Sphincter of Oddi dysfunction: SOD after EPISOD, Now what do we do ?

Priya A. Jamidar, M.D., FASGE
Professor of Medicine,
Director of Endoscopy
Yale School

What is sphincter of Oddi dysfunction ?

"A riddle in a mystery wrapped inside an enigma"

John Baillie

ANNALI

DELL' UNIVERSITÀ LIBERA

DI PERUGIA

DI UNA SPECIALE DISPOSIZIONE A SFINTERE ALLO SBOCCO DEL COLEDOCO

RICERCHE

DI

RUGGERO ODDI

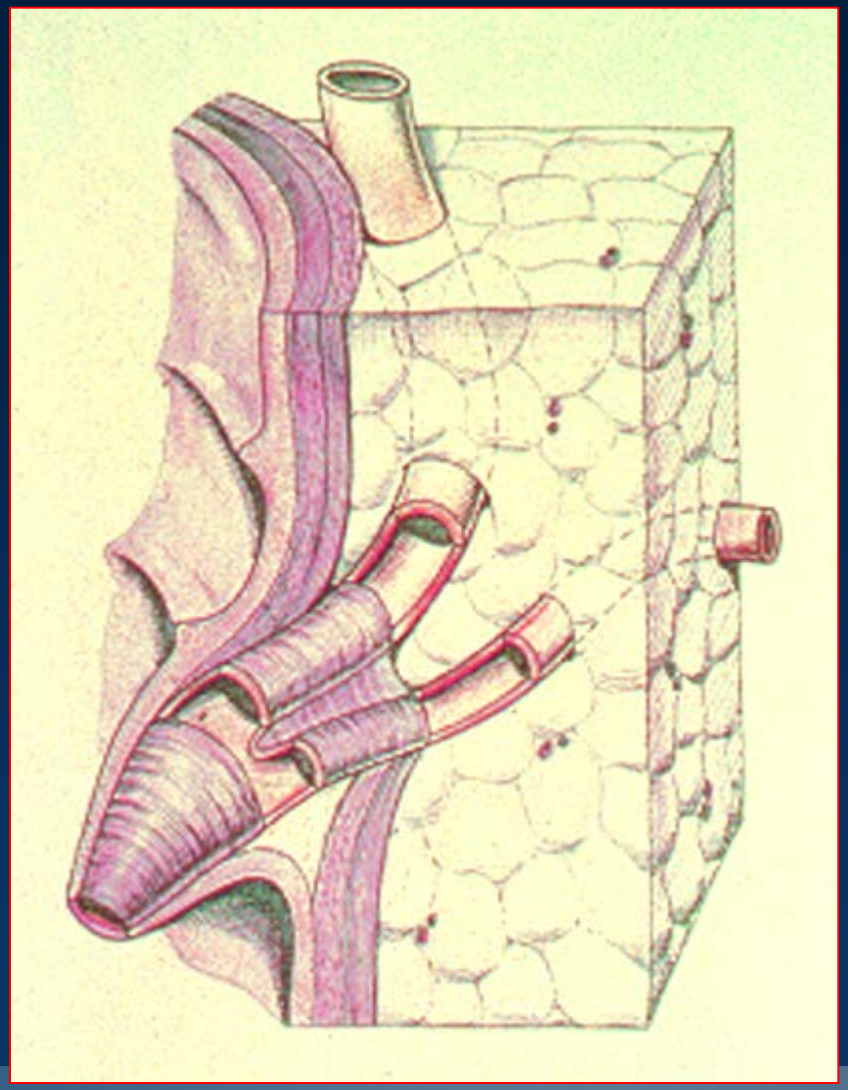
Desiderando fare uno studio comparativo sulla influenza che la bile poteva esercitare sulla digestione quando essa si versasse coscientemente nell' intestino, o allorchè io l' obbligava a riversarsi in modo non interrotto nello stomaco *) fui consigliato dal mio maestro professor Marcacci, ad escirpare la cistifellea. Privando così l' animale del serbatoio della bile, obbligava quest' ultima (almeno io lo credeva allora) a versarsi, via via che si formava, nello intestino, nel modo istesso che, nello stabilire la fistola colecisto-gastrica (previa legatura del coledoco), io l' obbligava a versarsi coscientemente nello stomaco. I due casi mi parvero allora assolutamente comparabili, per cui operai tre cani di questa escirpazione che, come ognuno sa, venne eseguita dallo Zambeccari sin dal tempo di Galileo e per consiglio di quest' ultimo. Ottenni facilmente la guarigione, riscontrando negli animali così operati veri fatti degni di nota, dei quali mi occuperò a parte. Quello che però debbo riferire, non solo perchè si collega direttamente col tema di cui ora mi occupo, ma

*) Ann. = Influenza della bile nella digestione gastrica studiata per mezzo della fistola colecisto gastrica = (Annali dell' Università libera di Perugia).

Papillary Stenosis: Definition

- *Benign noncalculous obstruction to flow of pancreatic juice or bile through the pancreaticobiliary duodenal junction (Sph. of Oddi) which may present with pain, pancreatitis, and/or cholestasis*

Relationship Between the Papillary Sphincters of the Common and Pancreatic Ducts with the Duodenal Wall



Type 1 Sphincter of Oddi dysfunction

SOD Clinical Features

- Usually female; CCX; 25-50 years old
- Pancreaticobiliary type pain
- Epigastric, RUQ, LUQ
- Radiation to back, scapulae, R shoulder
- Worse after meals; nocturnal; codeine, acid peptic Rx – no help

Classification of Biliary Sphincter disease

Type I: All of the following:

- Recurrent biliary pain
- Liver test elevations (AST or ALT) on two separate occasions (2x upper limit of normal) with resolution inbetween
- Dilated common bile duct (11 mm)

Type II: Recurrent biliary pain plus 1 of the above criteria

Type III: Biliary type pain only

Medical Rx of SOD

- Low fat diet
- Anticholinergics
- Nitrates
- Ca channel blockers
- Antidepressants
- Analgesics (avoid narcotics)

Complications of Biliary Sphincterotomy (MESH study)

- 2347 patients underwent Biliary ES
- 229 (9.8%) had complications
- Deaths 2.3 % (ERCP related 0.4%)
- ***Complications in 21.7% SOD vs 8.2% in non SOD patients***
- ***Severe complications > in SOD (3.7% vs 1.3%)***

Freeman M.L. et al, NEJM 1996;335:909-18.

Non-invasive tests of biliary SOD

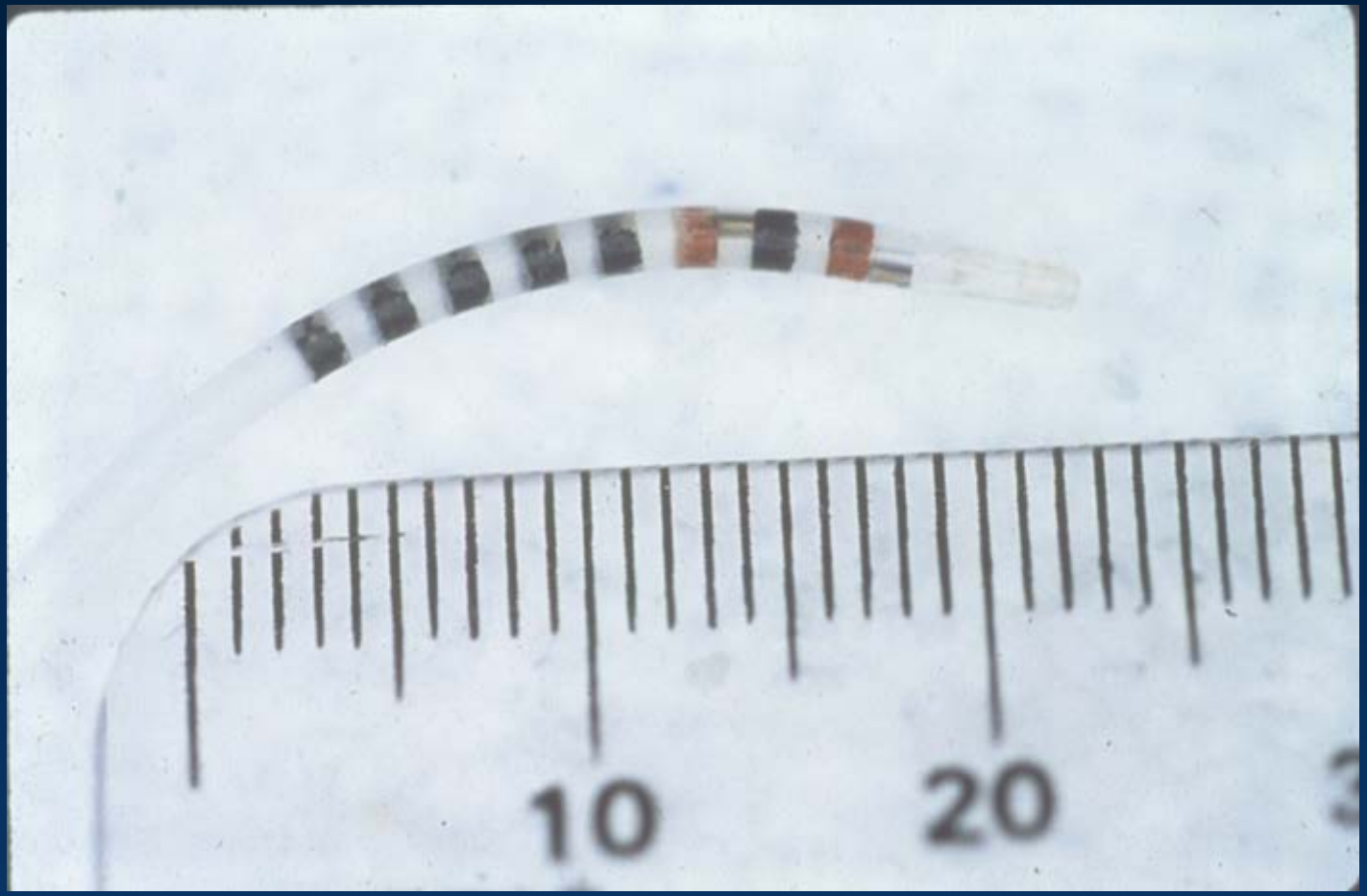
CBD

- **Hepatobiliary Scintigraphy ± CCK, Morphine**
- **Fatty Meal Sonography**

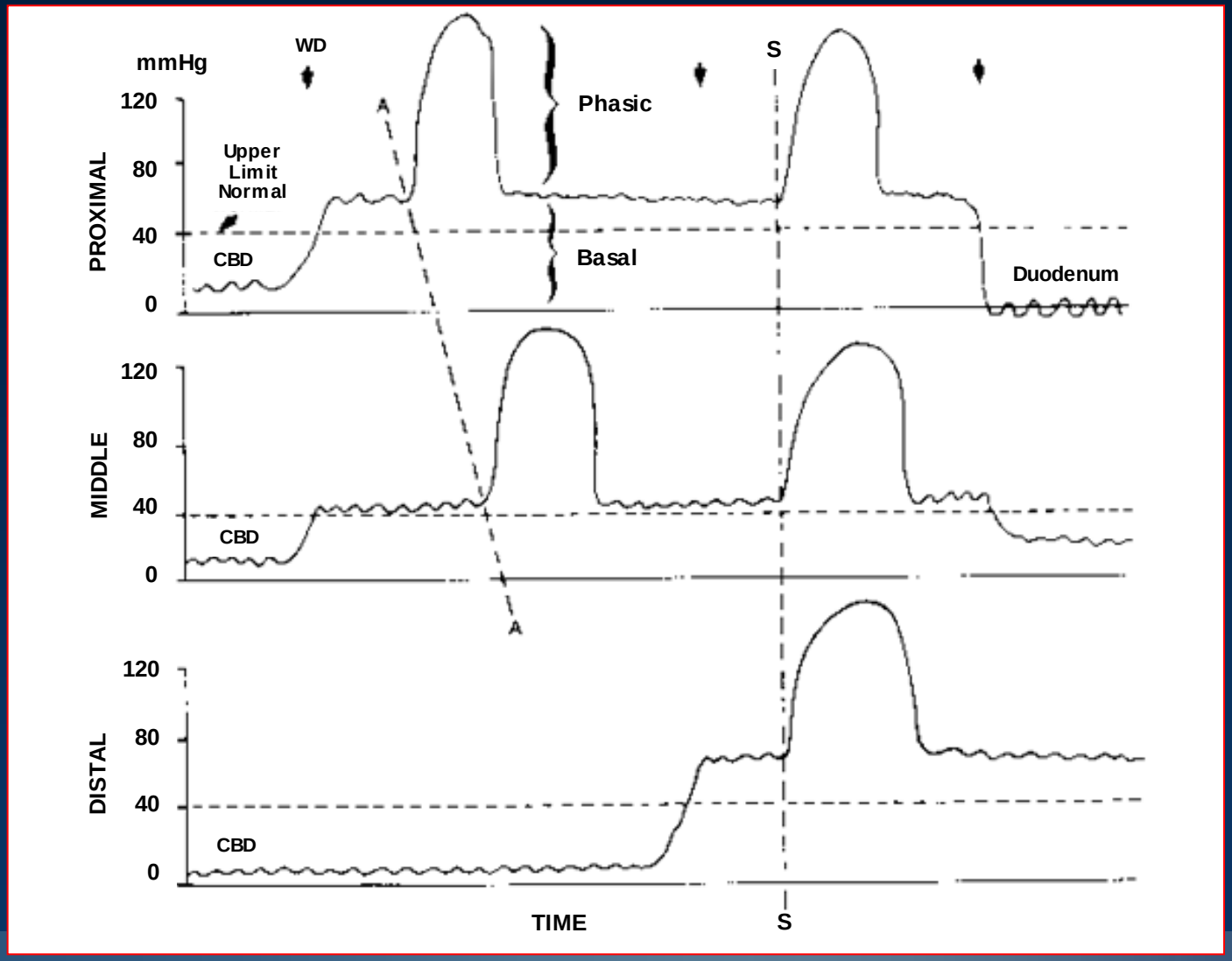
PD

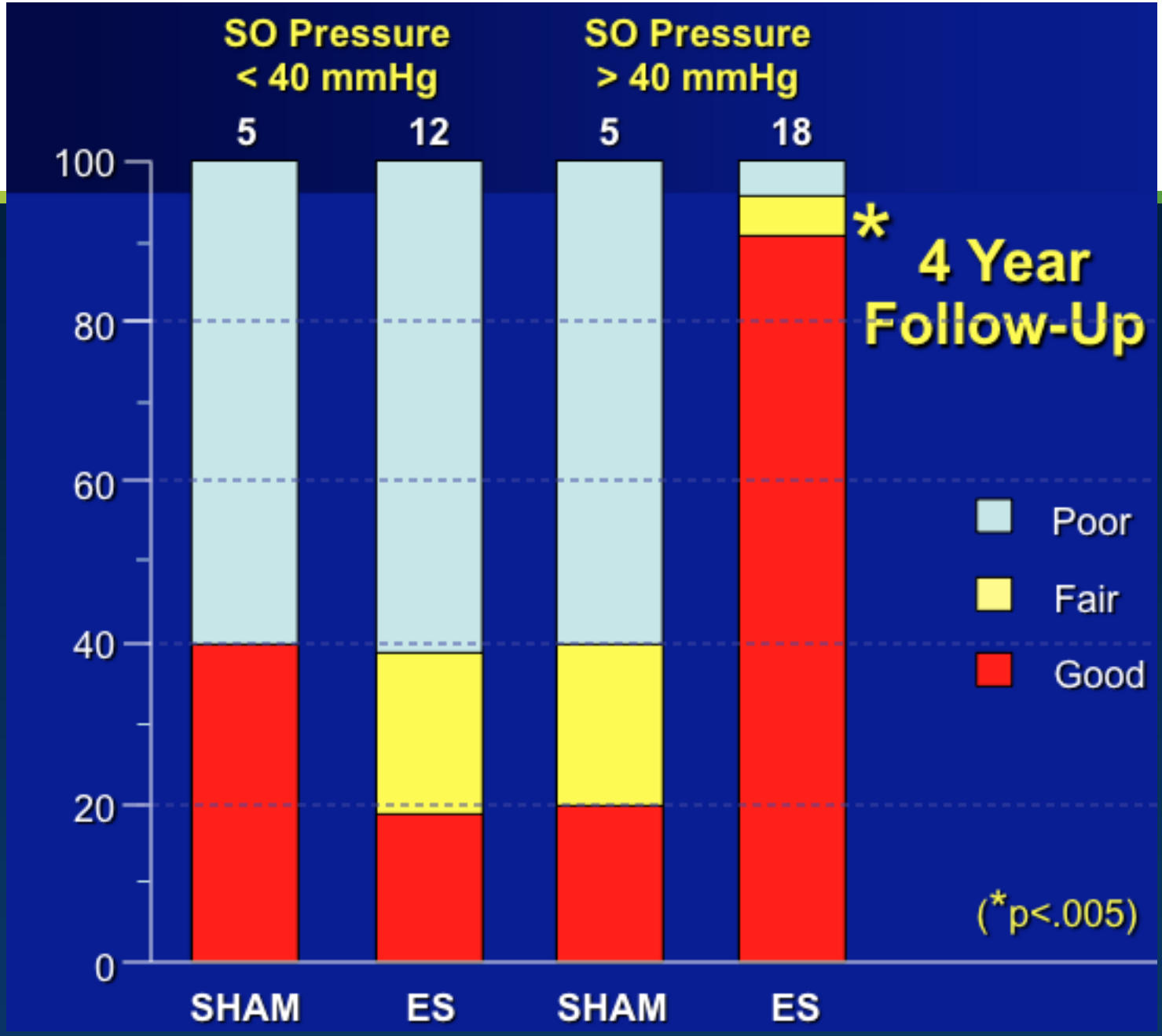
- **EUS + Secretin**
- **MRCP + Secretin**

Sphincter of Oddi Manometry



Sphincter of Oddi Manometry-Profile





Geenen JE et.al, NEJM 1989

RCT comparing ES, S-ES and SSP (with or without CCX)- Results

Therapy	FU (yrs)	Mean Pain Score		# Hosp. Days/Mo.		% Pts.
		Pre-Rx	Post-Rx	Pre-Rx	Post-Rx	Imp.
ES (n=19)	2.9	9.2	3.9*	.85	.26**	68***
S-ES (n=17)	2.0	9.4	6.7	.87	.97	29
SSp ± CCx (n=16)	3.1	9.4	3.3*	.94	.30**	69***

*p<.04; *p=.002; ***p=.02, ES and SSp + CCx vs. S-ES

EPISOD

Evaluating
Predictors and
Interventions in
Sphincter of
Oddi
Dysfunction

"SOD III" (pain only)

Post-cholecystectomy pain with

- normal liver labs and
- normal bile duct size (<10mm)

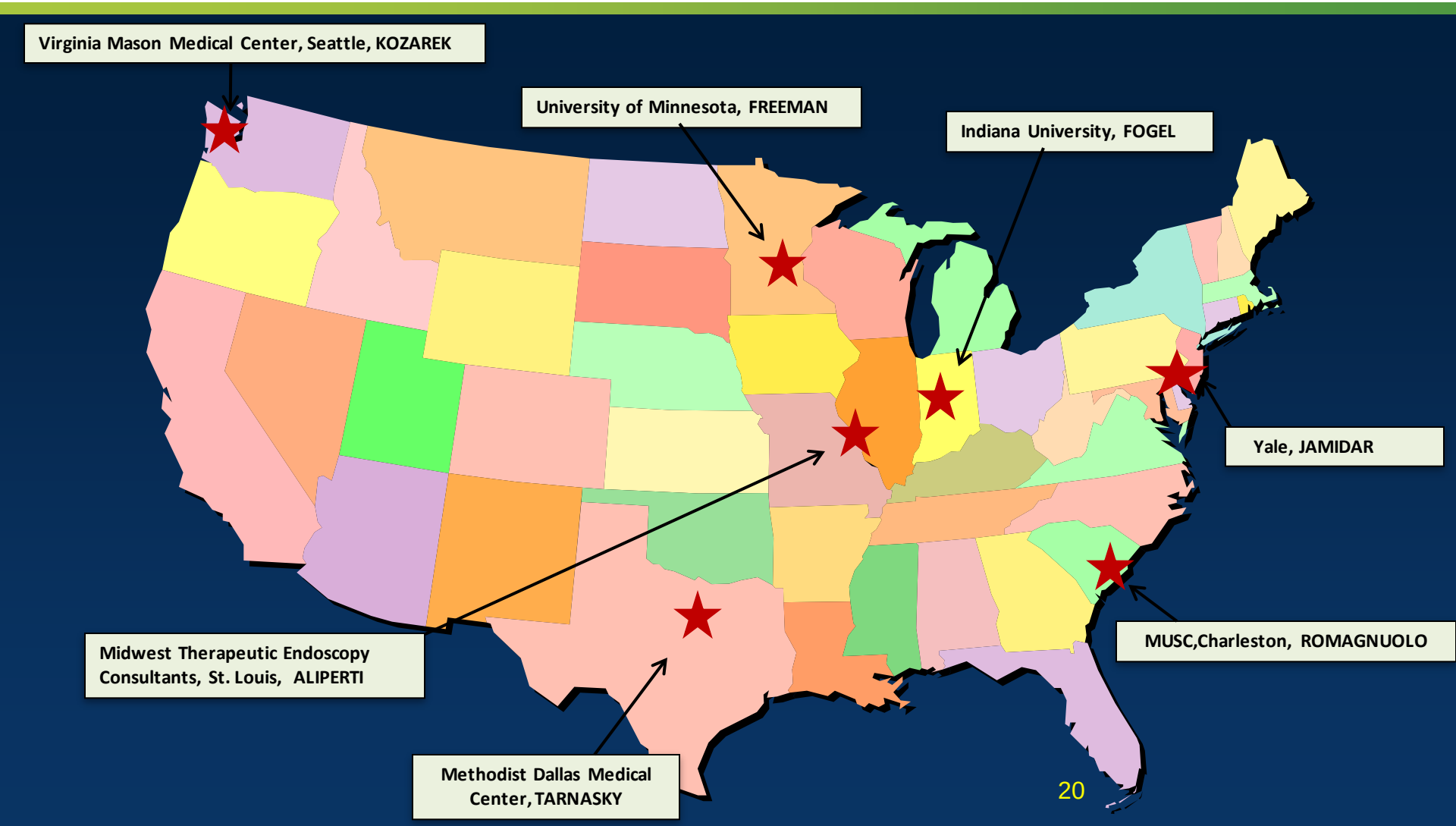
The problem of SOD III

- Results of ERCP/sphincterotomy unimpressive
  - *Unblinded cohort studies, one tiny RCT*
- Manometry is unproven as a predictor
- Risks are substantial
  - *Pancreatitis rate at least 15% . Perforations occur*
  - *Slippery slope of more procedures, and surgery*

Goals for EPISOD

- Which, if any, patients respond to biliary and/or pancreatic sphincterotomy?
- Are there clinical predictors of outcomes?
  - *pain pattern, reason for cholecystectomy and response to it, presence of other functional GI disorders, psychological status*
- Is manometry predictive?

EPISOD Study sites



EPISOD criteria

- Post-cholecystectomy (>3 m), aged 18-65
- Severe biliary pain
- No prior pancreatitis or sphincter treatment
- Normal EGD and scans, bile duct <10mm
- Labs (any time <6 months)
  - *Transaminases < 3xULN*
  - *Alk phos, Amylase, Lipase <2xULN*
- No daily narcotics or severe depression

Baseline characteristics (Brawman-Mintzer Am J Gastro 2014)

- 92% female, mean age 38
- Less psychologically distressed than expected
  - *9% anxiety, 7.5% depression, 17% trauma*
- 34% had IBS
- 26% had taken narcotics in prior month
- 38% on anti-depressants

Methods

- ERCP with manometry of both sphincters
- Randomized 2:1 sphincterotomy vs sham irrespective of manometry results
- Those randomized to sphincterotomy with elevated pancreatic pressures were re-randomized to biliary or dual sphincterotomy
- Temporary stent (all patients) to reduce pancreatitis

Primary outcome

Treatment	Number	Success
Sphincterotomy	141	31 (23%)
Sham	73	26 (37%)

Outcome in patients with PSH

Treatment	Number	Success
Biliary sphincterotomy	51	10 (20%)
Dual sphincterotomy	47	14 (30%)
Overall sham	73	26 (37%)

Manometry not predictive

Manometry		Sphincterotomy success	
Biliary	Pancreatic	Biliary	Dual
+	+	20%	33%
-	+	20%	23%
+	-	21%	
-	-	17%	

Factors predicting success/failure?

- Manometry
- No clinical feature predicted outcome
  - *pain daily or not, presence of IBS, minor lab abnormalities, psyche/anxiety status, reason for cholecystectomy and response to it*

Questions/limitations

- Excluded too many people?
  - *Those least likely to benefit (eg narcotics)*
- Success criteria too strict?
  - *Same with 50% pain reduction, allow narcs*
- Sham arm (ERCP/manometry/stent)
  - *Therapeutic?*
  - *Needed a no-touch arm?*

EPISOD conclusions

- Many subjects improved initially regardless of treatment allocation
- At one year, sphincterotomy was not superior to sham treatment
- Manometry did not predict primary outcome
- Significant risks even with experts
- Alternative approaches are needed for these challenging patients

??? Goodbye SOD types I, II, III

- Type III doesn't exist
- Type I can be diagnosed as stones or stenosis by EUS
- Leaving "Suspected SOD" based on
  - *Biliary type pain*
  - *Abnormal liver labs and/or dilating bile duct*
- More studies needed

EPISOD Reaction

CLINICAL OPINION

Annals of Gastroenterology (2014) **27,** 427-428

EPISOD puts an end to sphincter of Oddi dysfunction type III

Jeffrey D. Mosko, Ram Chuttani

Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

ENDOSCOPIC SPHINCTEROTOMY FOR SPHINCTER OF ODDI DYSFUNCTION: INEFFICACIOUS THERAPY FOR A FICTITIOUS DISEASE

The Sphincter of Oddi Dysfunction Awareness and Education Network

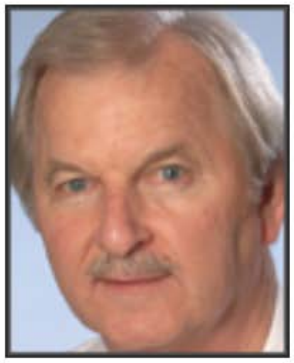
February 13 at 12:08am ·

SOD Advocacy Alert: The American Gastroenerological Association (AGA) refused to pull the damaging article, “Endoscopic Sphincterotomy for Sphincter of Oddi Dysfunction: Inefficacious Therapy for a Fictitious Disease" from circulation. The SODAE Network had formally requested the article be removed as the title alone promotes a discord between gastroenterologists and their patients; and infers that every type of SOD is fictitious. Although we are disappointed, the AGA has encouraged we send a "Letter to the Editor" regarding this matter, which will be sent next week. More details to follow.

AGA Perspectives Online

Sphincter of Oddi Dysfunction: Still Alive?

September 19, 2014



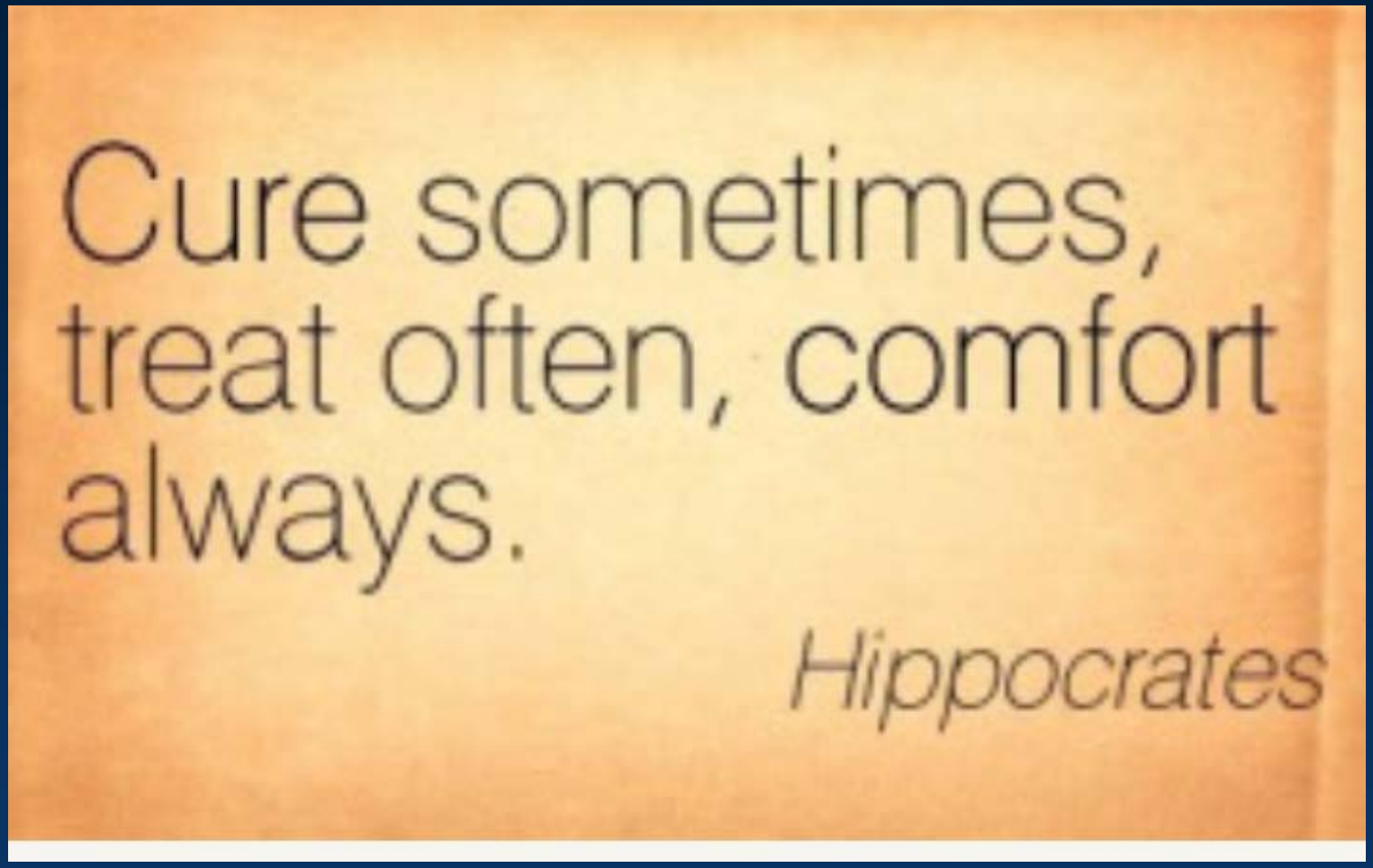
Glen A. Lehman, MD

Indiana University Department of Medicine

EPISOD-other considerations

- Around 3000 publications the last 150 years or so
- ? Adequate Pancreatic Sphincterotomies
- Is it fair to label patients that require retreatments as failures
- IBS 34% of cohort
- Hawthore effect
- What are “normal SO pressures”

What do we do with Type 111 patients now?



What do we do with Type 111 patients now?

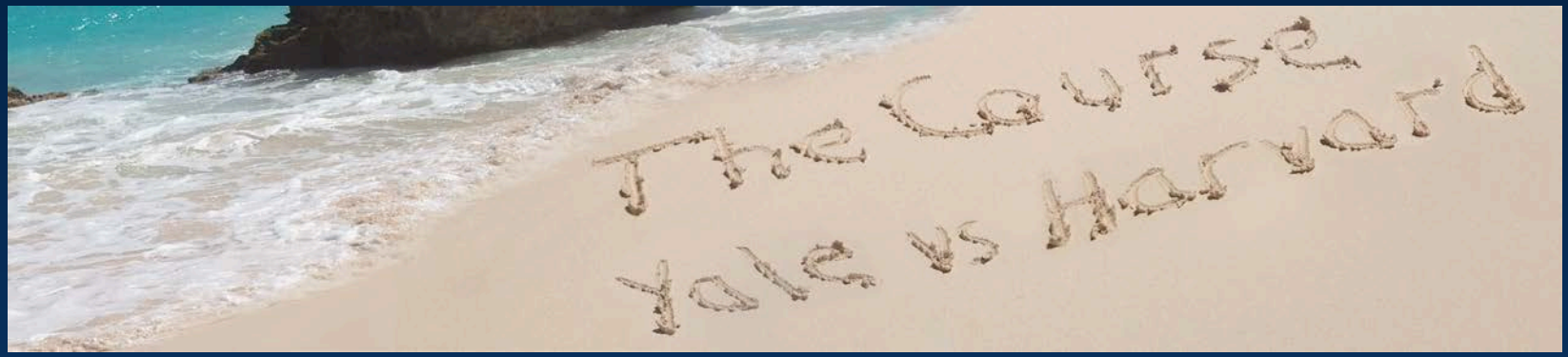
- Consider other diagnosis
  - *Chronic functional abdominal pain*
  - *Visceral hypersensitivity*
  - *Narcotic Bowel Syndome*
  - *Chronic pancreatitis*
  - *Irritable Bowel Syndrome*

What do we do with Type 111 patients ?

- ***DO NOT DO ERCP !!!!***
- Many desperate patients, referral for SOM is end of the road
- Long term pain management not a great option
- Trial of medical therapy i.e, low fat diet, antispasmodics, acid suppressive therapy etc
- Support and reassurance
- ? Role for Botox injections

The Course: Yale vs. Harvard, Hamilton Princess Hotel Bermuda. June 13 and 14, 2014

The Course: Yale vs. Harvard, Hamilton Princess Hotel Bermuda. June 13 and 14, 2014



The Course: Yale vs. Harvard, Southhampton Princess Hotel Bermuda. April 17 and 18, 2015

The Course: Yale vs. Harvard, SouthHampton Princess Hotel Bermuda. April 17 and 18, 2015