the early 20th century, with the pioneering efforts of Dr. William E. Ladd at Children's Hospital in Boston. Since that time, several generations of surgeons have dedicated their careers to the care of children, and pediatric surgery has become a well-established specialty.[1]

The specialty matured with the development of postgraduate training programs, the creation of the Section on Surgery of the American Academy of Pediatrics in 1948 and the American Pediatric Surgical Association in 1970, the founding of the *Journal of Pediatric Surgery* in 1965, and the establishment of certification in pediatric surgery in 1975.[2] Further evidence of the need for specialized surgical care for children has been the growth of pediatric surgical subspecialties, including cardiac surgery, neurosurgery, ophthalmology, orthopedic surgery, otolaryngology, plastic surgery, and urology.[3] Two previous articles in the *Journal,* published in 1973 and 1988, traced the evolution of pediatric surgery.[4,5]

The 764 board-certified pediatric surgeons in the United States constitute 1.7 percent of all board-certified general surgeons. During the past decade, the number of accredited North American training programs in pediatric surgery has grown from 20 to 37 (31 in the United States and 6 in Canada), and an average of 27 pediatric surgeons complete training each year. In a study that used computer-modeling techniques to estimate work-force requirements over the next 20 years on the basis of the current number of practicing pediatric surgeons and their ages, as well as population-based predictions of the number of children, it was predicted that there would be a surplus of pediatric general surgeons within the next two decades if the number of graduates per year exceeded 27.[6]

The impact of managed care on academic children's hospitals has altered the practice of pediatric surgery. In a recent study at a large, free-standing children's hospital, pediatric surgical specialists performed substantially more clinical work (measured in terms of operations and outpatient visits per surgeon) than pediatric surgeons did 10 years ago but at a lower overall rate of reimbursement, a difference that may affect teaching, research, and administrative responsibilities.[7] In response to economic pressures, a model of regional clinical networking was developed at the University of Michigan, which resulted in considerable increases in case volume and in the number of referrals of complex cases to surgeons in the network.[8] The concomitant economic benefit permitted the recruitment of faculty members and increased academic productivity while providing pediatric surgical care for a larger geographic area.

In this article, we focus on six areas of pediatric surgery in which there has been substantial progress in the past decade. First, surgical treatment has improved the management of several neonatal disorders. Second, minimally invasive techniques are now used routinely in children. Third, cooperative national oncology studies have helped define more effective multidisciplinary treatments for children with cancer. Fourth, innovative techniques of organ transplantation and improved immunosuppressive therapy have led to favorable outcomes in pediatric transplant recipients. Fifth, systems-management approaches for the prevention and treatment of childhood injuries have markedly reduced the rates of morbidity and mortality associated with trauma. Finally, fetal surgery is now a reality rather than science fiction (Fig. 1).

NEONATAL SURGERY

Congenital Diaphragmatic Hernia

Congenital diaphragmatic hernia is present in approximately 1 of every 2500 neonates. The disorder is usually characterized by pulmonary hypoplasia due to intrauterine compression of the developing lungs by the herniated viscera (Fig. 2). In addition to the effects of such compression, there may also be an underlying primary abnormality in airway branching that results in pulmonary hypoplasia.[9] The result is often a gravely ill neonate. The multicenter Congenital Di-

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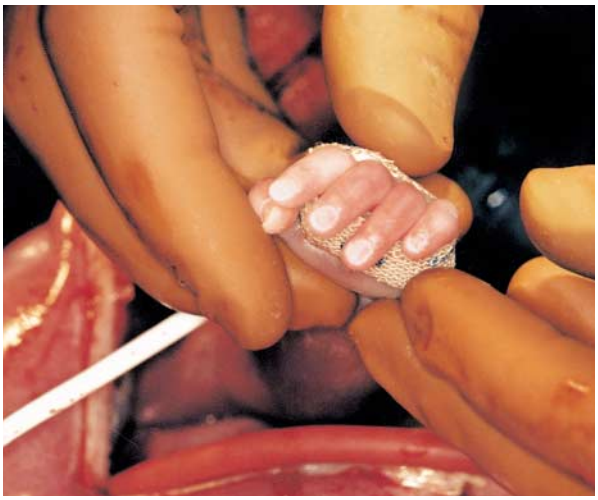


Figure 1. Application of a Pulse Oximeter to a 22-Week-Old Fetus Undergoing Thoracotomy and Resection of a Congenital Cystic Adenomatoid Lesion of the Lung Associated with Hydrops.

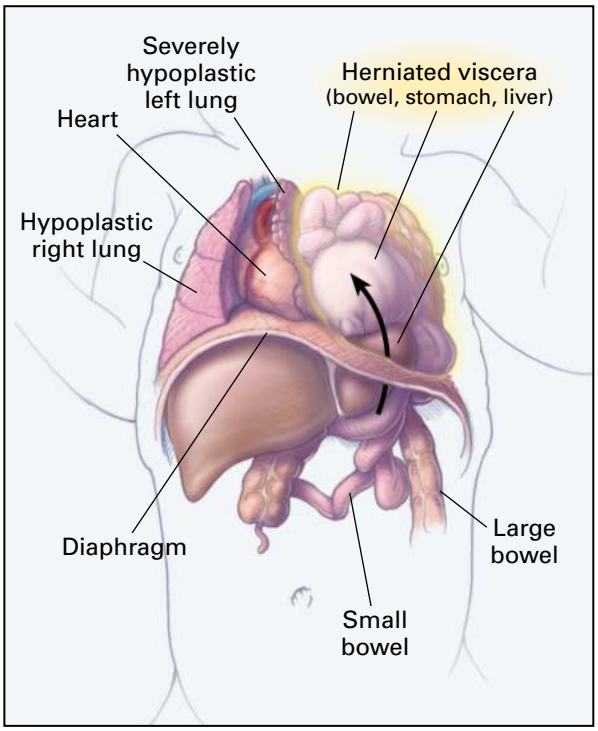


Figure 2. Congenital Diaphragmatic Hernia.
Herniation of abdominal viscera into the chest cavity (arrow) results in compression of the developing lungs and pulmonary hypoplasia.

aphragmatic Hernia Study Group recently reported a survival rate of only 63 percent in a study of 442 patients with congenital diaphragmatic hernia.[10] The disorder is no longer thought to require immediate surgery, since the primary problem after birth is not herniation of abdominal viscera into the chest but severe pulmonary hypoplasia and associated pulmonary hypertension.

New treatments have led to incremental increases in survival rates. Extracorporeal membrane oxygenation is a modified form of cardiopulmonary bypass that is used to treat severe neonatal respiratory failure. A review of data from the Congenital Diaphragmatic Hernia Study Group registry revealed that extracorporeal membrane oxygenation improves survival rates in a group of neonates with a predicted mortality rate of more than 80 percent in the absence of such treatment.[11]

Permissive hypercapnia with gentle ventilation, a strategy that permits supraphysiologic arterial carbon dioxide levels and marginal postductal oxygen saturation, is used in an effort to minimize airway inflating pressures and reduce barotrauma associated with ventilatory treatment of severe pulmonary hypoplasia. The survival rate associated with this approach (78 to 94 percent) is considerably better than the rates associated with traditional ventilatory strategies, with or without extracorporeal membrane oxygenation.[12,13]

Partial liquid ventilation, in which a perfluorocarbon liquid is instilled into the lungs, has shown promise in an animal model of congenital diaphragmatic hernia.[14] The perfluorocarbon liquid can dissolve large amounts of gases; thus it substantially augments the exchange of both oxygen and carbon dioxide at the alveolar level. In a study of four neonates with congenital diaphragmatic hernia who were treated with partial liquid ventilation, oxygenation and lung compliance improved, but survival was not increased.[15]

Other treatments for congenital diaphragmatic hernia have been disappointing. Inhaled nitric oxide, a selective pulmonary vasodilator, has been very beneficial in the treatment of other causes of neonatal pulmonary hypertension but has been ineffective in infants with congenital diaphragmatic hernia.[16] In some neonates, the lungs are relatively deficient in surfactant, yet anecdotal reports suggest that surfactant-replacement therapy does not improve survival.[17] Clinical trials of surfactant treatment after birth or maternal corticosteroid therapy before birth are needed. Long-term follow-up data on infants with congenital diaphragmatic hernia show substantial "hidden morbidity." Neurodevelopmental problems, gastroesophageal reflux, nutritional deficiencies, and skeletal anomalies are common, highlighting the need for close monitoring over a long period.[18]

Esophageal Atresia

Esophageal atresia affects about 1 in 4000 neonates. In the most common form of the disorder, the upper esophagus ends in a blind pouch, and the dis-

tal esophagus forms a tracheoesophageal fistula (Fig. 3). This defect was uniformly fatal before the first successful surgical repairs were performed, in the 1940s. The survival rate greatly improved in subsequent decades and is now higher than 90 percent.[19] The improvement in survival is due not only to surgical treatment but also to better neonatal intensive care, particularly the ability to meet the pulmonary and nutritional needs of these infants. Many of the infants grow up to lead normal lives. The group of infants with the highest risk of death are those weighing less than 1500 g at birth and those with associated cardiac or chromosomal anomalies.[20] Early deaths are the result of cardiac or chromosomal abnormalities, whereas later deaths are usually the result of respiratory complications. Correction of a long segment of esophageal atresia without an associated fistula remains a challenging problem. When primary esophageal anastomosis is not possible, the gap between the two ends of the esophagus is bridged by interposing a portion of the colon or jejunum or a tube made from the stomach or by bringing the entire stomach into the mediastinum as a gastric transposition.

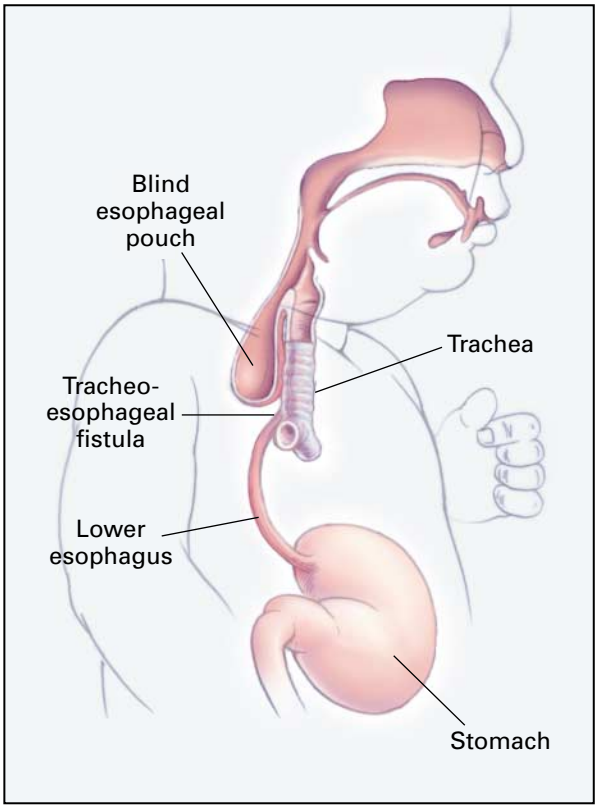


Figure 3. Esophageal Atresia.
In this form of the disorder, the upper esophagus ends in a blind pouch, and there is a fistula between the trachea and the lower esophagus.

Hirschsprung's Disease

Hirschsprung's disease is characterized by the absence of ganglion cells in the rectum. The disorder can extend proximally for some distance but is usually limited to the rectum and distal colon. In rare cases, it extends the entire length of the gastrointestinal tract, a condition that is often fatal. The absence of ganglion cells in patients with Hirschsprung's disease has been attributed to the failure of the migration of neural-crest cells.[21] On a molecular level, mutations of the *RET* proto-oncogene have been found in both the familial and sporadic forms of Hirschsprung's disease.[22] In a recent study of unselected patients with Hirschsprung's disease, a *RET* mutation was identified in 7 percent of the patients.[23] Mutations of the genes for endothelin-3 and endothelin-B receptors have also been linked to Hirschsprung's disease.[21,24] Once these mutations are better understood, they may prove useful as diagnostic markers or as targets for gene therapy. Studies of infants with Hirschsprung's disease have shown a deficiency of nitric oxide synthase activity in the affected intestinal wall. The lack of nitric oxide–producing nerve fibers in the aganglionic bowel probably contributes to the inability of intestinal smooth muscle to relax appropriately, thereby impairing peristalsis.[25,26]

A number of operations have been used to treat Hirschsprung's disease, all with generally satisfactory long-term results. The basic principle is to bring ganglionated bowel down to the anus. Recent efforts have focused on a single-stage repair through a transanal or combined abdominoperineal approach in the newborn period. In addition, a laparoscopically assisted approach has been reported.[27] These techniques eliminate the need for a preliminary colostomy and have favorable functional outcomes. Long-term follow-up studies have shown that surgical repair results in continence in virtually all patients, but 25 percent of patients need reoperation, and 19 to 25 percent have enterocolitis, with the specific rate depending on the type of repair that was used.[28]

Necrotizing Enterocolitis

Necrotizing enterocolitis usually occurs in premature neonates. Although an understanding of the pathogenesis of this condition remains elusive, the combination of an immature gastrointestinal mucosal barrier with an immature immune system has an important role. The pathologic outcome is the result of a hypoxic–ischemic event at the level of the intestinal mucosa. Additional putative causes include the presence of an intraluminal substrate (formula), since necrotizing enterocolitis is rare in unfed neonates. Infection probably also plays a part, since pathogens can be isolated from many affected neonates. However, whether infection is a cause or a consequence of necrotizing enterocolitis remains unclear.[29]

Most pediatric surgeons use signs of intestinal perforation or refractory sepsis as the indications for surgery. The mortality rate associated with laparotomy for perforated necrotizing enterocolitis is significantly higher among neonates with a body weight of less than 1000 g (usually those born at less than 27 weeks' gestation) than for larger neonates.[30] For this reason, bedside placement of peritoneal drains has been used initially in place of laparotomy for the management of perforation in the smallest newborns. Placement of drains can attenuate the source of sepsis by creating a point of egress through a controlled enterocutaneous fistula. With this approach, the overall survival rate among the smallest affected neonates (68 percent) approaches that among larger neonates who undergo laparotomy and intestinal resection.[31] Approximately one third of neonates treated with the placement of drains die from the disease, one third require subsequent laparotomy and bowel resection for necrotizing enterocolitis–related obstruction or undrained abscess, and one third do not require further surgery.

Imperforate Anus

The posterior sagittal approach for the correction of anorectal malformations was first described 18 years ago and has since become the gold standard for surgical repair of imperforate anus.[32] With the infant lying in the prone position, the tissues are divided in the midline from the coccyx to the perineum. This exposure facilitates accurate placement of the rectum within the pelvic muscle complex and allows the precise division and closure of the rectourinary or rectovaginal fistula.

The functional results of this procedure depend on the location of the associated fistula. More than 90 percent of infants with fistulas extending to the perineum or distal urinary tract have voluntary bowel movements, as compared with only 15 percent of those with defects extending to the neck of the bladder.[33] In all infants except those with perineal fistulas, a preliminary diverting colostomy is necessary. This approach has also been adapted for the repair of cloacal malformations in which the urinary tract, vagina, and rectum drain through a common channel. Use of the posterior approach, combined with advances in the repair of urinary tract anomalies, precise radiologic diagnosis, and state-of-the-art pediatric anesthesia and intensive care, has satisfactory results in infants with cloacae.[34] A single-stage laparoscopic correction of imperforate anus has recently been reported.[35]

Imperforate anus is often associated with other anomalies, which may complicate long-term care. The frequency of additional genitourinary abnormalities is 48 percent overall and ranges from 14 percent in infants with perineal fistulas to 90 percent in those with bladder fistulas.[36] In 24 percent of infants, the spinal cord is tethered and requires neurosurgical correction to prevent permanent neurologic deficits.[37]

Congenital Hyperinsulinism

Excessive secretion of insulin is the hallmark of congenital hyperinsulinism. This disorder is the most common cause of recurrent hypoglycemia in neonates and can lead to irreversible brain damage. Recent studies have shown that abnormalities of the K_{ATP} channel, encoded by the genes for the sulfonylurea receptor type 1 (SUR1) and the inward-rectifying potassium channel ($K_{IR}6.2$), are responsible for impaired control of insulin secretion. In response to hyperglycemia, the K_{ATP} channel closes, depolarizing the beta-cell membrane and initiating the calcium-dependent release of insulin from the beta-cell storage granules. Uncontrolled insulin secretion may occur if either the SUR1 or $K_{IR}6.2$ protein is defective.[38] This type of hyperinsulinism may not be controlled with drugs such as diazoxide, which acts on SUR1 to suppress insulin secretion, and pancreatectomy is often necessary. In contrast, the forms of hyperinsulinism that result from mutations of the gene for glucokinase or glutamate dehydrogenase are responsive to treatment with diazoxide, and surgery is usually not required.[39,40]

Neonates with hyperinsulinism may have either diffuse involvement of the pancreatic beta cells or focal adenomatous islet-cell hyperplasia. Mutations of the *SUR1* and *$K_{IR}6.2$* genes appear to be involved in both diffuse and focal hyperinsulinism. Diffuse disease often requires near-total pancreatectomy, which is associated with a long-term risk of diabetes mellitus. Conversely, focal disease may be cured with a partial pancreatectomy, with little risk of the subsequent development of diabetes. Preoperative transhepatic portal venous sampling and intraoperative histologic techniques have been used to differentiate between focal and diffuse disease, and additional diagnostic methods are being developed.[41,42]

MINIMALLY INVASIVE SURGERY

Many operations that previously required laparotomy or thoracotomy in children can now be performed with minimally invasive techniques. Improvements in instruments and the development of equipment of the appropriate size have made it possible to perform minimally invasive pediatric surgery. High-resolution cameras and telescopes that are 2 to 10 mm in diameter are introduced into the abdomen or thorax through small incisions. Instruments have been adapted for use through endoscopic ports to perform the procedures. The potential advantages of the endoscopic approach over laparotomy or thoracotomy include an improved cosmetic result, diminished postoperative pain, an accelerated recovery, a reduced degree of adhesion formation, and a shorter hospital stay.

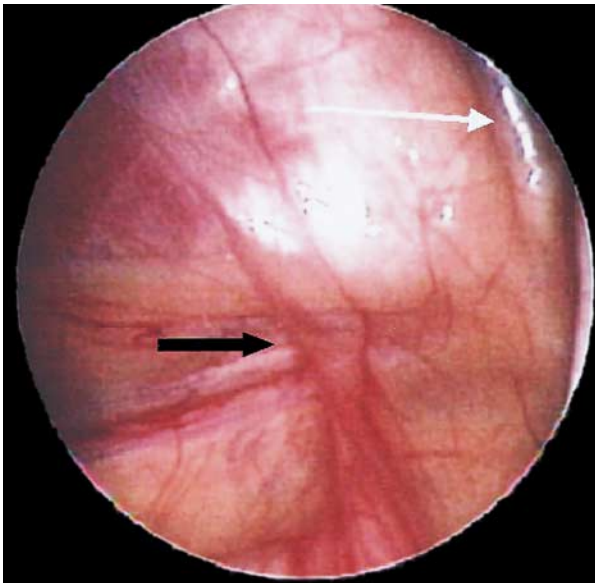
Gastroesophageal reflux in children can lead to esophagitis, aspiration pneumonia, esophageal stricture, anemia, and failure to thrive. Reflux that is re-

fractory to medical treatment often requires fundoplication, which can be performed laparoscopically even in small infants, with the use of operative techniques that are similar to those used in the open procedure. Laparoscopic fundoplication is associated with earlier initiation of feedings and shorter hospital stays than is the standard open procedure.[43] Although the follow-up period has been relatively short, the laparoscopic approach appears to be a promising alternative to the open procedure. Long-term follow-up studies will be required to determine whether the benefits of this approach are durable. Similarly, laparoscopic splenectomy for the treatment of hematologic disease is cosmetically superior, requires less postoperative analgesia, and results in an earlier discharge from the hospital than does open splenectomy.[44]

As an alternative to open inguinal exploration, laparoscopy can be used to rule out the presence of an unrecognized contralateral patent processus vaginalis in a child with a unilateral inguinal hernia. Laparoscopic exploration through the hernia sac to examine the contralateral side adds only a few minutes to the length of surgery and does not add to the cost, since reusable instruments are typically used (Fig. 4). In a meta-analysis of laparoscopic inguinal exploration in a total of 964 children, a contralateral patent processus vaginalis was detected in 39 percent of the children, with a procedural sensitivity of 99 percent.[45] A contralateral patent processus warrants operative repair.

The minimally invasive approach is routinely used for cholecystectomy in children. Laparoscopy may also be useful for evaluating a child with chronic abdominal pain, malrotation, an undescended testicle, or cancer. Although appendectomy for appendicitis, pyloromyotomy for pyloric stenosis, and inguinal hernia repair can be performed endoscopically, a laparoscopic approach to the repair of these conditions has not been widely accepted by pediatric surgeons.

A minimally invasive approach to the correction of pectus excavatum (funnel chest), developed a decade ago, involves the insertion of a stainless-steel strut across the anterior mediastinum under thoracoscopic guidance in order to elevate the sternum.[46] This maneuver permits the anterior chest wall to grow into the anatomically normal position. Overall, the results have been satisfactory in 93 percent of patients who have undergone the procedure. Since it does not require the excision of cartilage or sternal osteotomy, blood loss is minimal, the cosmetic outcome is good, and the small risk of postoperative asphyxiating thoracic dystrophy is eliminated. Most patients require a hospital stay of three to five days for postoperative recovery and the treatment of pain with thoracic epidural analgesia. Superior results and low operative morbidity have rapidly made this approach popular, and it has replaced the standard open approach at many centers. Initial results, with follow-up periods of up to 10 years, have been promising.



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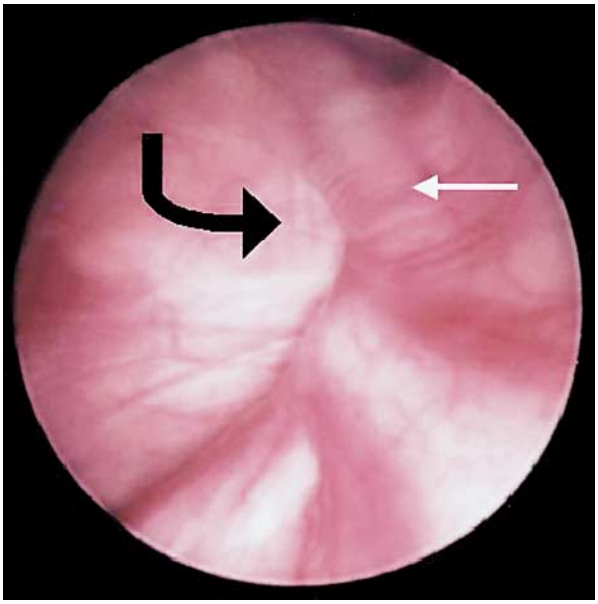

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Figure 4. Inguinal Anatomy as Viewed during Laparoscopic Exploration.

Panel A shows normal inguinal anatomy. The black arrow indicates the closed internal inguinal ring, and the white arrow the inferior epigastric vessels. Panel B shows an indirect inguinal hernia. The black arrow indicates the hernia sac, and the white arrow the inferior epigastric vessels.

The standard approach of long-term antibiotic treatment and hospitalization for pneumonia complicated by empyema has been challenged recently by advocates of early thoracoscopic decortication. The direct visualization afforded by thoracoscopy allows complete drainage of the pleural collection and facilitates the placement of the thoracostomy tube. In addition, débridement of the pleural space can be accomplished without resorting to thoracotomy. This approach results in an earlier resolution of fever and a shorter hospital stay than the standard approach, with minimal procedure-related morbidity.[47,48]

Thoracoscopy is ideally suited to lung biopsy, with random biopsies of diffuse interstitial processes or limited resection of discrete lesions easily accomplished. Surgical closure of a patent ductus arteriosus by thoracotomy was first reported by Gross and Hubbard in 1939.[49] In premature infants as small as 575 g, thoracoscopy is now used to place a metal clip across the patent duct.[50] Minimally invasive thoracic-surgery techniques have also been used to expose the anterior spine for the correction of scoliosis, sympathectomy, biopsy of mediastinal masses, and treatment of recurrent pneumothorax.[51]

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