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Expert

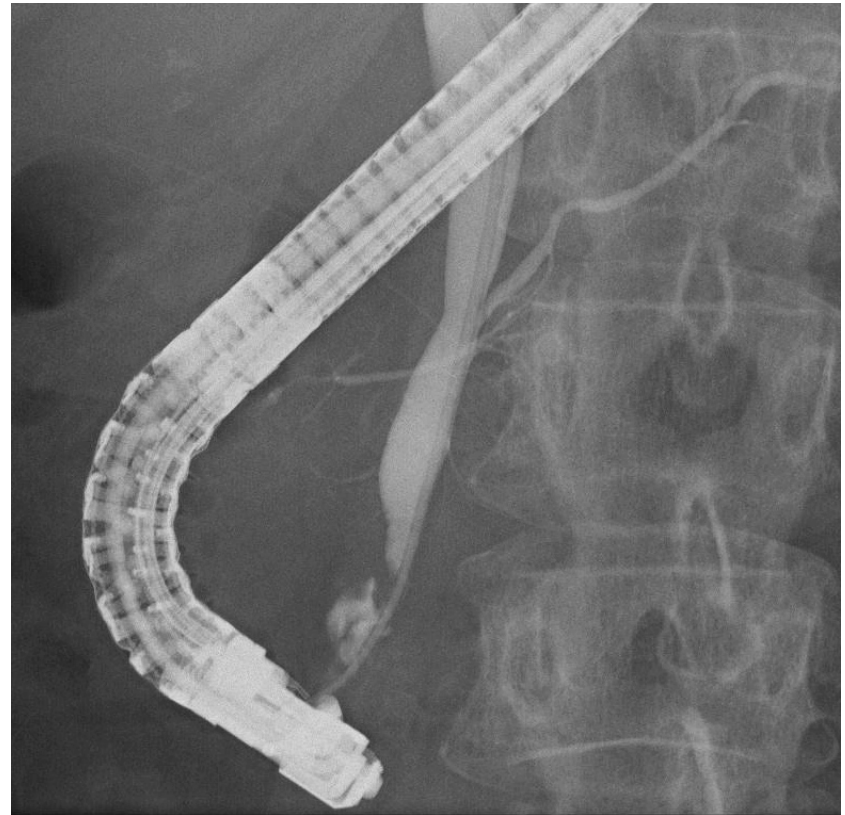
- Prenatal diagnosis,
Transitional type to Biliary Atresia 163–174

Advanced

Common channel & Narrow segment

First version, September 2024

Is the common channel a pancreatic duct or a bile duct?



PD branches coming out of the common channel support it is a PD.

Dilated common channel composed of both PD and BD

Proposed by Ando H in 1999

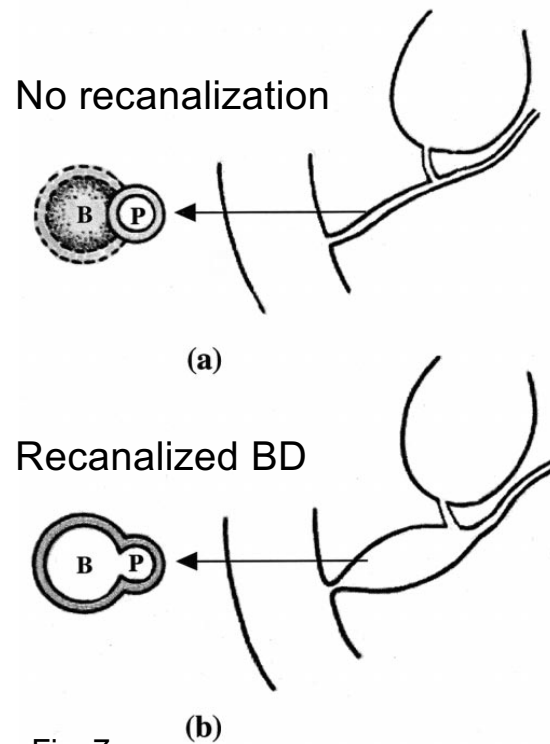
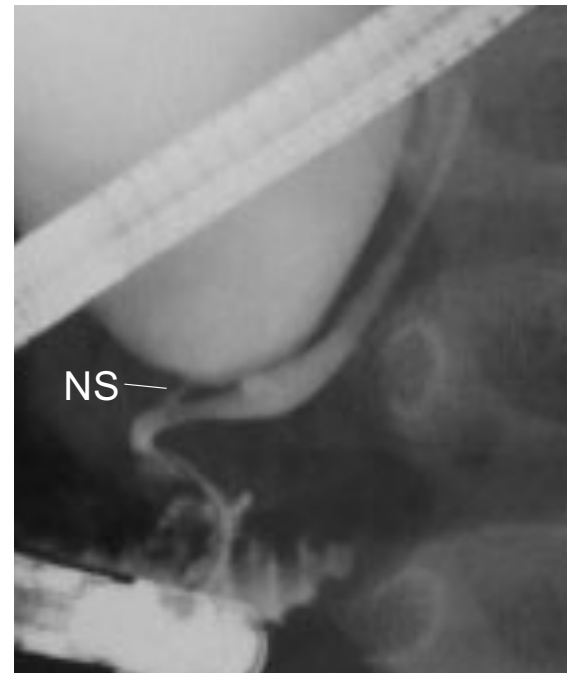
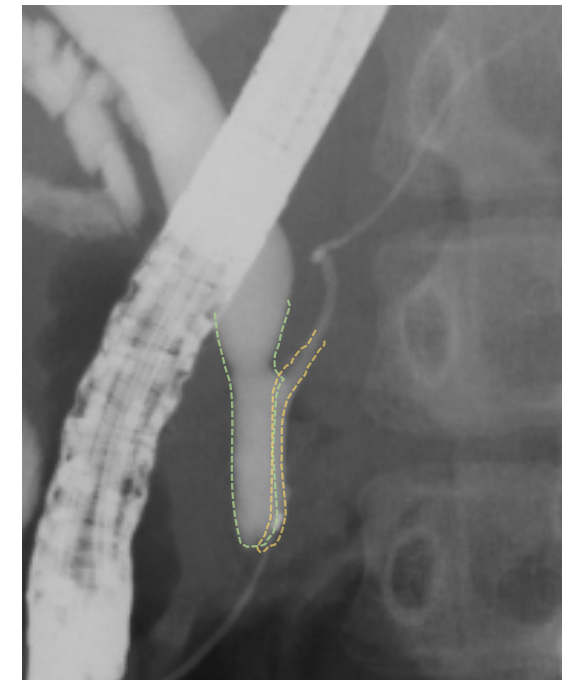


Fig. 7

Ando H, Kaneko K, Ito F, Seo T, Harada T, Watanabe Y.
Embryogenesis of pancreaticobiliary maljunction inferred
from development of duodenal atresia.
J Hepatobiliary Pancreat Surg 1999;6(1):50-4



PD alone



BD+PD

Case from *Basic Section*

See P43.

NS is a branch of PD

Histopathological demonstration

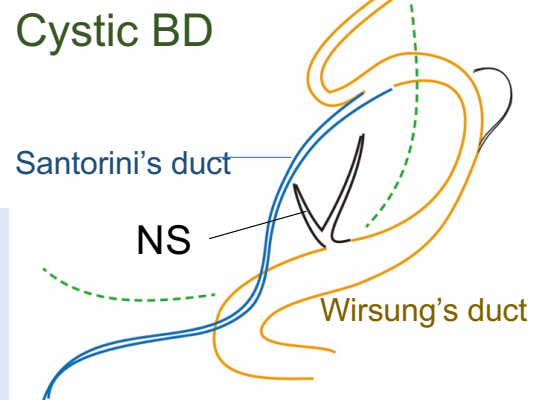
Suda K, Matsumoto Y, Miyano T.
Narrow duct segment distal to
choledochal cyst.

Am J Gastroenterol. 1991
Sep;86(9):1259-63. PMID:
1882808.

Case 9

ERCP in a 1-year-old
girl
Vomiting and elevated
levels of pancreatic
enzymes

Radiological demonstration



NS is one branch
of PD



Matsumoto's theory of PBM embryogenesis:
PBM is a result of BD misconnecting with
ventral PD or its branches. See P122.

Is NS really a PD branch?

In some cases of type Ic fusiform dilatation, the narrowed portion beneath the dilated BD may be considered as a normal BD rather than the narrow segment (NS). There is no abrupt narrowing in these cases.

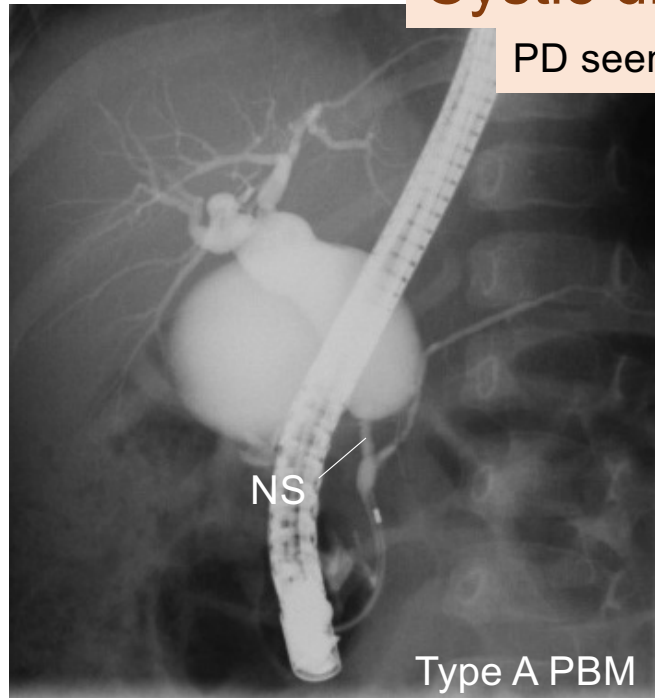
- JSGPBM classification (See P33.):
Type B, non-stenotic type rather than Type A, stenotic type
- The BD should be resected completely down to the PD using fluoroscopy with clips. See Next and P70.



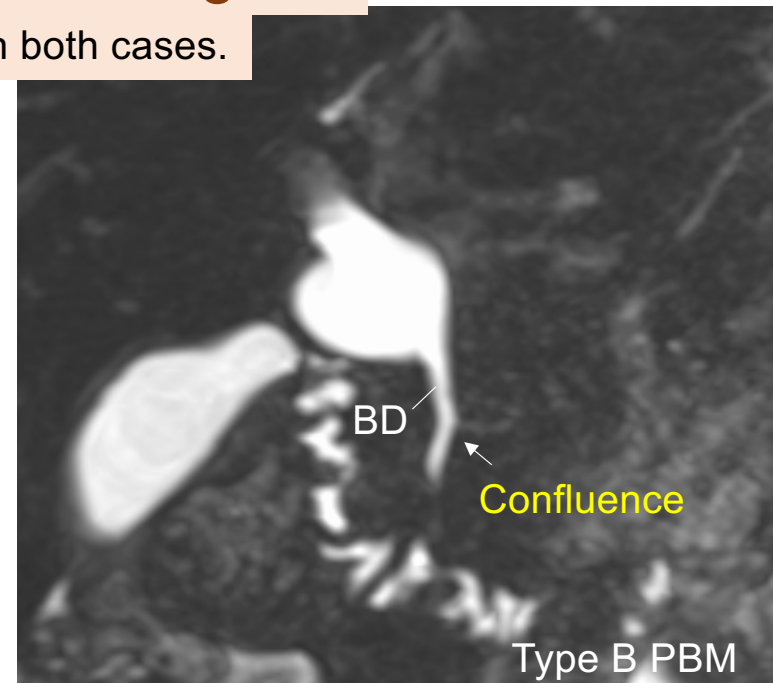
Is NS really a PD branch?

Cystic dilatation with a long NS

PD seems to enter BD in both cases.

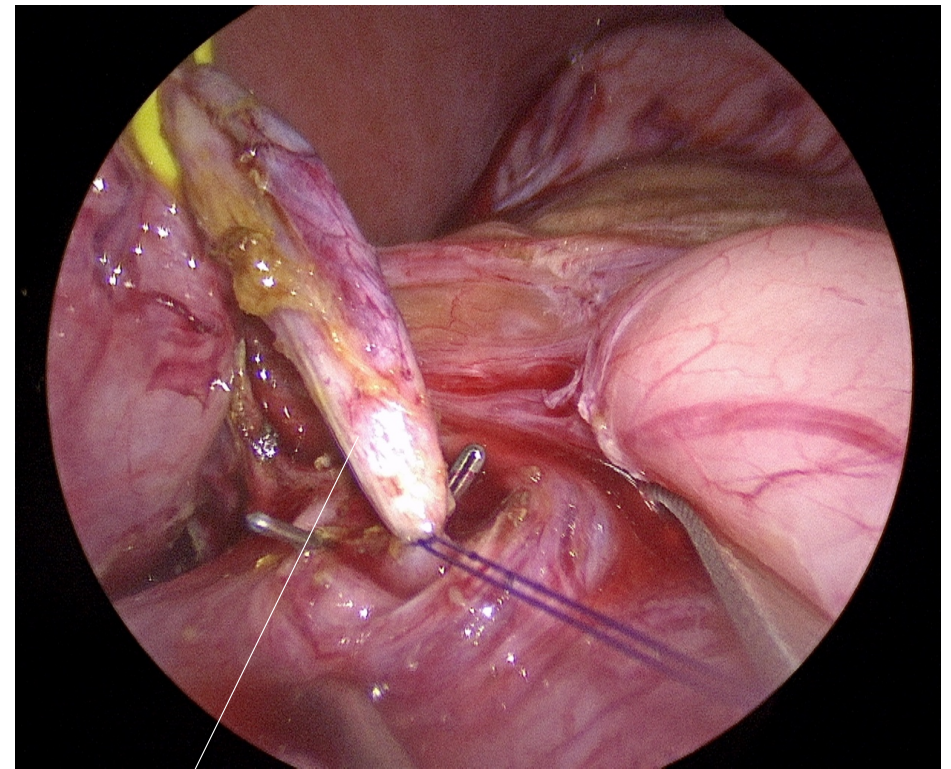
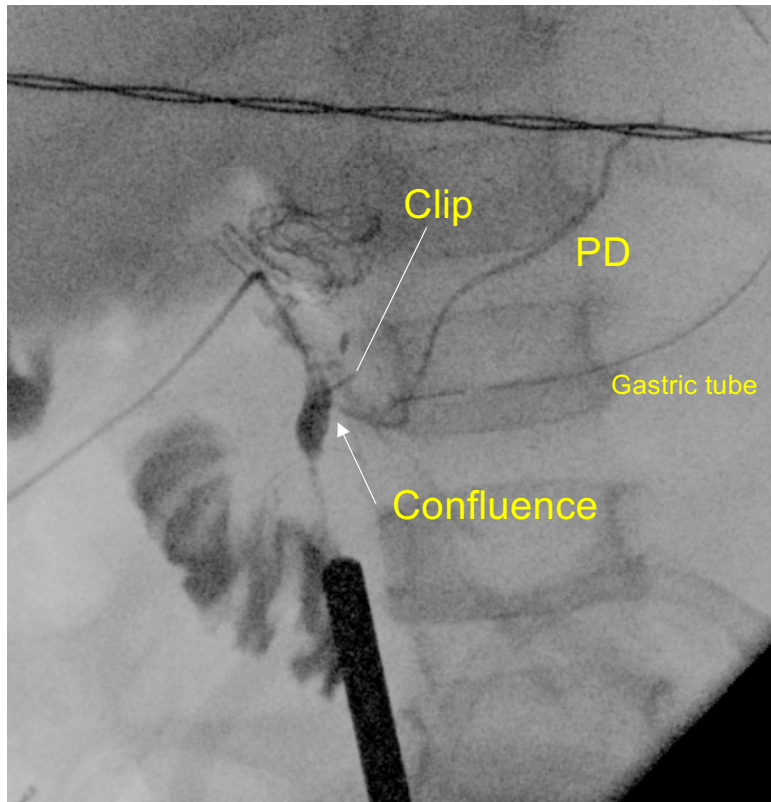


One-year-old child
Vomiting, elevated serum levels of liver enzymes and amylase
BD resected at the obvious NS.



Three-year-old girl
Abdominal pain, vomiting, and elevated serum levels of liver and biliary enzymes
No abrupt narrowing needed using fluoroscopy with clips. See next.

Surgery showed no NS.
BD was resected just above the PD using fluoroscopy with clips.



The narrowing portion on MRCP was a normal BD.

Is NS really a PD branch?

A PD branch and a narrowed BD may compose the NS

Pediatric case

Portion of BD
Portion of PD branch

Surgery confirmed NS

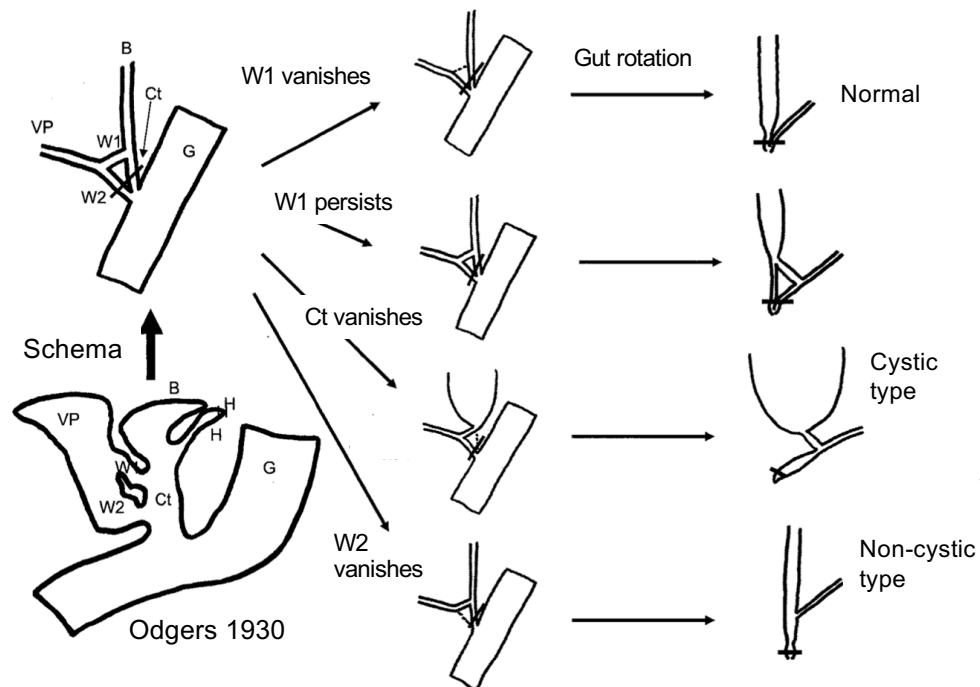
Adult case
Loop type of PD

Portion of BD
Portion of PD branch

Surgery confirmed NS

Matsumoto's theory of PBM embryogenesis:
PBM is the malformation where the choledochus misconnects with the ventral PD or its branches outside the duodenal wall. See next.

PBM embryogenesis



Cited from Itaru Oi. Tokyo Women's Medical University Journal 2008;78:55-60

Oi's theory of PBM embryogenesis in 1977
 Estimation based on Odgers's embryogenesis of PD (1930)
 W1, Left ventral pancreas duct; W2, right VP duct; Ct, terminal choledochus

Two classic theories

Confluence site of BD and ventral PD in congenital biliary dilatation



Cited from Yoshiro Matsumoto. Nippon Shokakibyo Gakkai Zasshi 1986;19:614-23

Matsumoto's theory of PBM embryogenesis in 1986
 Based on the fact that BD never enters a dorsal PD in PBM

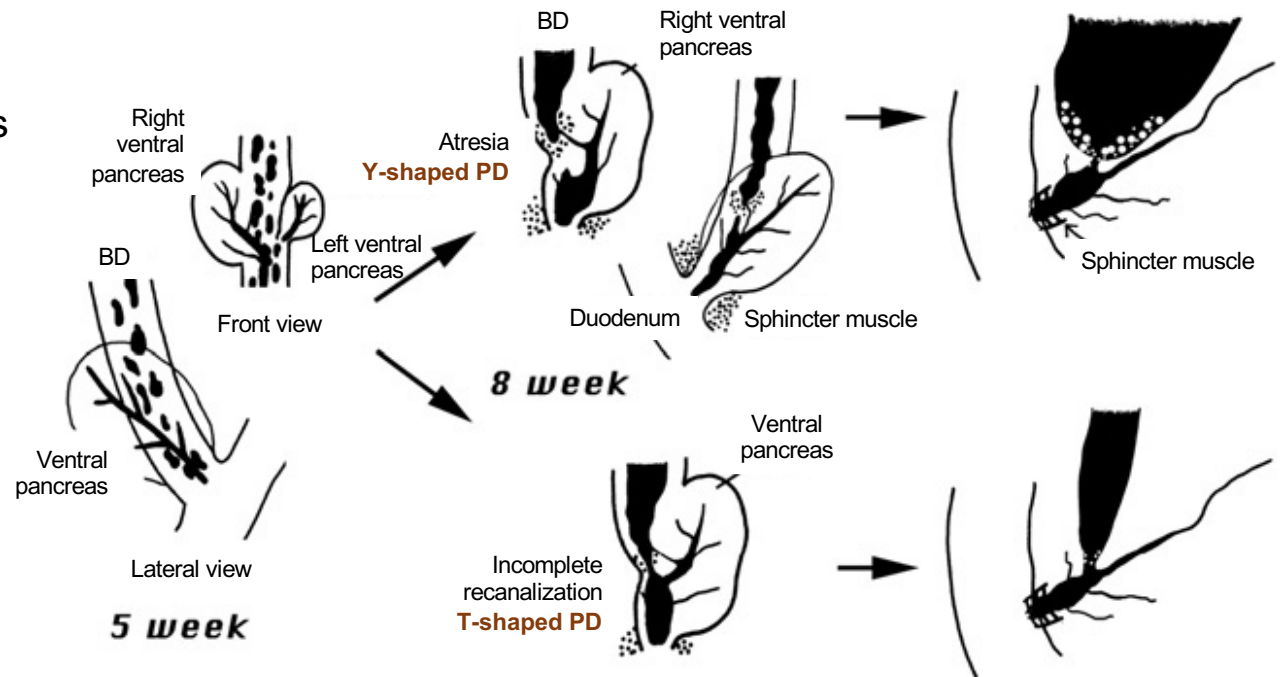
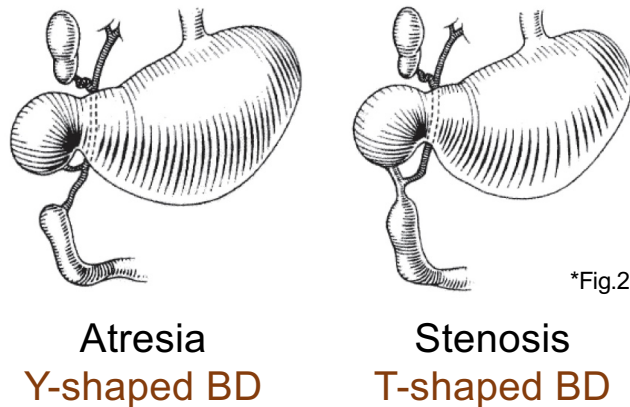
He thought that PD branches coming out of the common channel (CC) on cholangiopancreatography (See P115.) suggested that the CC was a PD. He estimated that PBM is the malformation where the choledochus misconnects with the ventral PD or its branches outside the duodenal wall.

See Cases 9* and 42**.

PBM embryogenesis

Ando H, Kaneko K, Ito F, Seo T, Harada T, Watanabe Y.
Embryogenesis of pancreaticobiliary maljunction inferred from
development of duodenal atresia.
J Hepatobiliary Pancreat Surg 1999;6(1):50-4*

Congenital duodenal atresia and stenosis
Disorder of recanalization from the solid stage



Cited from Hisami Ando. Tando
(Biliary Tract) 2008;22:175-80

Inferred from embryogenesis of congenital duodenal atresia and stenosis
BD has a solid stage during its development as well as the duodenum,
while PD does not have a solid stage.

Because almost all congenital diseases with limited BD dilatation have PBM, there must be embryological relationship between them. However, does regurgitation due to PBM really cause biliary dilatation?



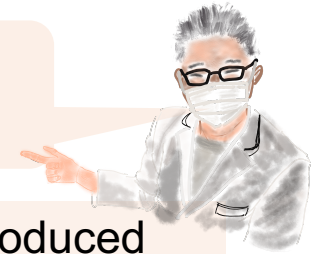
Advanced

What causes biliary dilatation?

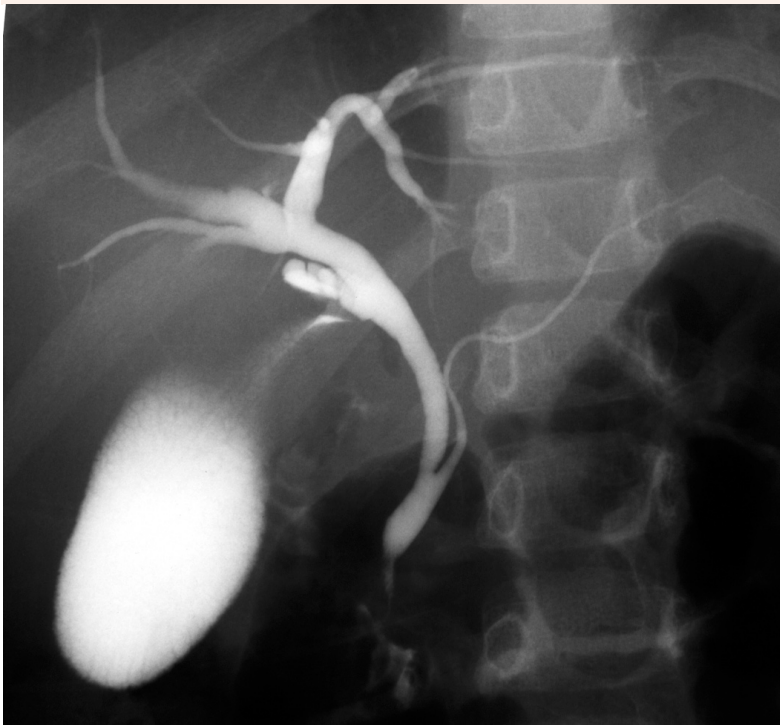
First version, September 2024

Regurgitation of pancreatic juice does not cause biliary dilatation

When the idea of PBM became popular in Japan, it was thought that bile duct injury due to pancreatobiliary reflux was the cause of dilatation.



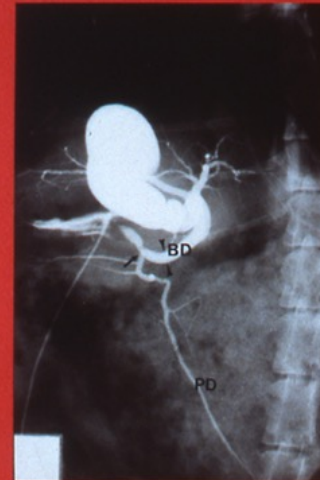
Non-dilated type of PBM exists



Pediatric case of non-dilated PBM
The common channel is dilated but BD is not.

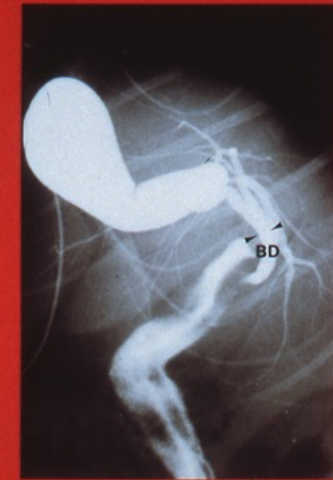
Cystic dilatation was not produced in animal PBM models

Cholangiography



PBM model

2.72 ± 0.60 (mm)



Control

2.33 ± 0.76 (mm)

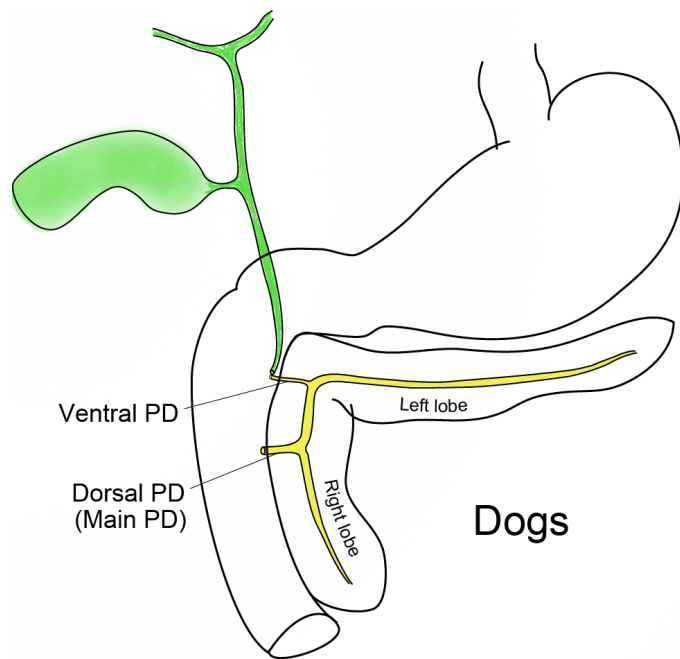
Cat model of PBM
BD did not dilate.

Pancreatobiliary anatomy differs among animals

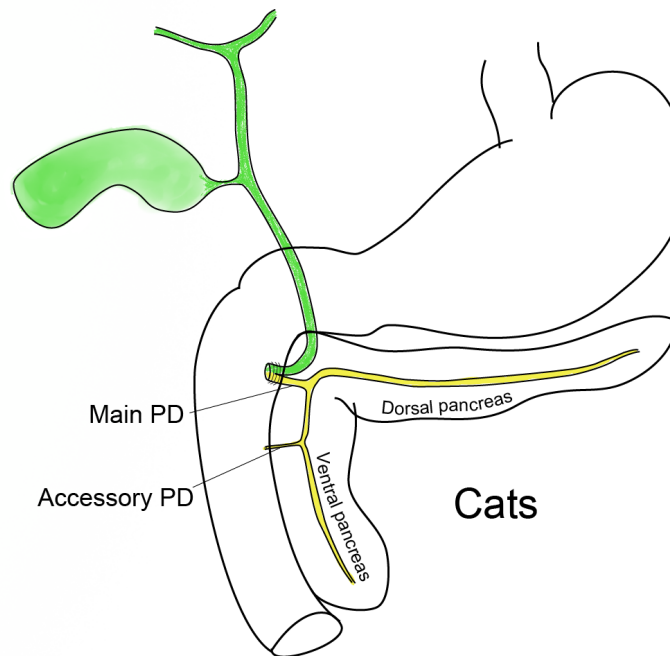
BD joins the accessory PD

Similar to human anatomy

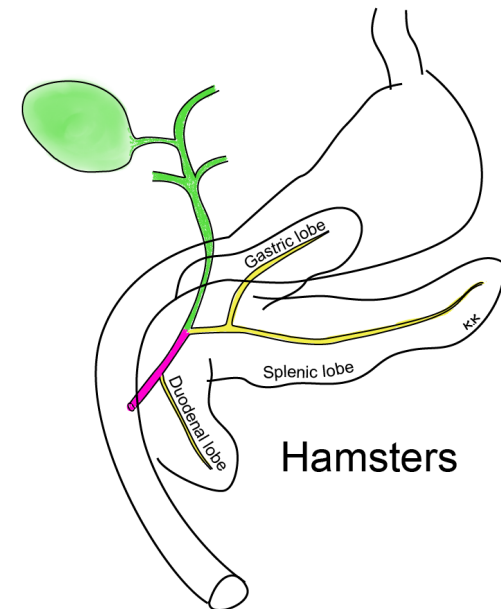
PBM is normal in
rodents, goats, and sheep



Dogs



Cats



Hamsters

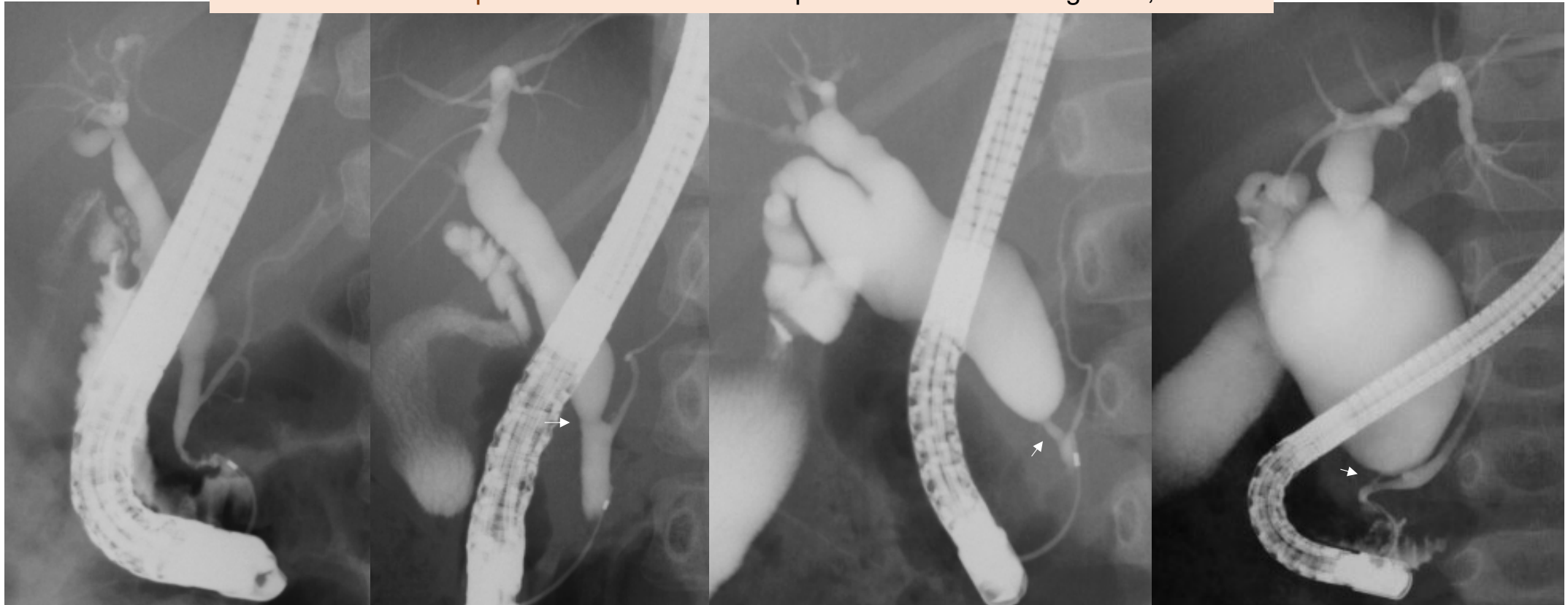
The cause may be the narrow segment (NS)

Dilatation related with NS length

Increased intraductal pressure due to NS

Ando H. Jpn J Surgery 1983;84:1174-85

Davenport et al. J Pediatr Surg 2005;40:331-5



No NS

Slight constriction

Thick NS

Thin NS

NS alone cannot explain characteristic dilatation

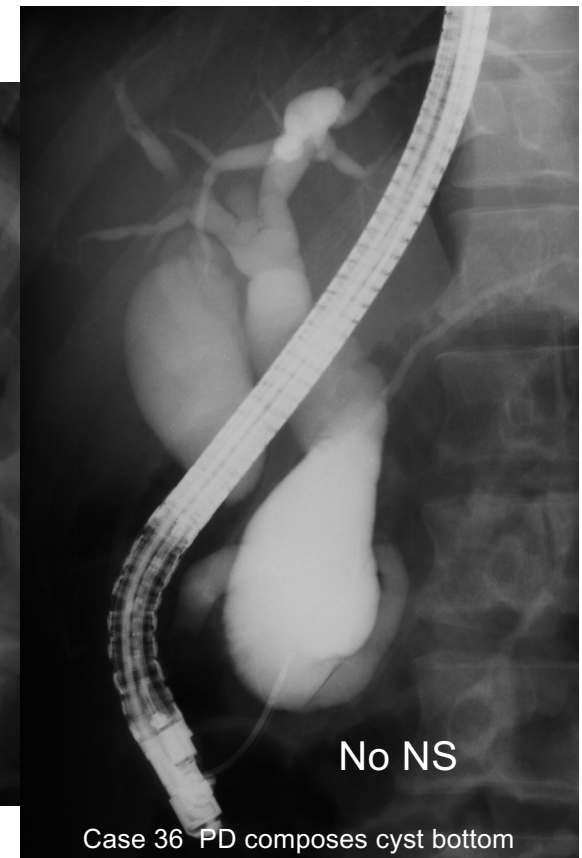
Increased ductal pressure cannot cause limited dilatation See P11.



Limited dilatation

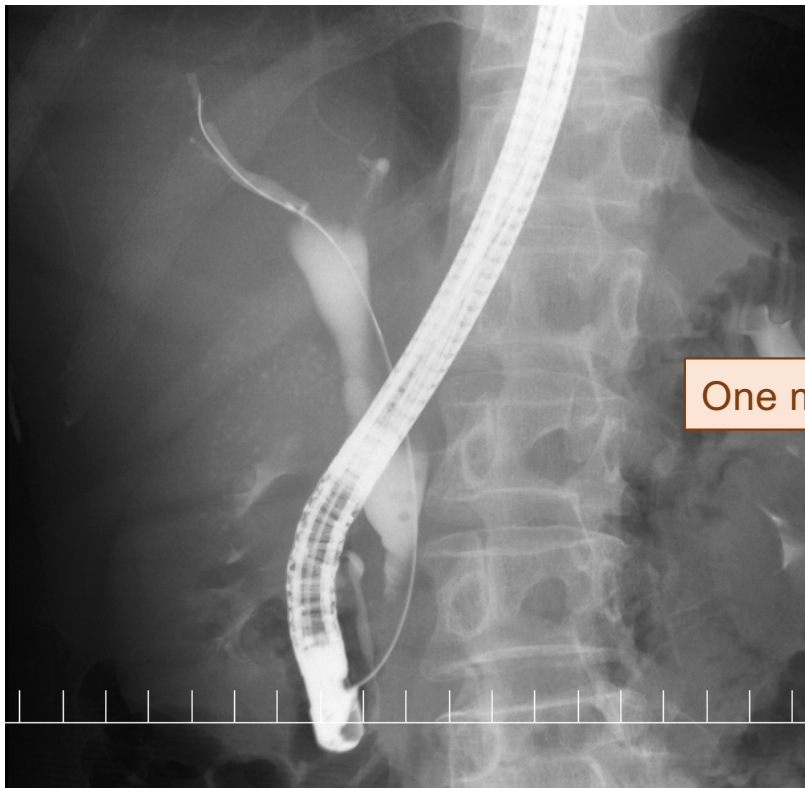


Limited dilatation
Intrahepatic bile ducts are more dilated

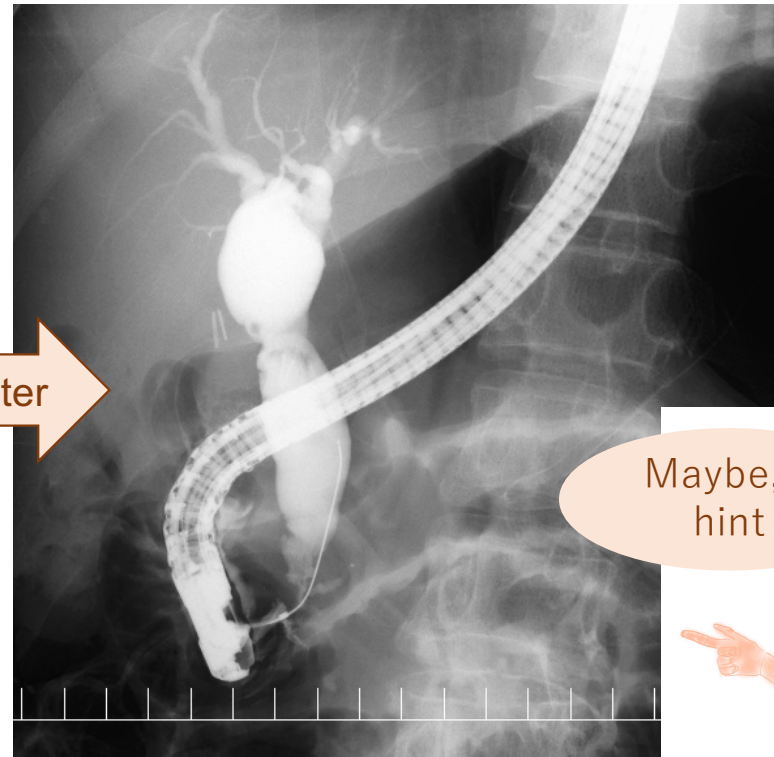


Acquired limited BD dilatation

Chronic intermittent increase of intraductal pressure



One month later



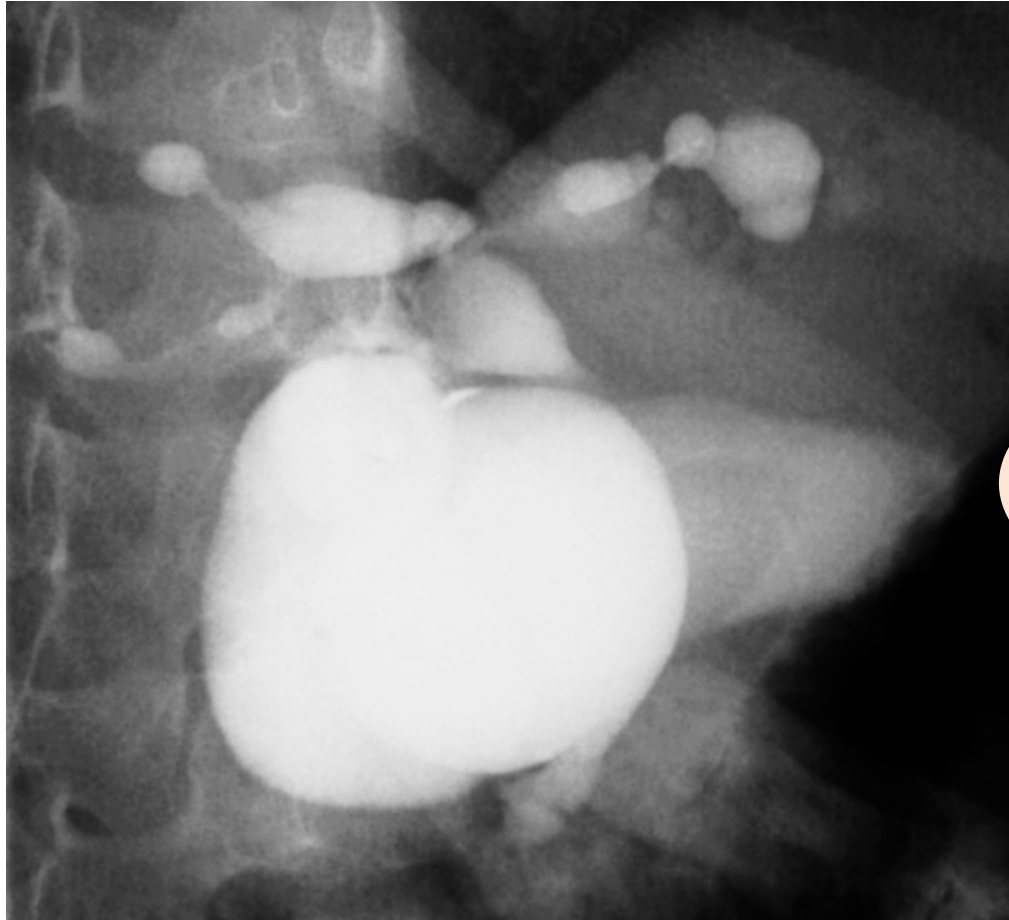
Maybe, a hint



Male in his fifties, Bile duct stones

The common hepatic duct became larger but upstream BDs did not dilate.

Peripheral cystic dilatation of Intrahepatic BDs

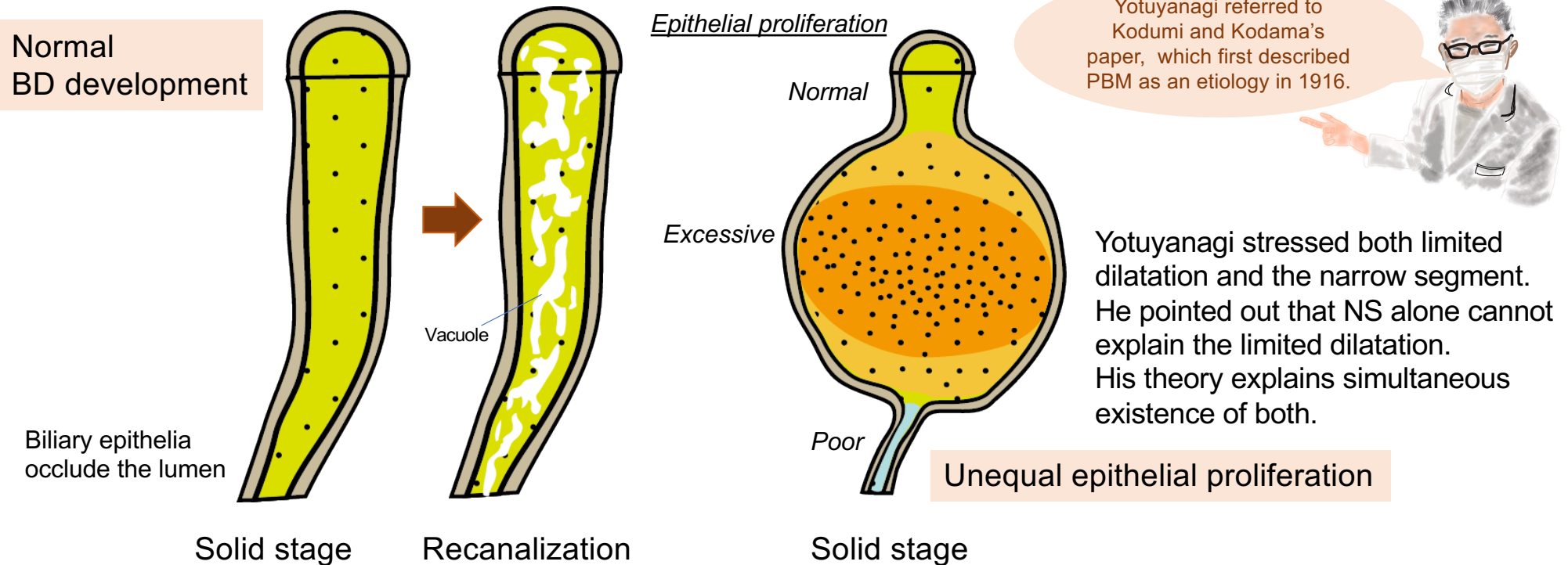


However, it is difficult to explain this phenomenon only by high pressure.



Yotuyanagi's etiological theory in 1936

Limited dilatation in congenital biliary dilatation



Yotuyanagi S. Contributions to the aetiology and pathogeny of idiopathic cystic dilatation of the common bile-duct with report of three cases; A new aetiological theory based on supposed unequal epithelial proliferation at the stage of the physiological epithelial occlusion of the primitive choledochus. Gann 1936;30:601-52

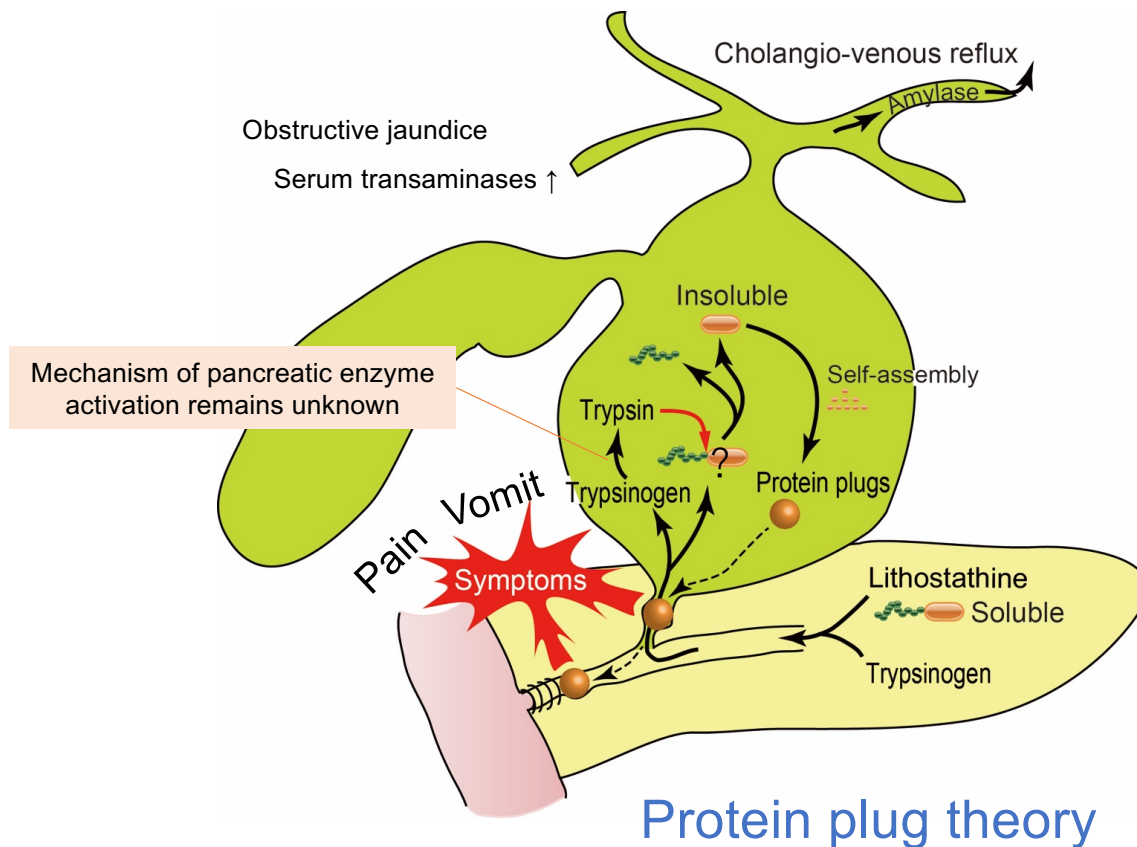
Advanced

Pathophysiology in pediatric patients

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Symptomatology in childhood

See Basic Section, P18-23.



Fragile protein plugs occlude the narrow segment or the common channel, producing a transient increase of intraductal pressure and cause the symptoms.

Findings supporting protein plug theory

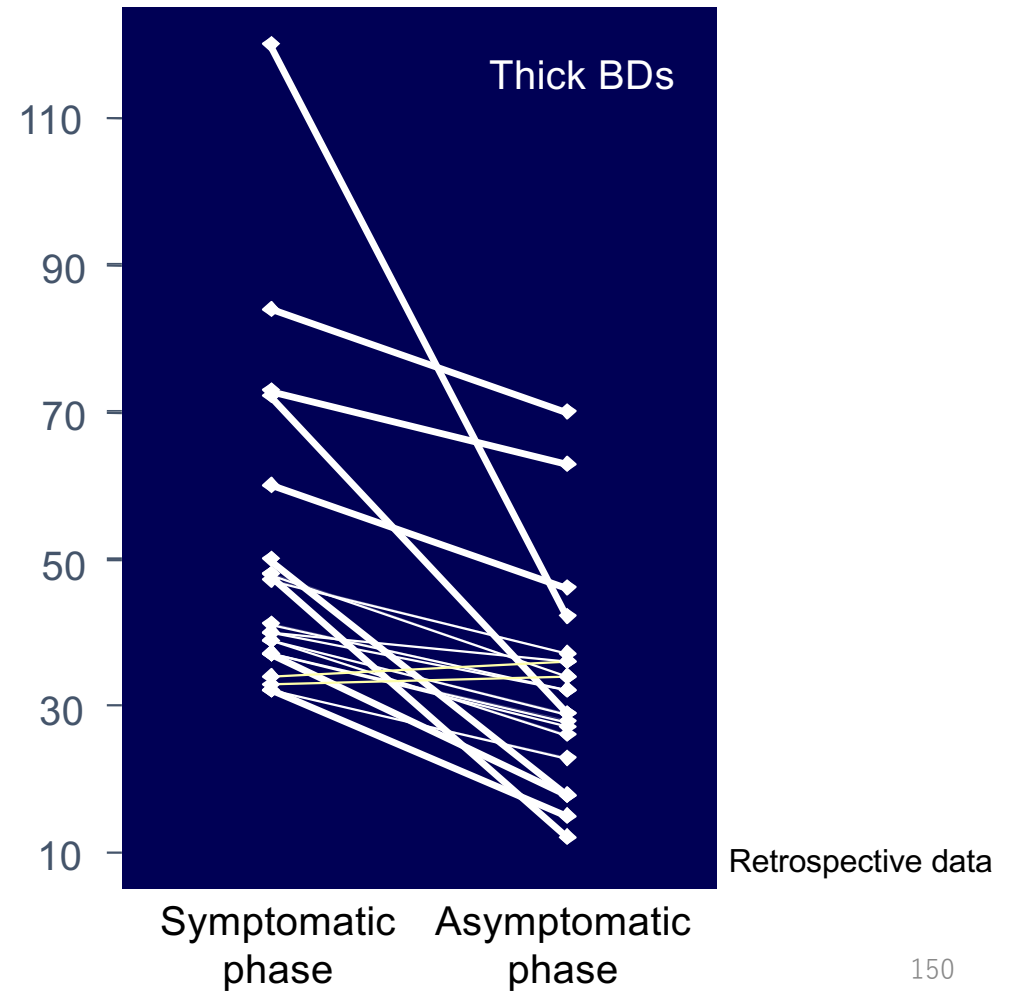
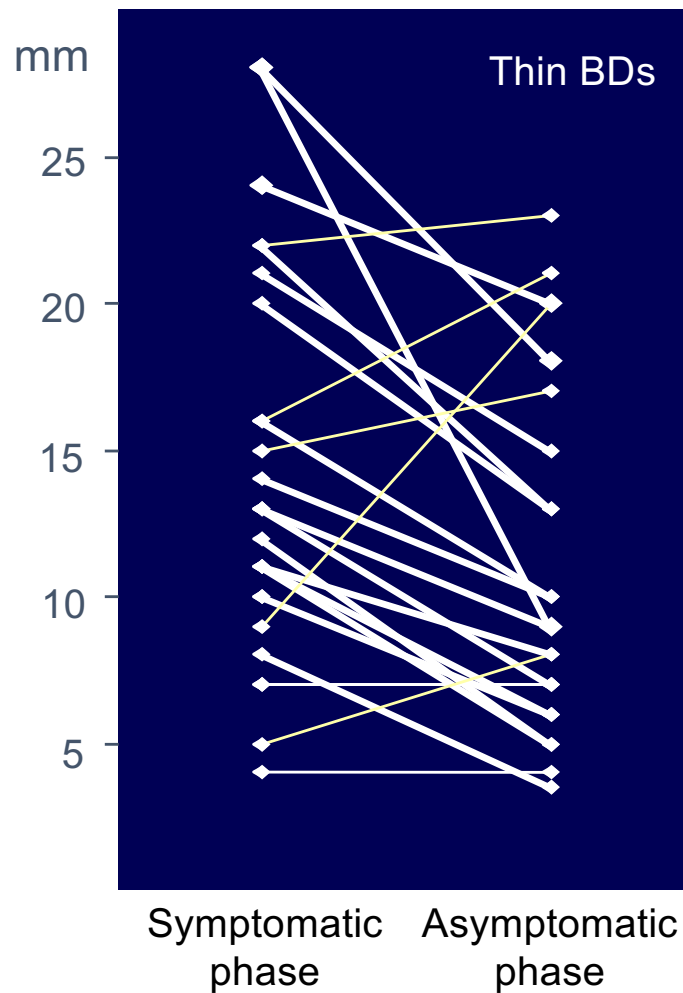
Endoscopic drainage promptly relieves persistent or exacerbated symptoms



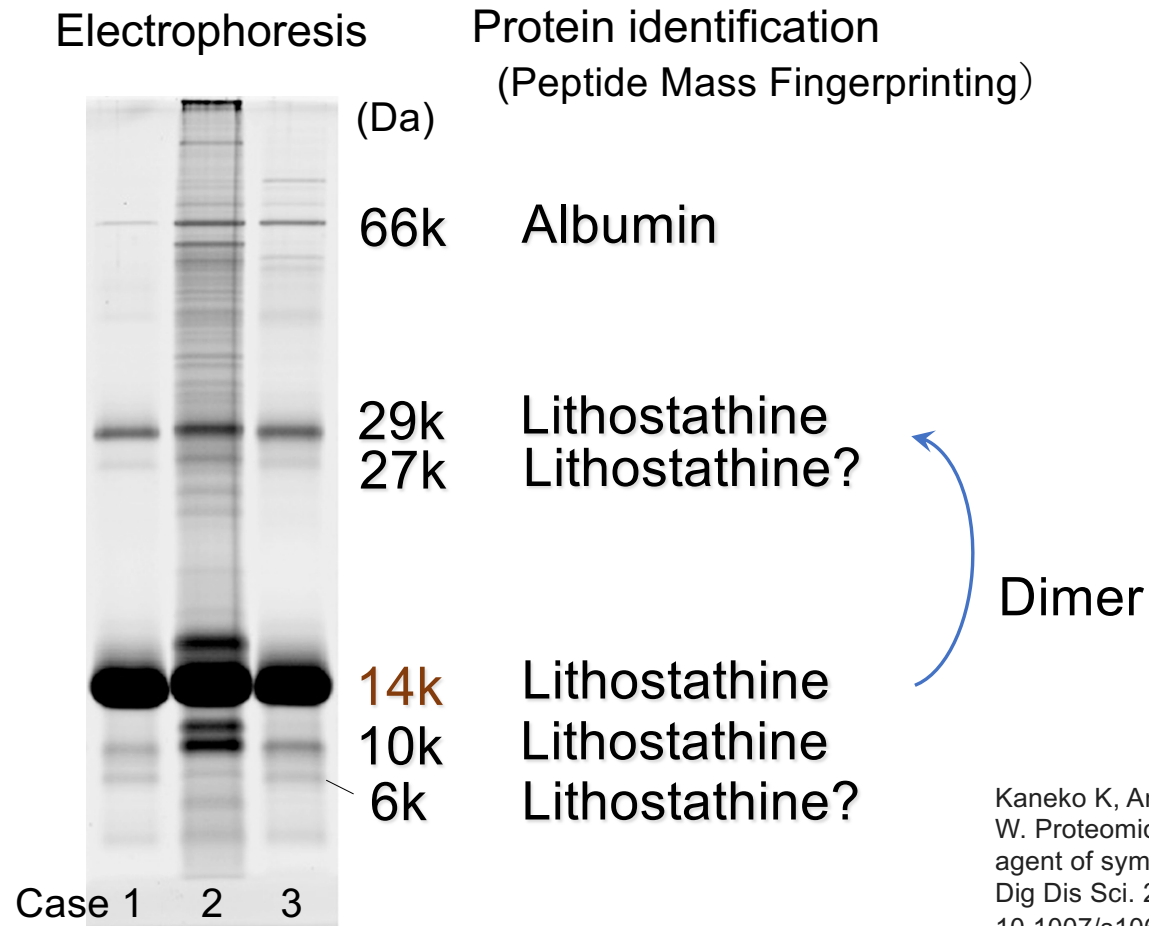
Tsuchiya H, Kaneko K, Itoh A, Kawashima H, Ono Y, Tainaka T, Murase N, Ando H. Endoscopic biliary drainage for children with persistent or exacerbated symptoms of choledochal cysts. J Hepatobiliary Pancreat Sci. 2013 Mar;20(3):303-6. doi: 10.1007/s00534-012-0519-5. PMID: 22581057. Fig. 1

Findings supporting protein plug theory

Diameter of the common bile duct is larger in symptomatic phase



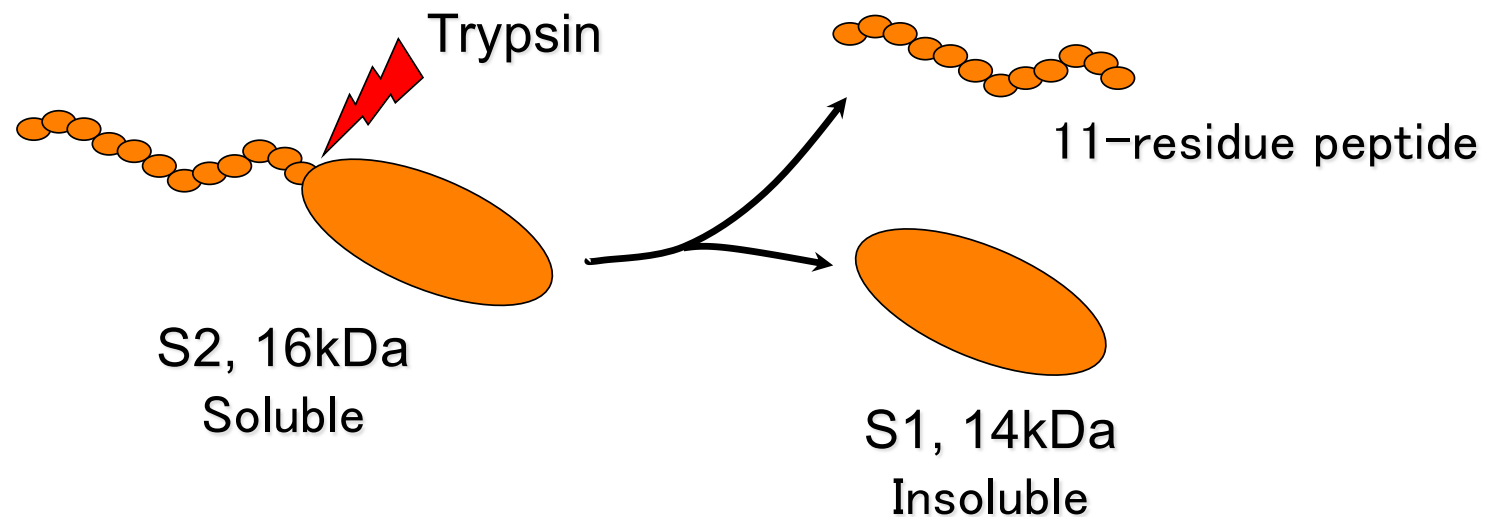
Protein plugs are composed of lithostathine



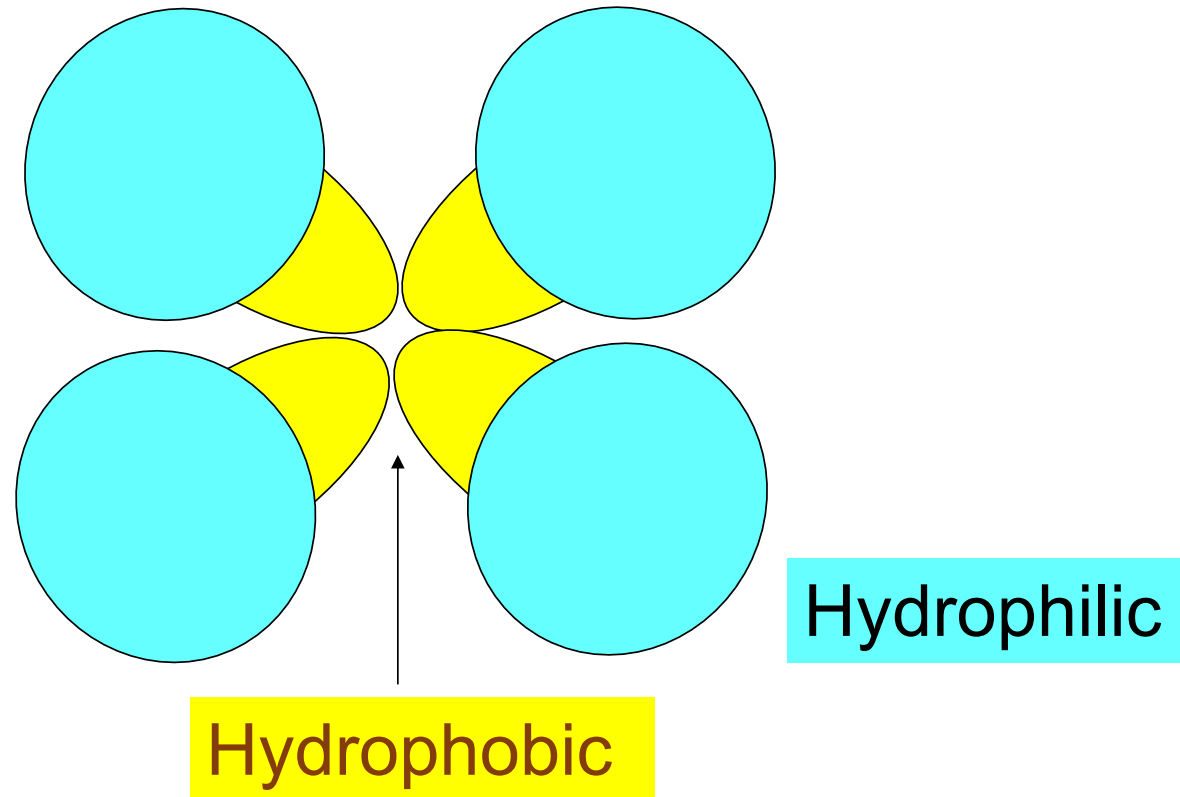
Kaneko K, Ando H, Seo T, Ono Y, Tainaka T, Sumida W. Proteomic analysis of protein plugs: causative agent of symptoms in patients with choledochal cyst. Dig Dis Sci. 2007 Aug;52(8):1979-86. doi: 10.1007/s10620-006-9398-4. Epub 2007 Apr 6. PMID: 17415647.

Lithostathine

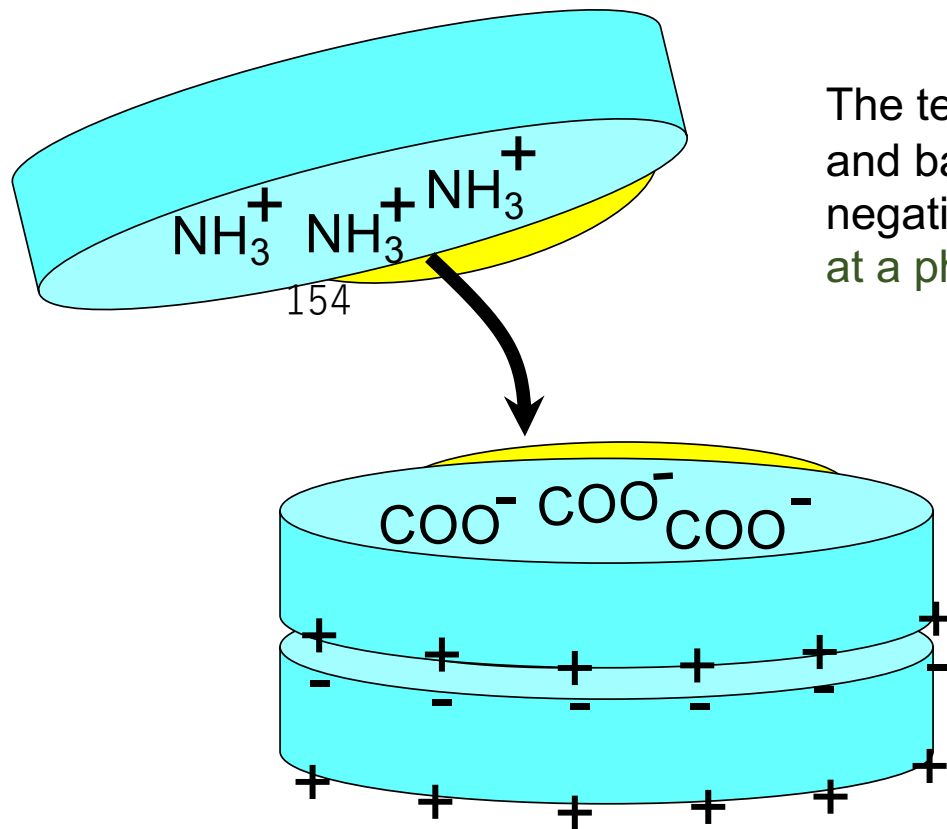
- Soluble 144-amino acid glycoprotein secreted by pancreatic acinar cells
- Accounts for 5%-10% of proteins in pancreatic juice but unknown function
- Many other names such as pancreatic stone protein (PSP)



Lithostathine S1 forms tetramers by lateral hydrophobic interactions



Tetramers self-assemble by longitudinal electrostatic interactions

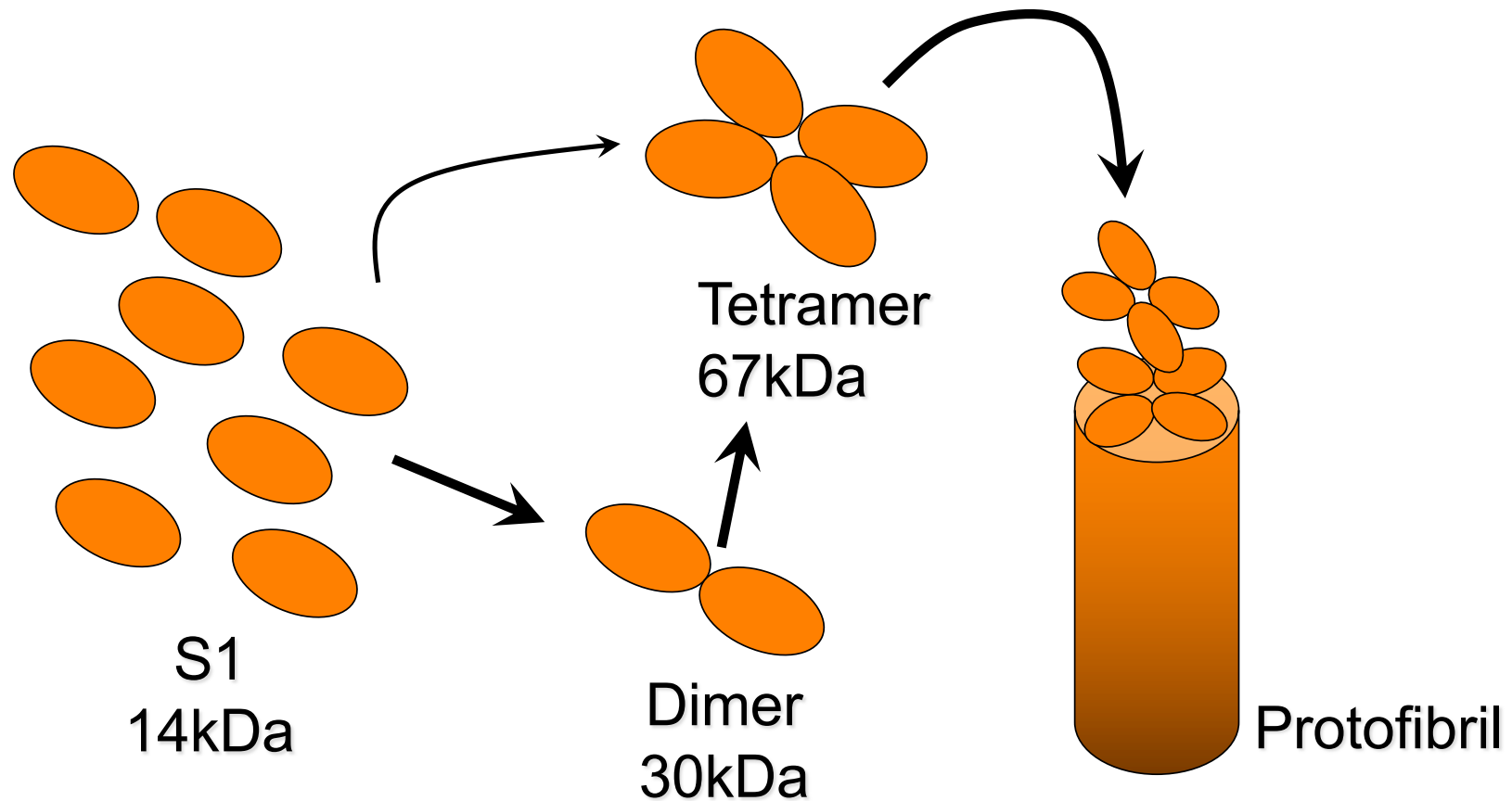


The tetramer has acidic residues on one side and basic residues on the other, contributing negative and positive charges, respectively, at a physiologic pH.

Low pH	Physiologic PH	High pH
$-\text{NH}_3^+$	$-\text{NH}_3^+$	$-\text{NH}_2$
$-\text{COOH}$	$-\text{COO}^-$	$-\text{COO}^-$

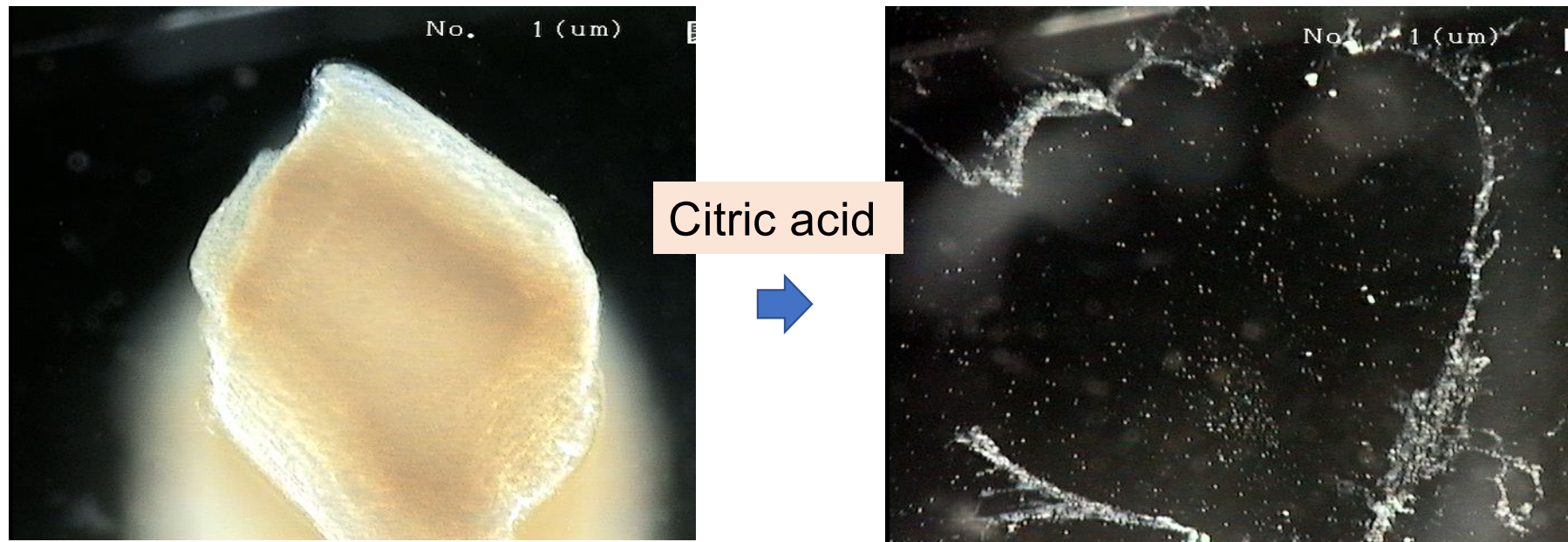
Gregoire et al. EMBO J 2001;20:3313–3321

Cleaved lithostathine (S1) self-assembles into protofibrils at a physiologic pH



Gregoire et al. EMBO J 2001;20:3313–3321

Acidic and basic solutions dissolve protein plugs



Proof that electrostatic interactions work only at a physiologic pH

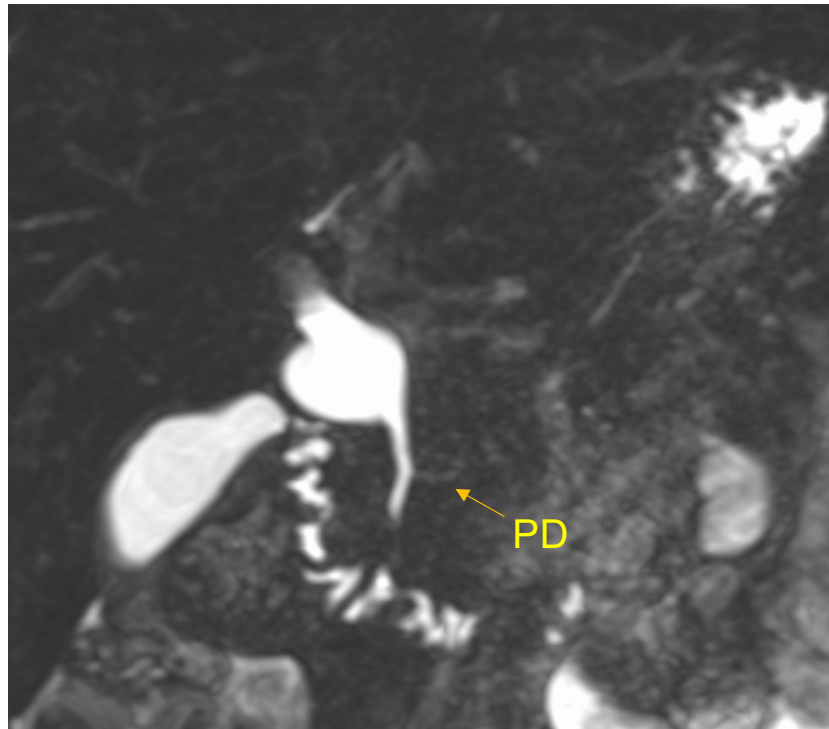
Kaneko K, Ono Y, Tainaka T, Sumida W, Ando H. Acidic and basic solutions dissolve protein plugs made of lithostathine complicating choledochal cyst/pancreaticobiliary maljunction. *Dig Dis Sci.* 2009 Jul;54(7):1475-80. doi: 10.1007/s10620-008-0503-8. Epub 2008 Nov 7. PMID: 18989781.

Where protein plugs form?

Case 4 from Basic Section

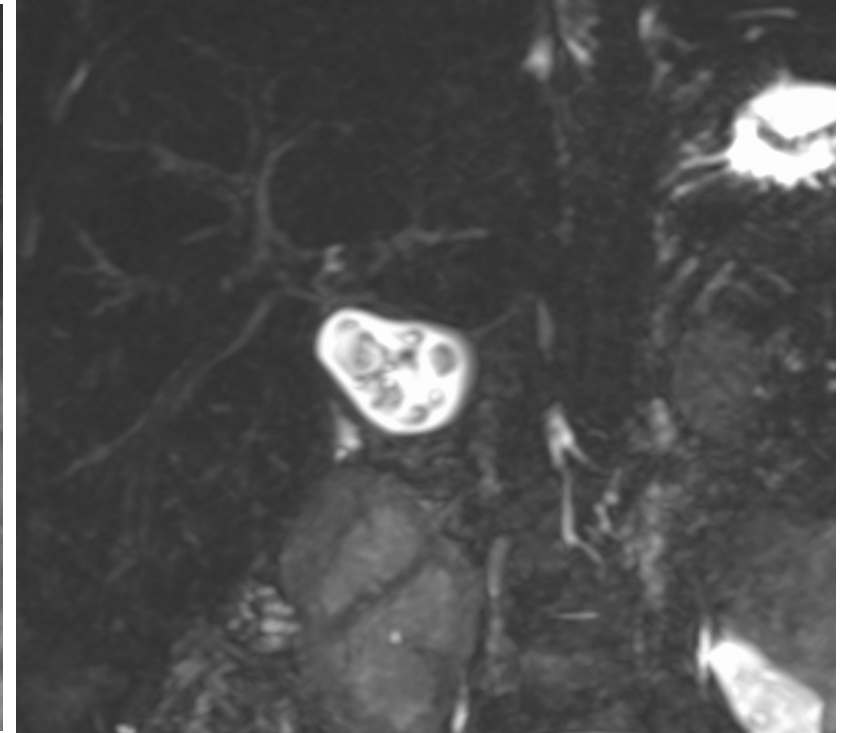
- Onset with abdominal pain and vomiting
- Elevated serum levels of liver and biliary enzymes
- No elevation of serum levels of pancreatic enzymes

Protein plugs are often found in the dilated common channel. However, plugs are formed as well in cases without dilatation of the common channel like this case. Most of plugs are presumed to form in the dilated BD or the gallbladder, where bile stagnates.



No dilatation at the common channel

Probably, here



Many filling defects at the dorsal side in the choledochus

Advanced

Symptomatology besides protein plugs

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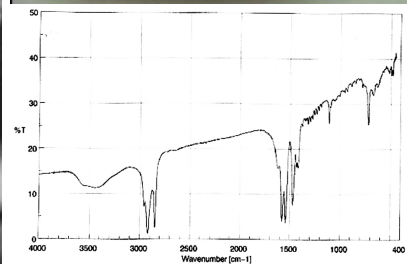
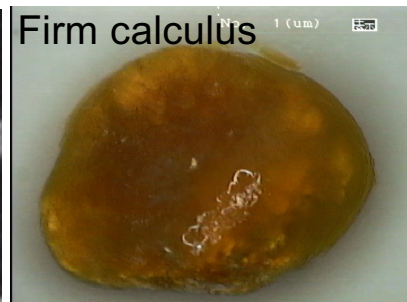
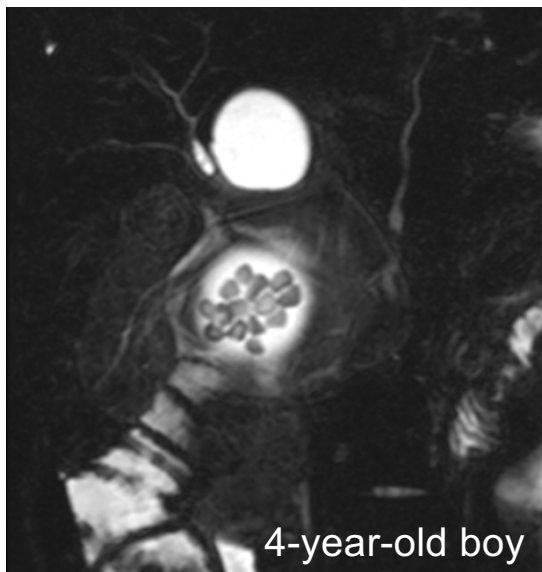
There is no theory without exceptions.



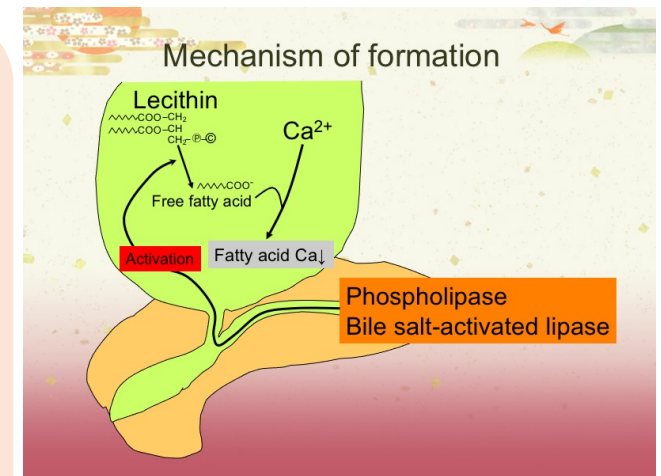
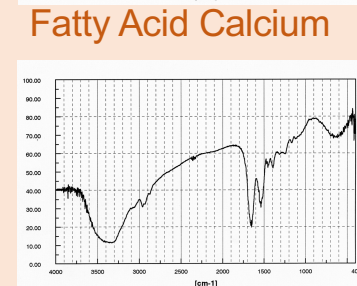
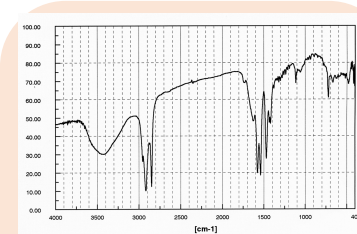
Symptomatology besides protein plug

The protein plug theory explains symptoms in most pediatric cases. However, there are a few exceptions.

- Fatty acid calcium stones causing occlusion, but extremely rare
- Early onset in neonates and early infants

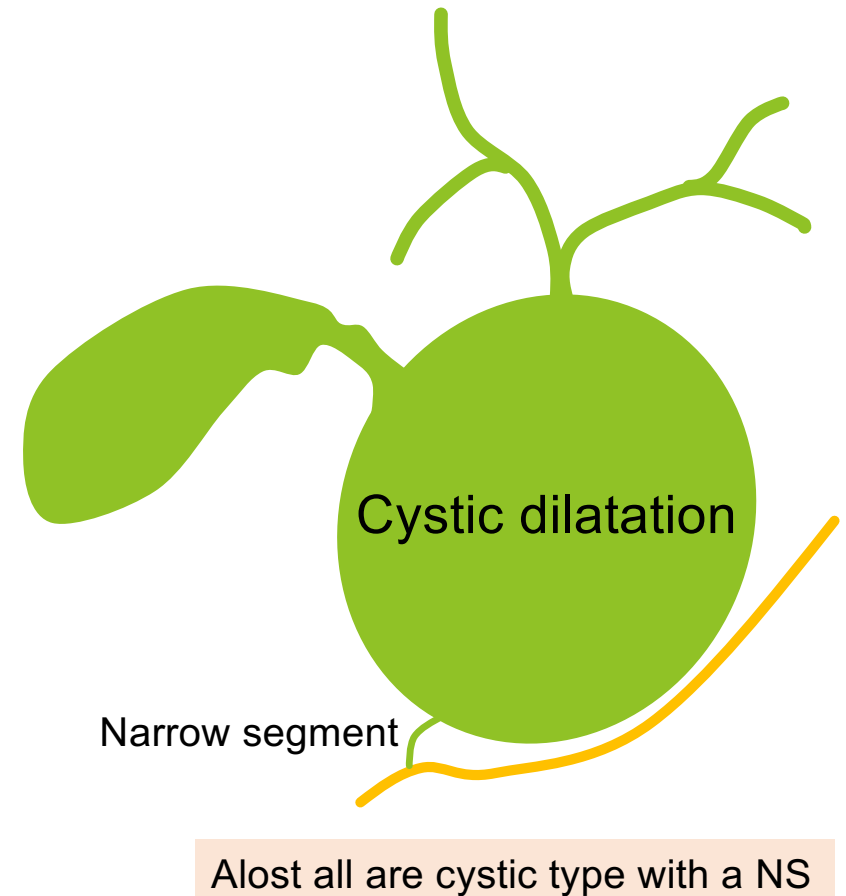
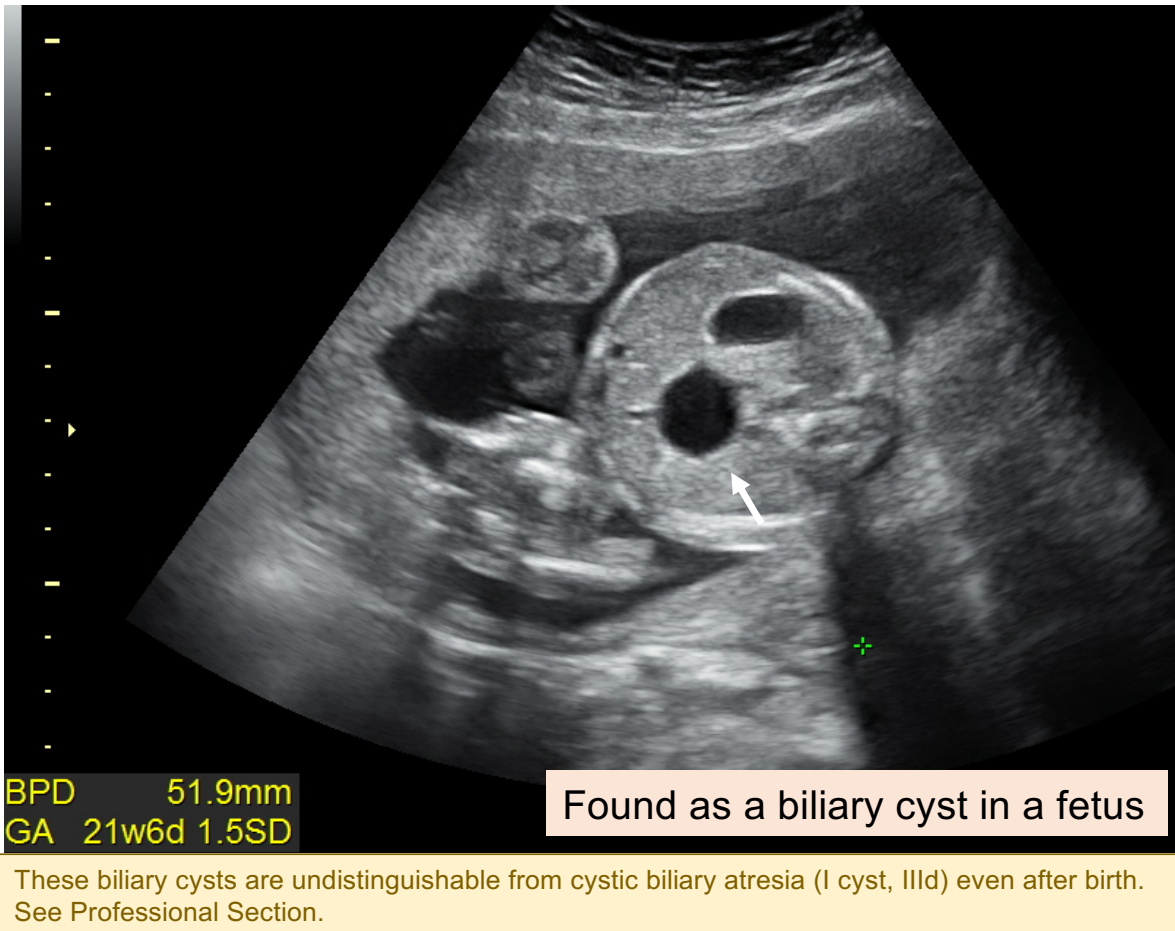


cf. Spectra of standard materials

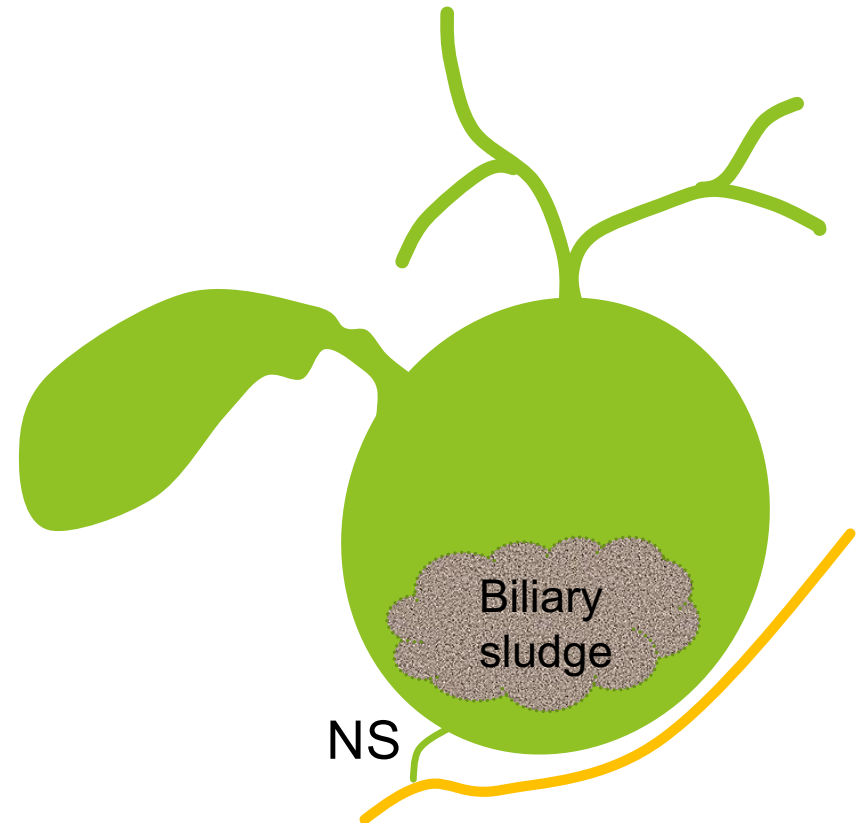
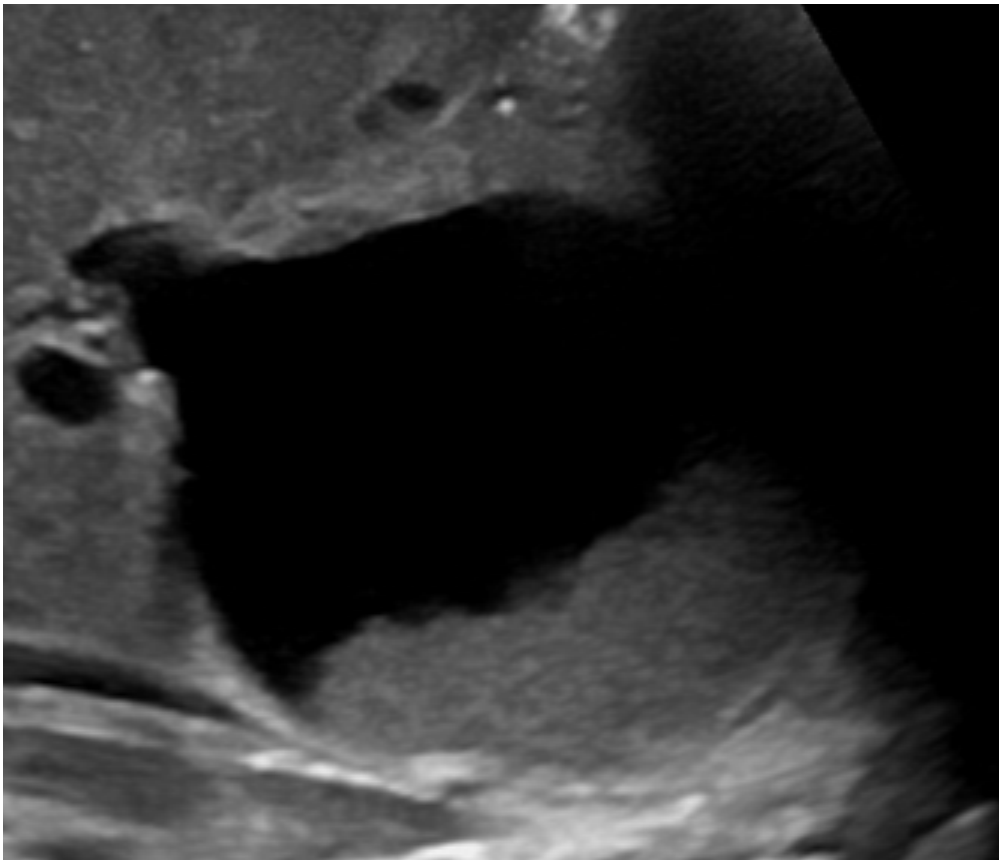


Kaneko K, Ono Y, Tainaka T, Sumida W, Ando H. Fatty acid calcium stones in patients with pancreaticobiliary maljunction/choledochal cyst as another cause of obstructive symptoms besides protein plugs. J Pediatr Surg. 2008 Mar;43(3):564-7. doi: 10.1016/j.jpedsurg.2007.11.004. PMID: 18358304.

Onset in neonates and early infants



Debris appears in the cyst before symptoms occur

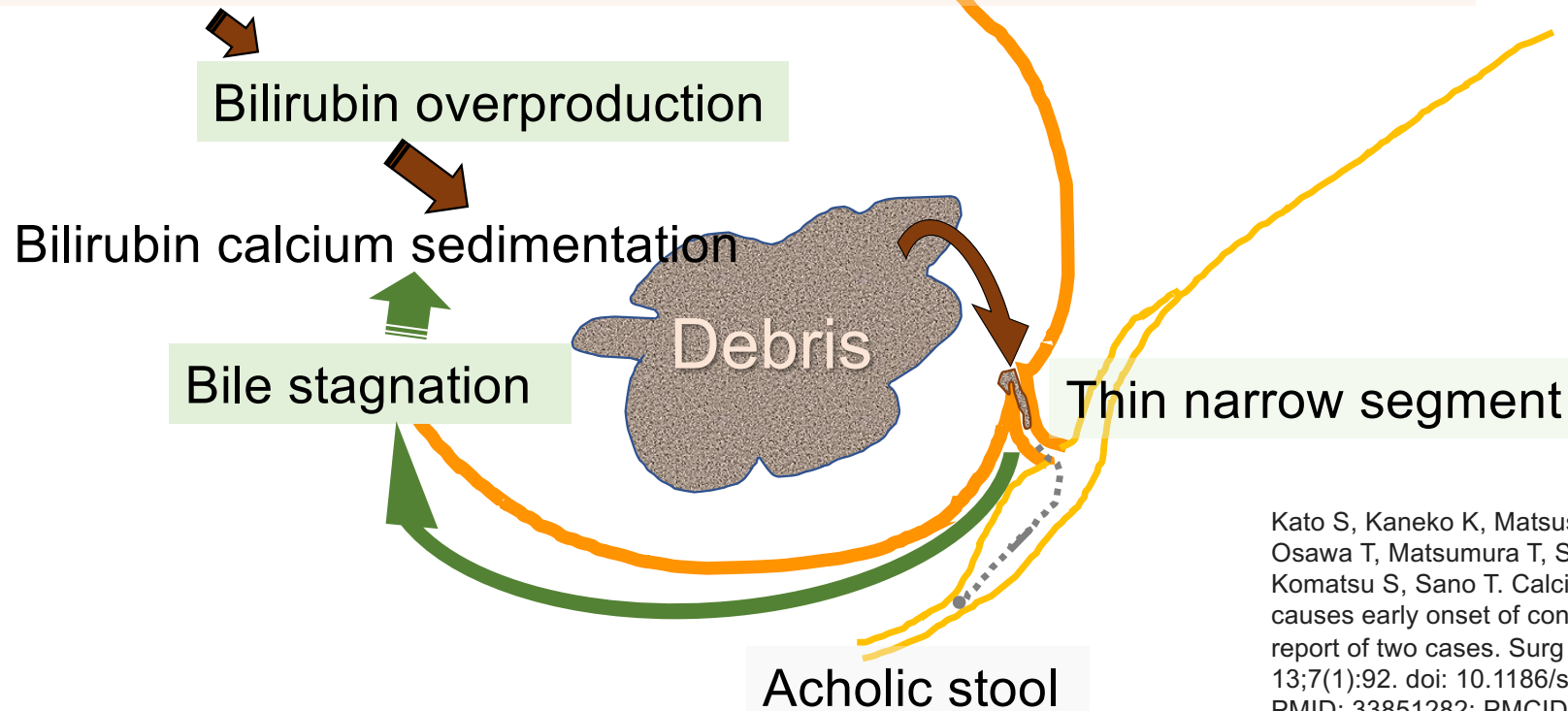


Infrared absorption spectrometry shows the sludge is composed of **Bilirubin Calcium**.

Proposed mechanism of early onset

Accelerated **hemolysis** due to neonatal hematologic features

- Physiological **polycythemia** of red blood cells (RBC)
- High percentage of **Hb F** RBC with a **shorter life span**



Kato S, Kaneko K, Matsushita N, Kurahashi S, Osawa T, Matsumura T, Saito T, Fukami Y, Komatsu S, Sano T. Calcium bilirubinate sludge causes early onset of congenital biliary dilatation: a report of two cases. Surg Case Rep. 2021 Apr 13;7(1):92. doi: 10.1186/s40792-021-01175-x. PMID: 33851282; PMCID: PMC8044275.