

Gastrointestinal Manifestations of Epidermolysis Bullosa

大疱性表皮松解症的胃肠道表现

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EB的胃肠道症状

GI Manifestations in EB

- Pyloric atresia
- Esophageal strictures
- Gastroesophageal reflux
- Constipation, anal stenosis



幽门闭锁
食道狭窄
胃食道返流
便秘，肛门狭窄



Frequency of gastrointestinal tract findings and symptoms by major type of EB in the NEBR

国家EB资料库中各主要EB亚型的胃肠道症状频率

Abnormality 病症	EBS	JEB	DEB-u	DDEB	RDEB
Anal stricture 肛门狭窄	0.6 %	2.4 %	2.4 %	1.1 %	6.4 %
Chronic constipation 慢性便秘	8.1	17.4	32.9	15.5	45.2
Pyloric atresia 幽门闭锁	0.0	3.0	1.2	0.0	0.0
Dysphagia (difficult swallowing) 吞咽困难	3.0	19.0	20.0	14.1	56.9
Esophageal stricture 食道狭窄	0.6	3.7	8.5	2.6	37.2

Severe Constipation 严重的便秘

- Painful defecation 排便疼痛
- Blood on stool 便血
- Retentive behaviors 忍便不排的行为
- Megacolon 巨结肠
- Anal fissures 肛裂
- Anal stenosis 肛门狭窄
- Cramping abdominal pain 腹痛痉挛
- Loss of appetite, 食欲不振
- Growth failure 发育障碍



Management of Constipation

便秘的处理

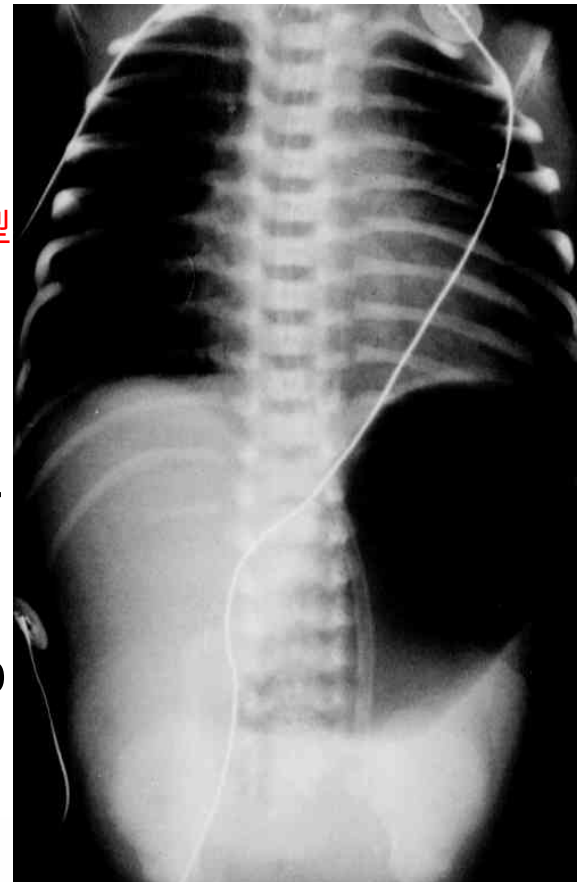
- Anal stricture may require dilatation 肛门狭窄可能需要扩张
- Lubrication and analgesics for anal fissures 对肛裂使用润滑和止疼药
- High fluid intake for dehydration 脱水时要大量补水
- Increased fiber in diet 膳食中增加纤维
- Laxatives 使用泻药
 - “Miralax” (Polyethylene glycol, an osmotic agent) 常用剂量：1mg/kg体重。滴定到有效剂量
 - Mineral oil 矿物油
 - Beware of aspiration, 注意肛门漏油
 - vitamin malabsorption 维生素吸收障碍
 - Lactulose 乳果糖
 - Others 其它



Junctional EB –Pyloric Atresia

- 常染色体隐性遗传，JEB-6 β 4整合素， β 4整合素基因。
- 单纯型EB，PLEC1突变

- Autosomal recessive entity JEB
 - 6 β 4 integrin, β 4 integrin genes
- PLEC1 mutation in EB simplex
- Dominant dystrophic EB
- Affected infants present with skin and mucosal fragility and inability to feed due to intestinal obstruction. · 显性营养不良型
- Despite successful surgical repair of the anatomical defect, the outcome is poor owing to poor feeding, malabsorption, failure to thrive, and sepsis
- Lethal and non-lethal disease variants; >65% mortality <1 year · 患病的婴儿皮肤和粘膜脆弱，由于胃肠道阻塞无法进食



- 通过手术修复了阻塞，但由于进食少、吸收不良、发育迟缓、败血症，效果不佳
- 致死性和非致死性亚型：>65%在<1年时间内死亡

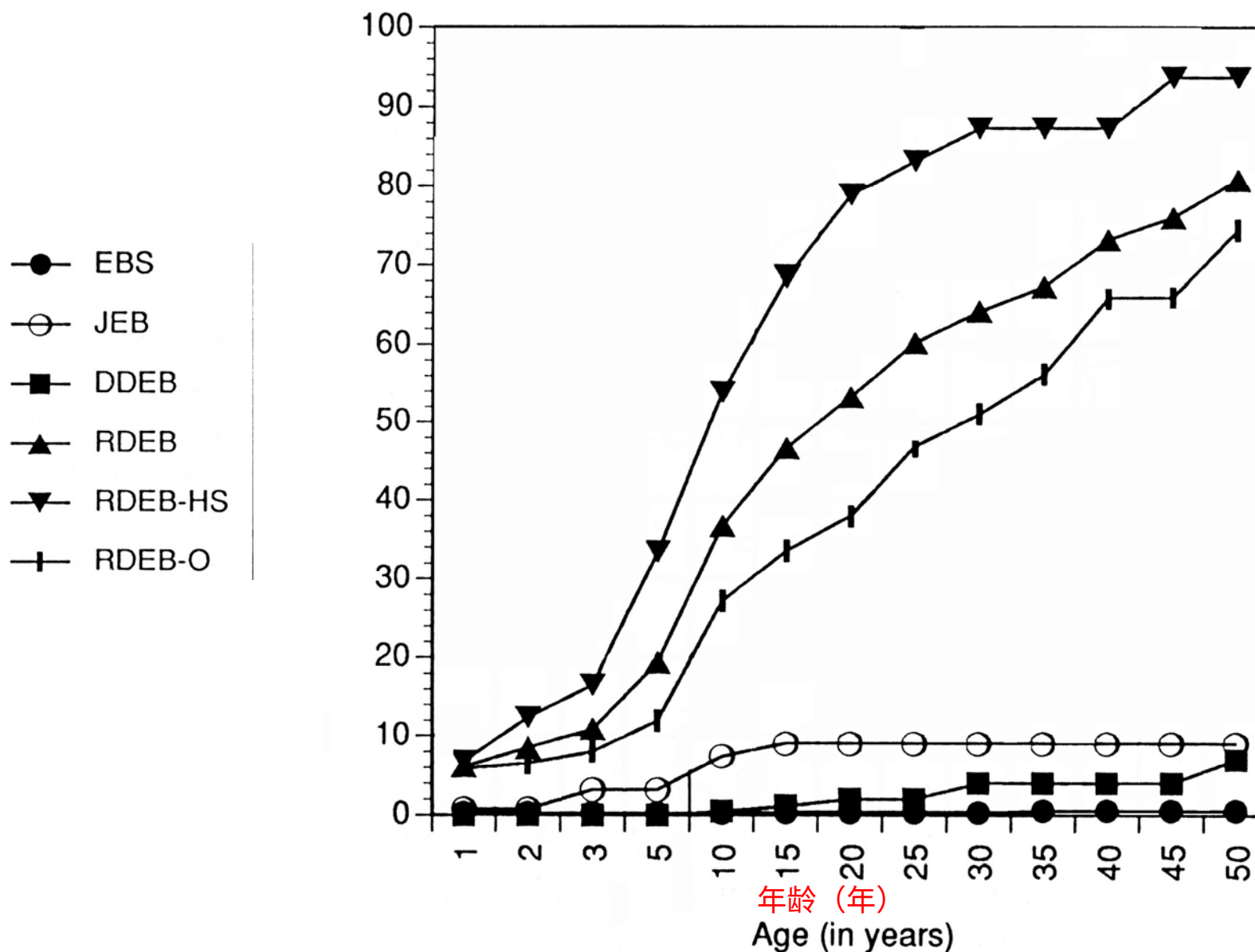
Esophageal Strictures - RDEB

- Present with painful and difficult swallowing · 吞咽困难并疼痛
- Food lodges at site of strictures · 食物会滞留在狭窄的位置
- Food ingested is progressively softer and eventually pureed · 吃的食物越来越软，最后发展到打碎了吃
- Liquids do not go down quickly and pool above stricture · 水也不会很快下去，会聚集在狭窄处
- Coughing and aspiration · 咳嗽、清喉咙
- Weight loss, dehydration and nutritional failure
- Growth disturbances · 体重减轻，脱水，营养不良
· 发育障碍

EB各亚型发生食道狭窄的累积频率

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Cumulative Probability of Esophageal Strictures in EB subtypes



食道狭窄

Esophageal Strictures

- Proximal esophagus involved in almost all symptomatic patients. Approximately 60% that is only site
- Approximately 1/3 have 2 significant strictures
- Remainder have 3 or more strictures

- 几乎所有有症状的患者都涉及到近端食道。
大约60%只有这一处
- 大约1/3有两处明显的狭窄
- 余下的有3处或更多狭窄



钡餐

Barium Swallow

- Most proximal stricture frequently missed by less experienced radiologists especially when initial symptoms necessitate initial investigation
- Requires careful view of neck area. May be captured by video-fluoroscopy
 - 经验不足的放射科医生无法发现多数近端狭窄，特别是初期症状做首次检查的时候
 - 需要仔细检查脖子区域。可以用视频荧光透视



大疱性表皮松解症

Epidermolysis Bullosa

- How are significant esophageal strictures in EB patients treated? EB患者明显的食道狭窄怎样治疗？
- What are the long-term consequences of esophageal strictures and dilatation? 食道狭窄和扩张的长期效果怎样？
- Are there options for maintaining adequate nutritional support when dilatations have limited effectiveness?

当扩张的效果有限时，有没有别的方案可以维持足够的营养支持？

食道扩张技术

Techniques used for Esophageal Dilatation

- Blind bouginage

盲探条扩张

- Rigid esophagoscopy with bouginage

刚性食道镜探条扩张

- Flexible esophagoscopy with balloon dilatation

柔性食道镜球囊扩张

- Fluoroscopically guided balloon dilatation

荧光镜引导球囊扩张

食道扩张技术

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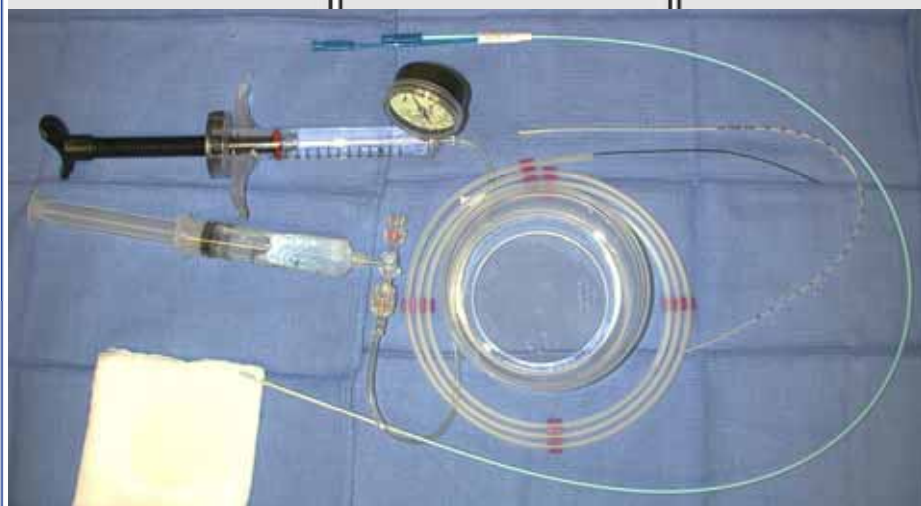
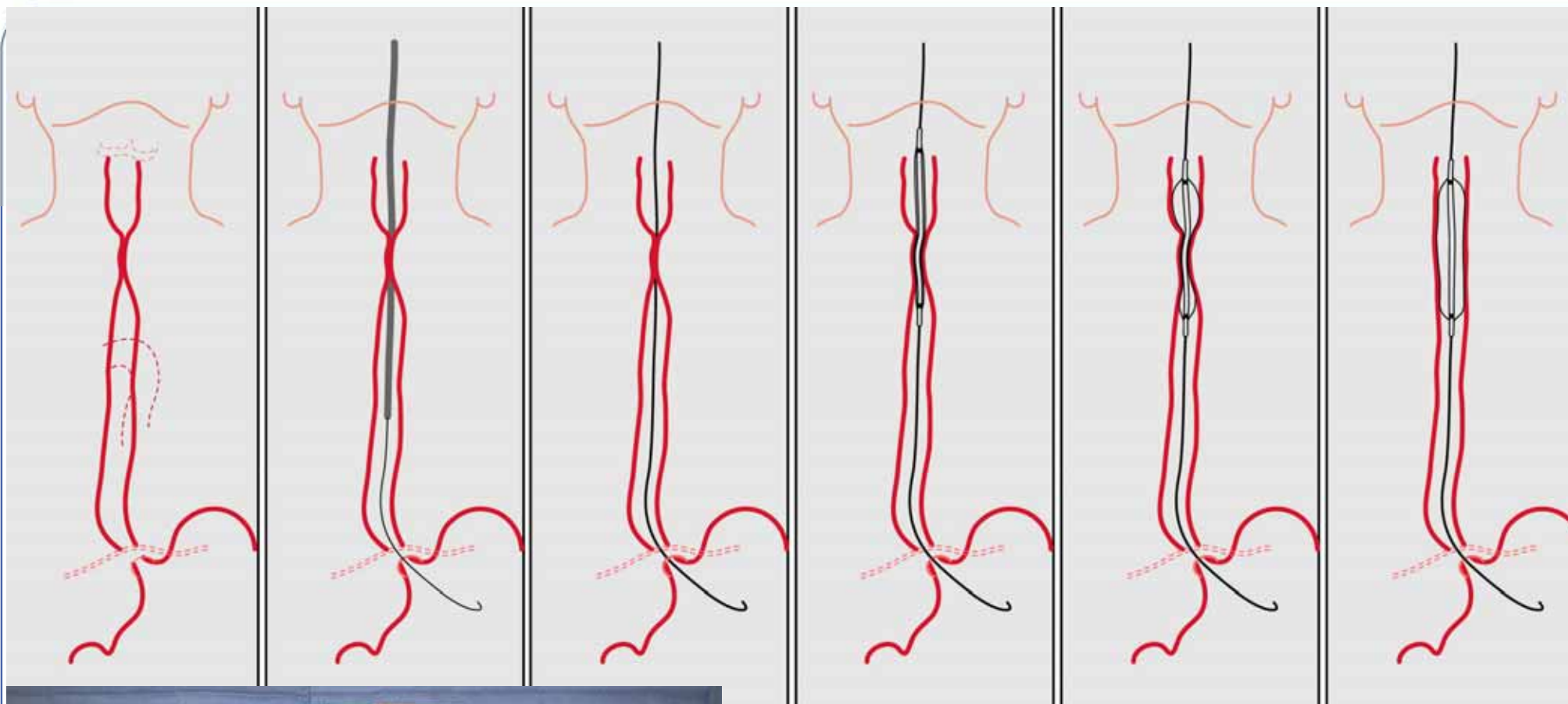
刚性食道镜探条扩张

- Flexible esophagoscopy with balloon dilatation

柔性食道镜球囊扩张

- Fluoroscopically guided balloon dilatation

荧光镜引导球囊扩张



Hydrostatic balloon dilatation
of esophageal strictures under
general anesthesia

全身麻醉下食道的液压球囊扩张

Technique

Hydrostatic Balloon Dilatation

液压球囊扩张技术

- General Anesthesia 全身麻醉
 - Endotracheal Intubation 气管插管
 - No Adhesives 不用胶带
- No Endoscope 不用内窥镜
 - Fluoroscopic x-ray control X光荧光镜控制
 - Live monitoring 实时监控
- Minimally invasive 最小化侵入伤
 - Umbilical Artery Catheter 5-8Fr
 - Hydrostatic balloon catheter 12-22mm
 - 5-8Fr的脐动脉导管
 - 12-22mm的液压球囊导管

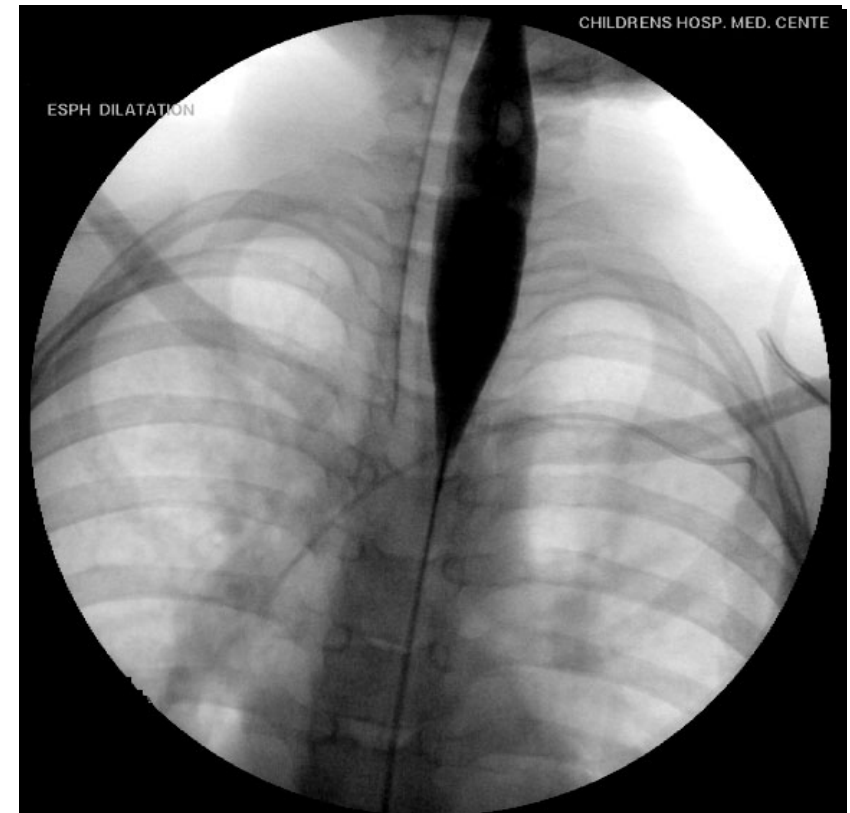


Technique

Hydrostatic Balloon Dilatation

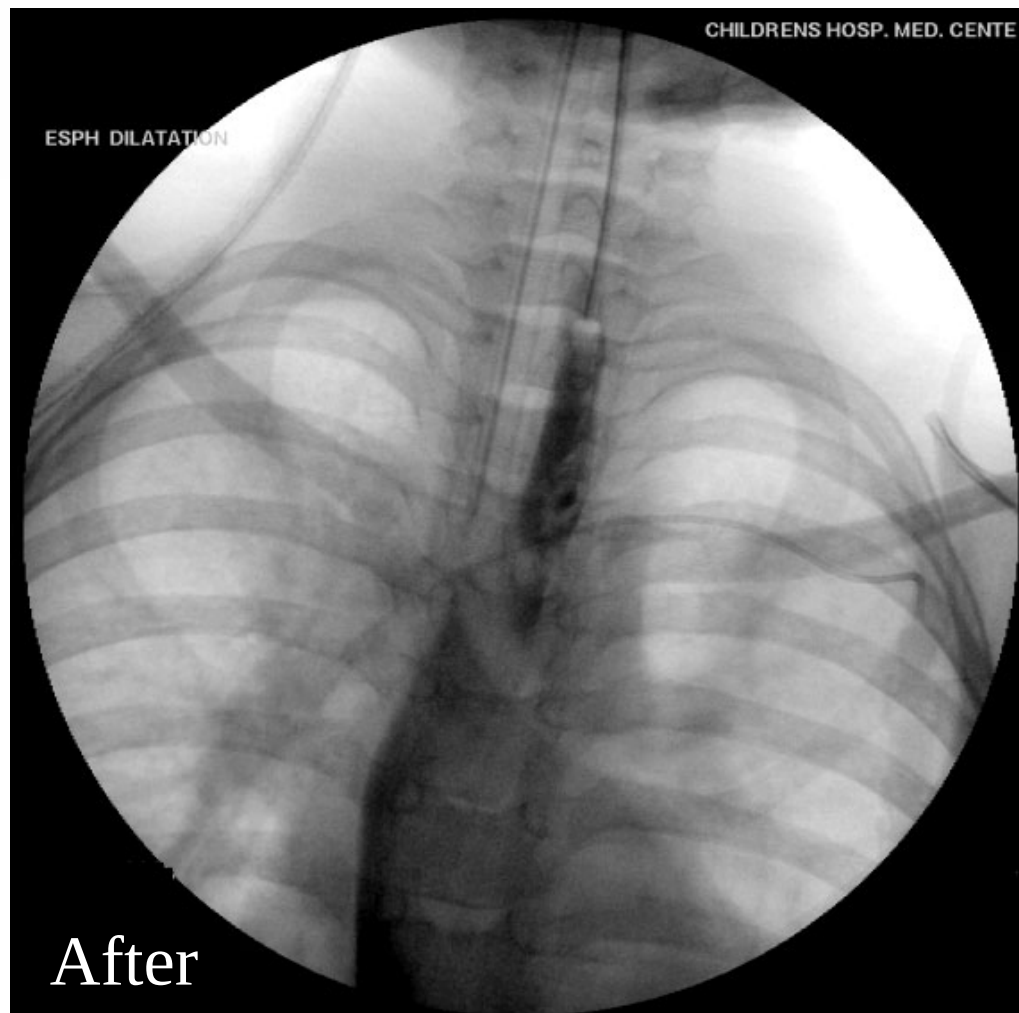
液压球囊扩张技术

- General Anesthesia 文字与上页一样
 - Endotracheal Intubation
 - No Adhesives
- No Endoscope
 - Fluoroscopic x-ray control
 - Live monitoring
- Minimally invasive
 - Umbilical Artery Catheter 5-8Fr
 - Hydrostatic balloon catheter 12-22mm





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术后

**Watersoluble contrast to
rule out perforation**

水溶性对照剂可排除穿孔



食道扩张

Esophageal dilatation

- Patient receives intravenous steroids at the time of dilatation 扩张时患者静脉注入类固醇
- Liquid prednisolone for daily 1 week with rapid taper 每天注射泼尼松龙，1周内快速减量
 - 1-2 mg/kg initial dose 初始剂量1-2mg/kg
- If reflux is a consideration – add H-2 blocker (ranitidine) or proton pump inhibitor (pantaprazole) to reduce gastric acidity 如需要控制反流 - 加H-2受体阻滞剂（雷尼替丁）或质子泵抑制剂（泮托拉唑）以减少胃酸
- This regimen seems to lengthen interval between dilatations 此方案似乎可延长扩张的间隔

Hydrostatic balloon esophageal dilatation outcomes over last 15 years

- >75 patients ages 2 to 45yr >75名患者，从2岁到25岁
- 16-22 mm balloon size most commonly used 最常用的球囊是16-22mm
- >200 dilatations – vast majority < 23 hour stay >200次扩张 - 绝大多数住院<23小时
- Immediate relief of symptoms in majority of patients 多数患者症状立刻缓解
- Most able to resume adequate oral feedings by the following day 多数在术后几天能恢复充足的口腔进食
- One localized and limited perforation resolved with non-operative treatment (antibiotics and no oral feedings for 3 days 一例局部和有限的穿孔通过非手术方式解决了 (抗生素并停止口腔进食3天)
- 1 patient aspirated post-op after extensive dental work
- Interval to next required dilatation varies - minimum 2 mos - 8 yrs; ave. @1 yr
 - 一名患者做了大量牙齿治疗，术后做了吸液。
 - 到下次需要扩张的间隔：最小2个月 - 8年；平均1年

荧光镜引导球囊扩张

Fluoroscopy Guided Balloon Dilatation

- First Line of Treatment

一线治疗方案
安全、可重复、成功

 - Safe, Repeatable, Successful
- Minimizes Oropharyngeal Trauma

最小化口咽处损伤
不使用内窥镜

 - Eliminates Endoscope
- Maximizes Esophageal Diameter

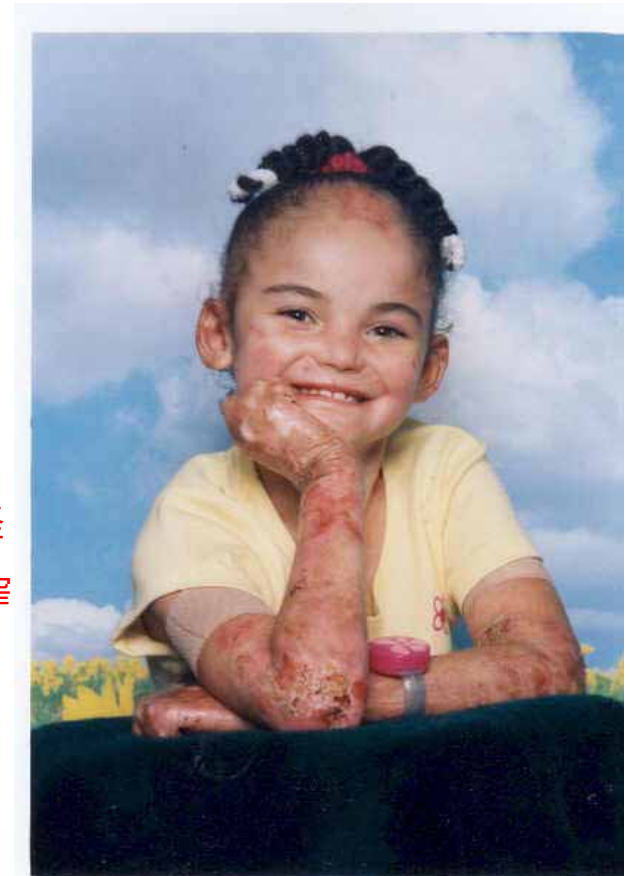
最大化食道直径
大球囊，软狭窄

 - Large Balloons, Soft Strictures
- Maintain Nutritional Status

维持营养状况

 - Independent of G-tube 不依赖胃饲管
- Quality of Life

生活质量



Gastrostomy

- 旷日持久的发育障碍，需要反复扩张，无法获得适当的护理，行为问题 - 大约1/3的患者需要
- Protracted growth failure, need for repeated frequent dilatation, access issues to appropriate care, behavioral issues – required in approximately 1/3 patients
- Operative gastrostomy 胃造瘘术
 - Open 开放
 - Laparoscopic 腹腔镜
- Percutaneous gastrostomy 经皮胃造瘘术
 - Percutaneous endoscopic gastrostomy (PEG) 经皮内镜下胃造瘘术
 - Non-endoscopic Push technique 非内镜推进术

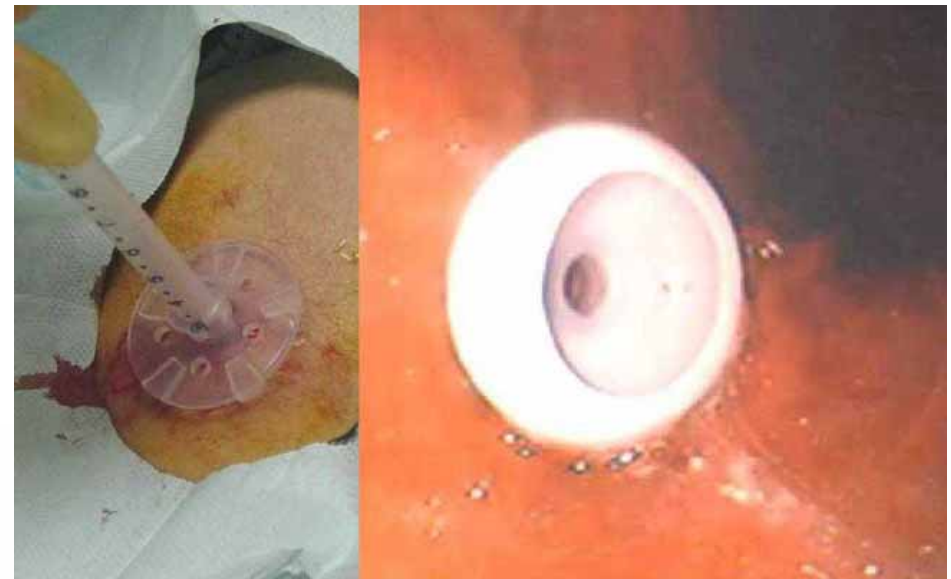
Surgical Gastrostomy

- Most surgeons trained with this procedure 多数外科医生学过这种手术
- May performed with preexisting esophageal strictures 已有食道狭窄的情况下也可以做
- Risk of wound complications especially infection higher 10-12% 创口发生并发症，特别是感染的风险高，10-20%
- Laparoscopic approach not recommended as extensive abdominal wall blistering a theoretic risk because of abdominal insufflation 不推荐采用腹腔镜方法，因为呼吸时腹部运动理论上会产生广泛的腹壁水疱
- Gastrostomy tube (silicone) anchored to underside of abdominal wall – not changed for 8 weeks 胃造瘘管（硅胶）锚定在腹壁下部 - 8周没有更换

Percutaneous Endoscopic Gastrostomy

在北美广泛应用，使用柔性内窥镜

- Also widely performed in North America uses a flexible endoscope
- May be difficult to perform with preexisting esophageal strictures but dilation could proceed PEG
- Procedure may further traumatize oropharynx, esophagus
- Risk of colocutaneous fistula – uncommon <1%
- Initial tube not changed for 12-16 weeks
- 手术过程可能会进一步损伤口咽和食道
- 结肠皮肤瘘的风险 - 不常见 <1%
- 初始胃管12-16周没有更换



Gastrostomy tube in place with ring and button positioned properly.

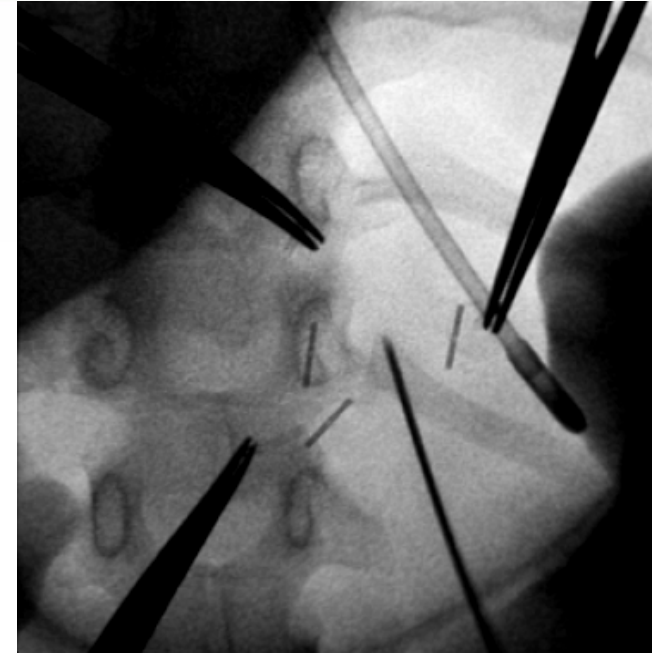
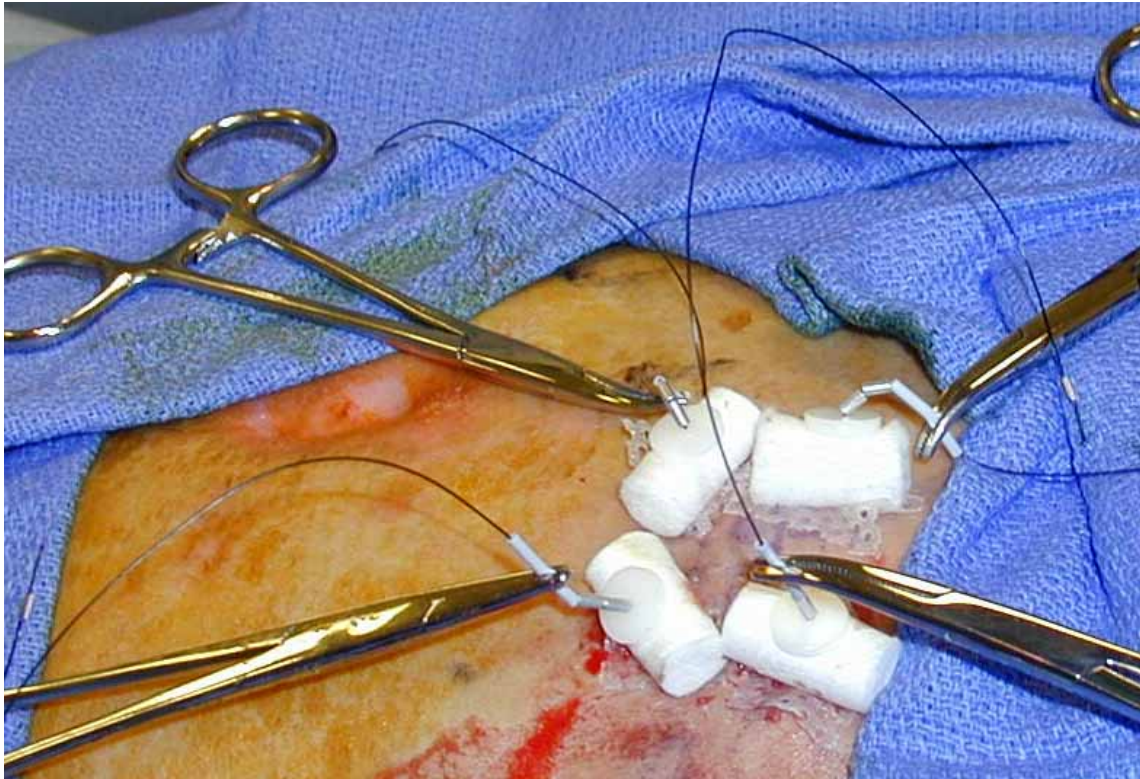
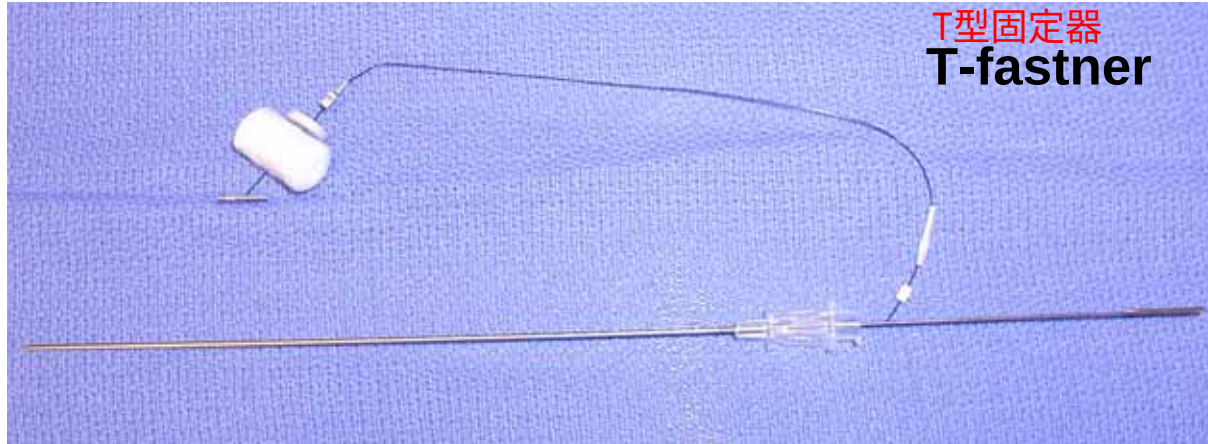
胃造瘘管设置好了，环和钮位置合适

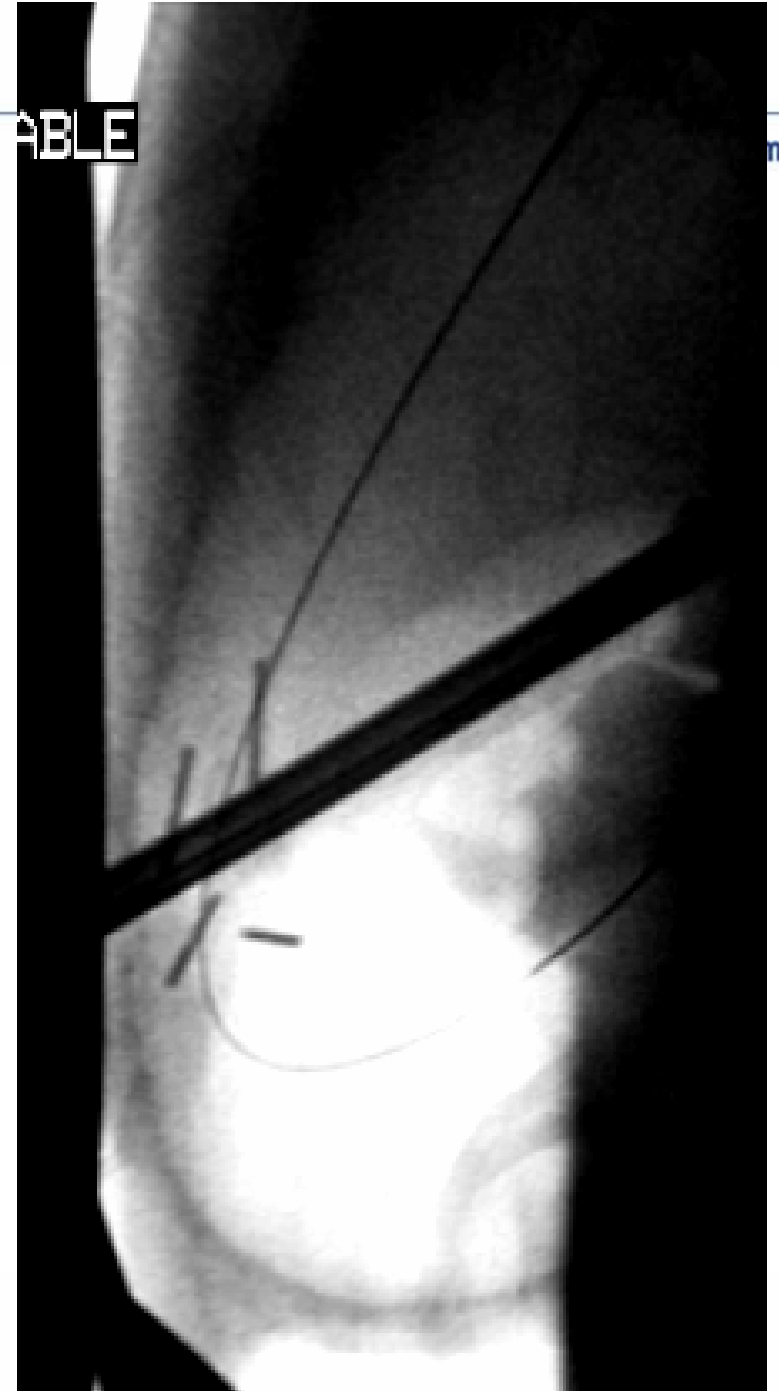
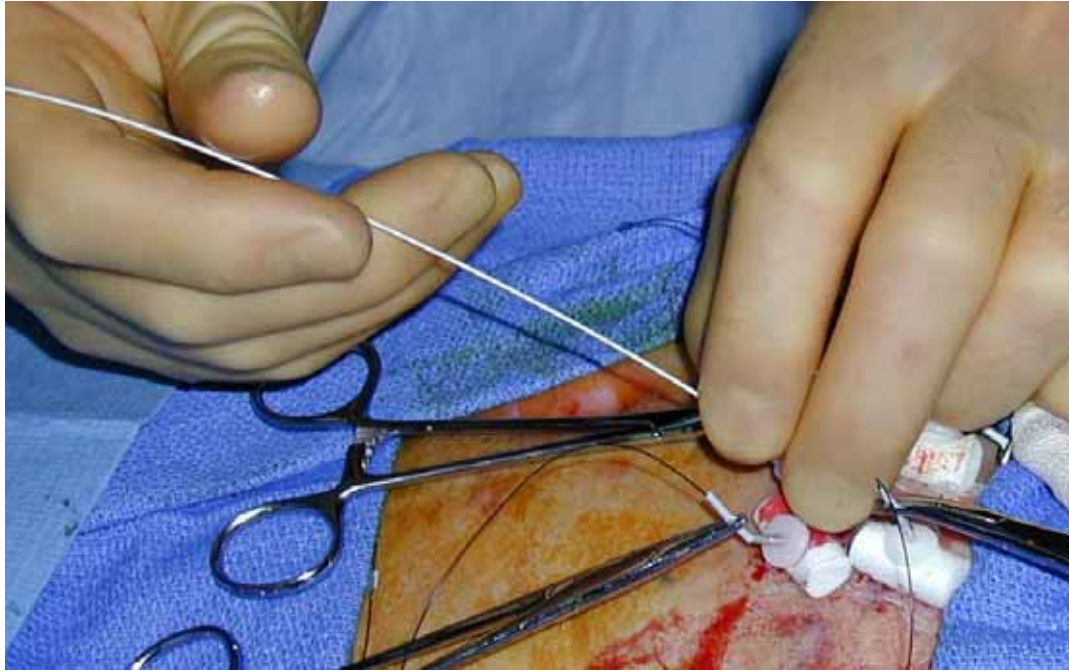
推式经皮胃造瘘术

Push Percutaneous Gastrostomy

- 水溶性对照剂灌肠，显示出左边和横结肠
- 腹部超声，定位靠近胃一侧肝的边缘
- Water soluble contrast enema to outline left and transverse colon
- Abdominal Ultrasound to locate edge of liver in relation to stomach
- Small orogastric tube to insufflate air (2-300 ml) into stomach
- Fluoroscopic guidance to perform cannulation of stomach
- 3 EB patients have had this procedure in Cincinnati
- 通过小的口胃管往胃里吹气 (2-300ml)
- 透视引导执行胃插管
- 3名EB患者在辛辛那提医院做过这个手术

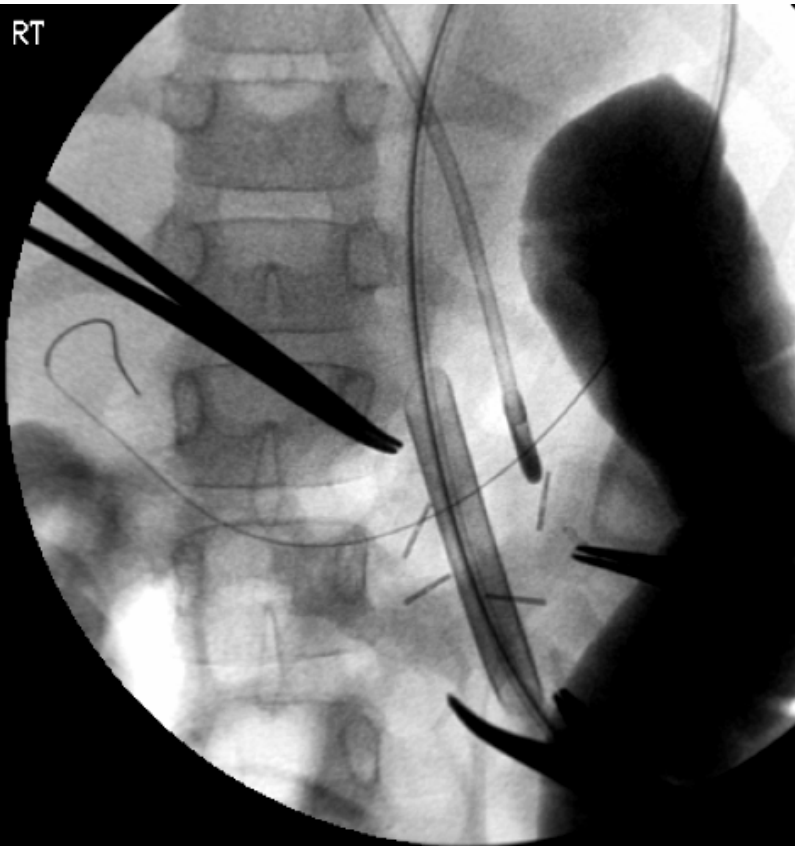




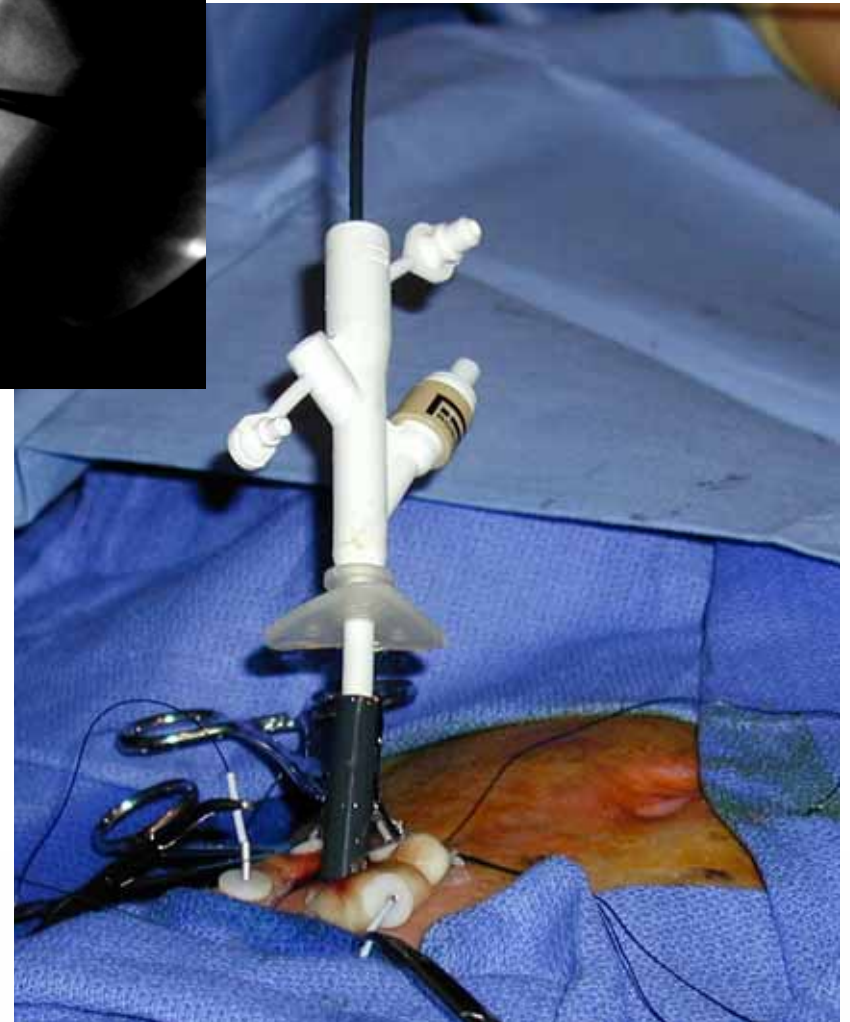
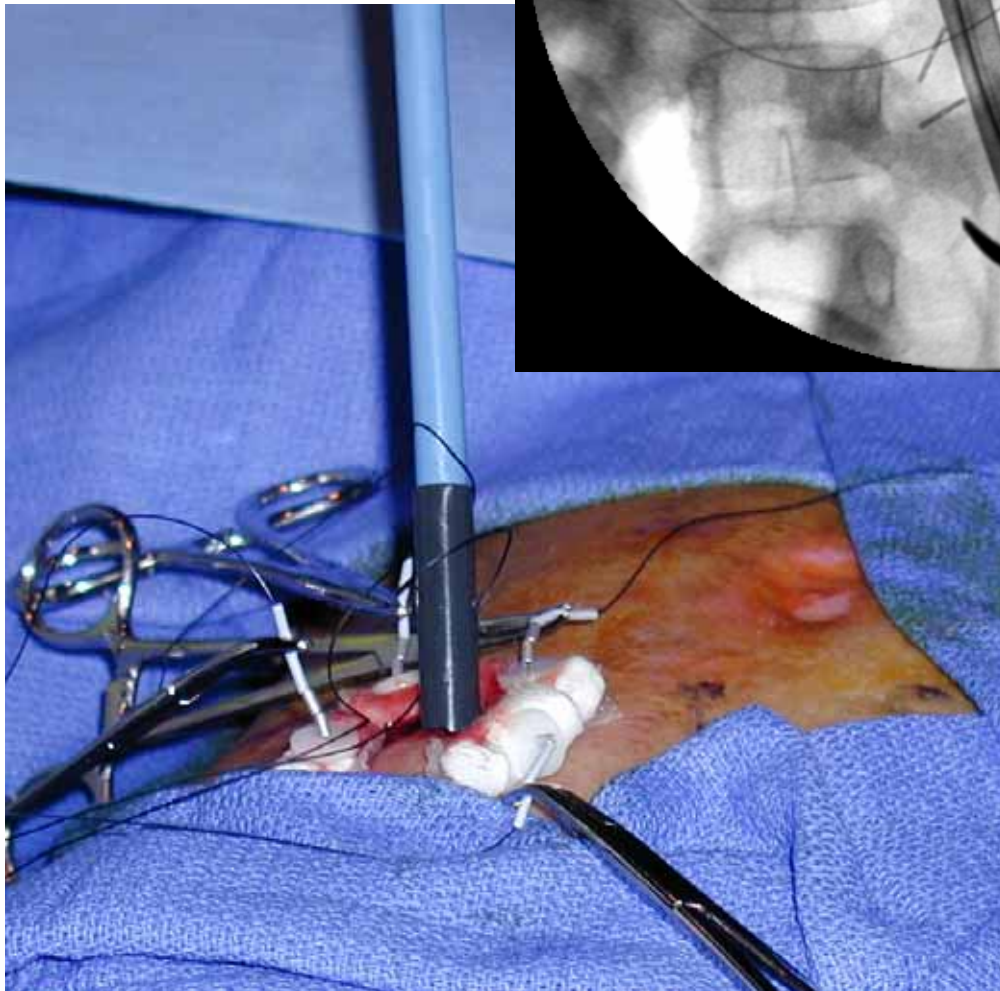


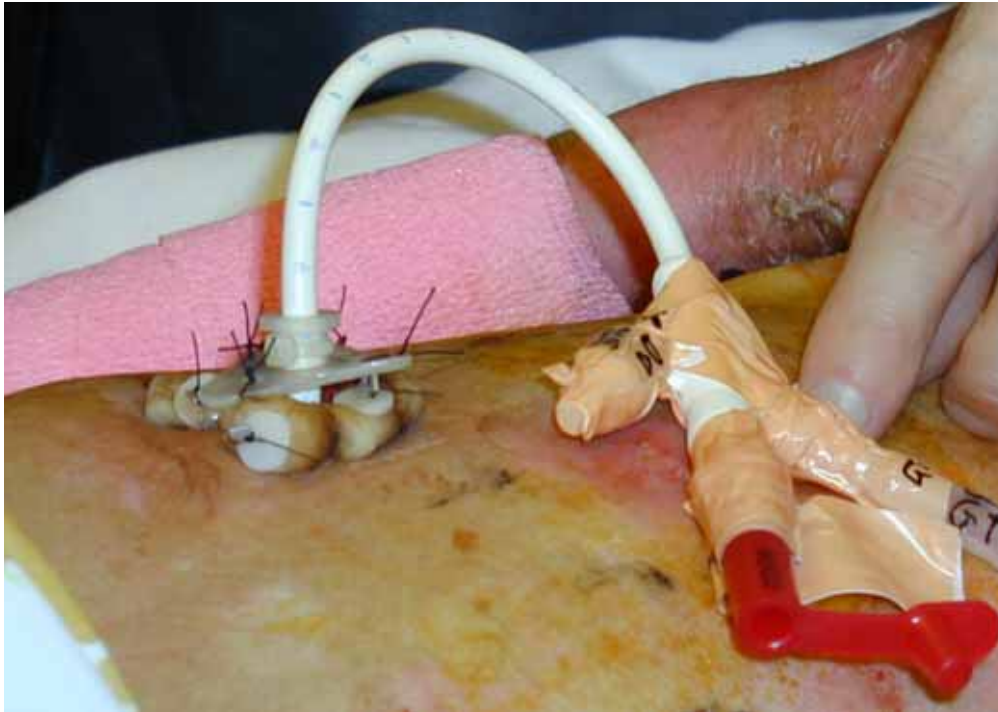
ABLE

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- G-tube anchored to the T-fastener
dental rolls not skin 胃饲管固定在牙科棉卷上的
T型固定器上，不是在皮肤上
- Feedings started the next day in small
quantities 第二天开始少量喂食
- Tube not changed for 12-16 weeks 12-16周没有更换胃饲管
- Replaced with a low profile G-tube 换了一个小号胃饲管



Gastroesophageal Reflux Disease

- Most patients with esophageal not carefully evaluated for GERD 多数患者没有仔细检查胃食道反流
 - Barium swallows not complete 钡餐吞咽不全
 - UGI not sensitive enough to discriminate pathological reflux 上消化道钡餐造影不够敏感，分辨不出病理性反流
 - pH probes and impedance study may be traumatic to patient – probe catheter placed into esophagus through the nose for 12-24 hours
 - Esophagoscopy and esophageal biopsy traumatic
 - pH值和电阻测量可能对患者造成创伤 - 探头需要通过鼻子放到食道12-24小时
 - 食道镜和食道活检也有创伤

胃食道反流

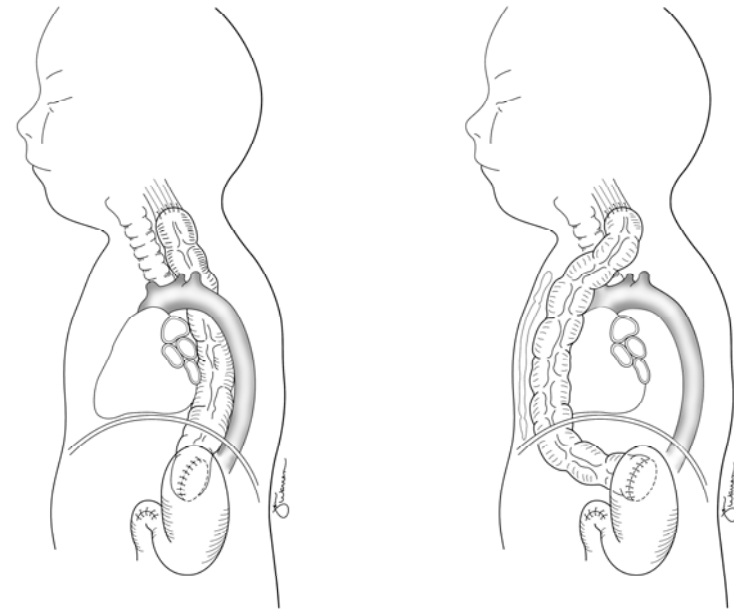
Gastroesophageal Reflux Disease

- Most EB patients with esophageal strictures are treated with proton pump inhibitors or H2 blockers empirically to reduce acid impact on strictures
多数有食道狭窄的EB患者依经验使用质子泵抑制剂或H2受体拮抗剂，以减少胃酸对狭窄的影响
 - Anti-reflux operations rarely performed in RDEB
 - Anti-reflux procedures more likely required in Junctional EB patients especially those that have airway involvement and a tracheostomy
- RDEB患者极少做阻止反流的手术
 - 阻止胃酸的手术更常见于JEB患者中，特别是那些呼吸道受影响的和做过气管切开术的。

结肠移位

Colon Transposition

- Complete obstruction of the esophagus 食道完全阻塞
- Replacement of the native esophagus with a vascularized segment of colon 把本来的食道换成带血管的结肠
- Kralik-1975, Harmel - 1986, Touloukian -1988: reported successful colon interpositions in children with EB



这几个人报道过对EB儿童做过成功的结肠移位

结肠植入

Colon Interposition

· 技术复杂，有显著风险 - 对很多患者不推荐

- Technically complex with significant risks - limited option for many patients.
 - Mortality for non-EB patients is 3% 非EB患者的死亡率是3%
 - Complications 25-30% including esophageal leak, strictures, long-term issues
 - Rarely performed (<5% of RDEB patients)
 - Those who have had good results are very happy and satisfied patients
- 25-30%有并发症，包括食道漏，狭窄，长期问题
· 极少做（RDEB患者<5%）
· 手术效果好的患者非常高兴和满意

总结

Summary

Constipation and anal pathology are very common in EB patients. Treatment consists of good hydration and nutrition as well as stool osmotic agents and laxatives

便秘和肛门病变在EB患者中很常见。治疗方法包括补水和增加营养，以及粪便渗透剂和泻药

Patients with epidermolysis bullosa and esophageal strictures have life-long issues in maintaining adequate oral nutrition.

有食道狭窄的表皮松解症患者终生面临维持充足口腔进食营养的问题

Using a variety of strategies, enteral nutrition and appropriate growth can be maintained for almost all patients.

通过各种策略，几乎可以为所有患者维持肠内营养和适宜的发育

Cincinnati Children's Hospital Medical Center

Thank you!!!!!!!!!!

