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Author(s)	佐々木, 常雄
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## Intravenous Cholegraphy applied to pseudo-cholera infantum (Hakuri) and infantile jaundice

By

Tsuneo Sasaki, M.D.

Department of Radiology, Nagoya University Hospital, Nagoya, Japan.

(Director: Prof. S. Takahashi)

### 乳児の胆嚢造影—白痢及び乳児黄疸について—

名古屋大学医学部放射線医学教室 (主任 高橋信次教授)

佐々木常雄

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乳児疾患殊に乳白色下痢便のため胆道の通過障害を疑われる白痢(仮性小児コレラ), また胆道の閉塞或は肝機能障害などによると思われる乳児黄疸の症例にビリグラフィンを用いて胆嚢造影法を施行しこれらの疾患の病因の一端を明かにせんとした。

研究の対象として選ばれた乳児は白痢14例, 乳児黄疸20例で, いずれもほゞ一年未満の乳児である。これらに早朝空腹時に30%ビリグラフィンを体重1kg当り1.5cc静脈内に注射し, 注射後1, 2, 3時間の3回胆嚢の撮影を行つた。注射前15~30分には眼瞼結膜内にビリグラフィン1~2滴点眼したと同時に0.1cc皮内注射してヨードに対する過敏性の有無をテストした。撮影は蓄電器放電装置(1 $\mu$ F)を用い管球フィルム間距離100cm, 管電圧60KVで行い, 乳児は仰臥位をとらせ

固定しX線中心線を右上腹部に合せて撮影した。

白痢では全例に胆嚢が造影され, 胆嚢の異常拡大を認めず, 卵黄一個投与後の追加撮影で胆嚢の収縮能は良好であり, 造影剤が小腸内に認められて胆道の通過障害は認められなかつた。(Table 1, Fig. 1)

乳児黄疸では全例に胆嚢は造影されず胆道の通過異常が推定された。この中5例は手術により胆道の閉塞が確認された。しかし2例は肝炎であつて他の症例同様胆嚢造影は不成功であつて眞の胆道閉塞との鑑別は確実に行いようとは云い難かつた。しかし臨床所見及び疾病の経過の観察とこの胆嚢造影所見とを併せ考えれば十分鑑別診断に役立つものと考えられる。なお, この検査を施行しても副作用は何等認められなかつた。(Table 2, Fig. 2)

### Introduction

In order to make clear the pathogenesis of the various pediatric diseases such as pseudo-cholera infantum (Hakuri) suspected the presence of disturbance of passage of the biliary tract because of milky-white stool, and infantile jaundice caused probably by biliary atresia or liver damage, the cholegraphy with Biligradin was performed.

### Method and material

The selected cases, 14 of pseudo-cholera infantum and 20 of infantile jaundice, were below 13 months of age. No food or liquid was given to the infants during the 3 hours

period prior to injecting Biligradin, taking 5 minutes for injection of about 1.5 ml of 30% Biligradin per kilogram of the body weight intravenously (mainly into the jugular vein).

At 15 to 30 minutes before the examination, the sensitivity test was carried out by dropping one or two drops of Biligradin into the conjunctiva of the eye and simultaneously to this, by injecting 1/10 ml of Biligradin intracutaneously. But no serious reactions such as reddening accompanied with induration were observed. The sensitivity test for iodine was all negative.

The radiograms were taken at the end of 1st, 2nd and 3rd hour after injection of the Biligradin. And the radiograms were taken in the supine position with the central rays directed towards the right upper abdomen.

The films used were 6 1/2' x 8 1/2' or 8' x 10' in size. It was used the X-ray unit of a condenser type with a capacity of 1  $\mu$ F. The tube-film distance was 100 cm. The tension between the tube terminal was 60 KV, and the stationary grid was used.

When the gall bladder was imaged, the radiogram was again taken after 30 minutes after administering one egg yolk for the contraction test.

### Results

#### 1) Pseudo-cholera infantum.

The cholegraphic examination was carried out on fourteen typical cases, 11 males and 3 females, of pseudo-cholera infantum<sup>14)15)</sup> in the peak of the illness, which were considered to be bearable to the examination.

Table 1. Cases of Hakuri

No.	Sex	Age	Clinical findings	Urinary system				Gall bladder				Intestinal tract			
				1h	2h	3h	PC	1h	2h	3h	PC	1h	2h	3h	PC
1	F	6m	Vomit. 3/d, Diarh. 2-3/d.	—	—	—		+	+	+		—	—	—	
2	M	8	Vomit. 3/d, Diarh. 2/d.	P	—	—		+	+	+		—	—	—	
3	M	10	Vomit. 2/d, Diarh. 2-5/d.	B	B	B	B	+	+	+	1/2	—	—	—	+
4	F	12	Vomit. 3/d, Diarh. 3/d.	B	B	B		+	+	+	1/3	—	—	—	+
5	M	4	Vomit. 4-5/d, Diarh. 4-5/d. Fever 38.0°C	B	B	B		+	+	+		—	—	—	
6	M	7	Vomit. 10/d, Diarh. 10/d.	P B	B	B		+	+	+		—	—	—	
7	M	7	Vomit. 5-6/d, Diarh. 3/d.	P B	B	B		—	+	+		—	—	+	
8	M	3	Vomit. 3/d, Diarh. 4/d.	B	B	B		+	+	+		—	—	—	
9	M	11	Vomit. 1-2/d, Diarh. 8/d.	B	B	B		+	+	+		—	—	+	
10	F	9	Vomit. 3/d, Diarh. 5/d.	B	B	B		+	+	+		—	—	—	
11	M	4	Vomit. 5/d, Diarh. 4/d. Fever 38.0°C	B	B	—		+	+	+	1/2	—	—	—	+
12	F	7	Vomit. 4/d, Diarh. 5/d. Fever 38.0°C	B	B	B		—	+	+	1/3	—	—	—	+
13	M	9	Vomit. 2/d, Diarh. 3/d Fever	B	B	B		+	+	+	1/2	—	—	—	+
14	M	9	Vomit. 4/d, Diarh. 5/d	P B	B	B		+	+	+	1/2	—	—	—	+

PB: Pyelogram and Cystogram positive  
B: Cystogram positive

The gall bladders were demonstrated in 12 cases at the end of 1st hour after the injection of Biligradin and in all cases at the end of 2nd hour. The gall bladders were of a small pear shape and located beneath the suspected shadow of the liver in the right upper abdomen.

The opacity of the gall bladder reached maximum about two hours after injection.

Out of 14 cases only 6 cases were administered with the egg yolk and the gall bladders in those 6 cases were contracted to one half or one thirds of their original size in 30 minutes after the administration of the egg yolk.

At this time the image of contrast medium was faintly visible in the intestinal tract. The common bile duct was not seen at the end of 1st hour after the injection but it was seen in two cases at the end of 2nd hour and in one case in 30 minutes after administering the egg yolk.

The urinary pelvis was visualized in four out of 14 cases at the end of 1st hour

Table 2. Cases of cong biliary atresia.

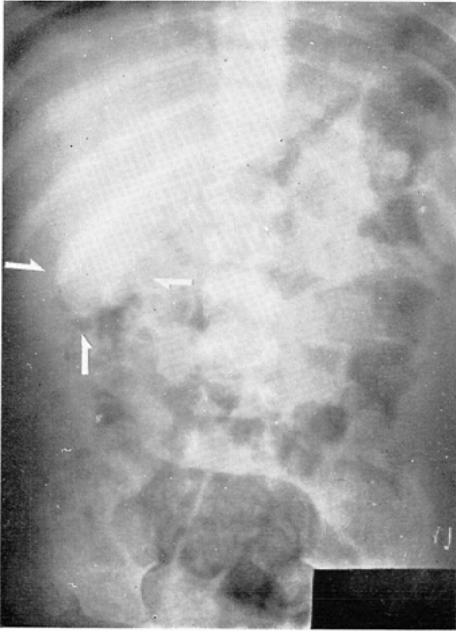
No.	Sex	Age	Clinical Diag.	Clinical findings	Urinary system			Gall bladder			Intestinal tract		
					1h	2h	3h	1h	2h	3h	1h	2h	3h
1	F	6m	Cong Atresia of the Biliary Tract	Liver 3 FB Icterus (+)	P	B	B	-	-	-	-	-	-
2	F	7	"	Liver at level of navel, Icterus (+)	P	B	B	-	-	-	-	-	-
3	M	3	" (op)	Liver at the level of navel, Icterus (+)	P	B	B	-	-	-	-	-	-
4	F	3	" (op)	Liver 2 FB. Icterus (+) Meulengracht 36	P	B	-	-	-	-	-	-	-
5	F	4	" (op)	Liver 3 FB. Icterus (+)	B	-	-	-	-	-	-	-	-
6	M	2	" (op)	Liver 3 FB. Icterus (+)	P	B	-	-	-	-	-	-	-
7	M	4	"	Liver 4 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
8	F	6	"	Liver 3 FB. Icterus (+)	P	B	B	-	-	-	-	-	-
9	F	6	"	Liver 2 1/2FB. Meulengracht 90	P	B	B	-	-	-	-	-	-
10	M	2	"	Liver 2 1/2FB. Icterus (+)	B	B	B	-	-	-	-	-	-
11	M	2	"	Liver 2 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
12	F	6	"	Liver 3 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
13	M	6	"	Liver 2 FB. Icterus (+)	P	B	B	-	-	-	-	-	-
14	F	4	"	Liver 3 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
15	M	2	"	Liver 2 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
16	F	2	"	Liver 4 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
17	M	13	" (op)	Liver 3 FB. Icterus (+) Meulengracht 52	B	B	B	-	-	-	-	-	-
18	F	2	Neonatal Hepatitis	Liver 2 1/2FB. Icterus (+)	B	B	B	-	-	-	-	-	-
19	M	6	Cong Atresia of the Biliary Tract	Liver 2 FB. Icterus (+)	B	B	B	-	-	-	-	-	-
20	M	12	Virus Hepatitis	Liver 3 FB. Icterus (+) Meulengracht 24	P	B	B	-	-	-	-	-	-

OP: Surgical operation  
FB: Finger breadth

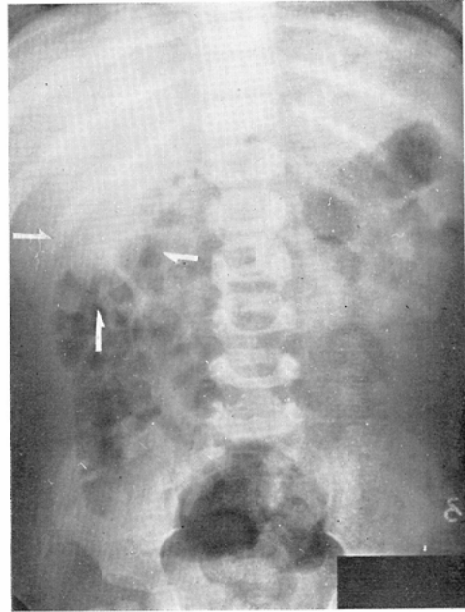
PB: Pyelogram and Cystogram  
B: Cystogram

Fig. 1. Case of Hakuri: Injecting 9.1 ml of Biligradin the radiograms were taken at the end of 1st, 2nd, 3rd hour. Thirty minutes after administering the egg yolk. The image of the gall bladder (arrows) was increased its density to 1st, 2nd and 3rd hours roentgenographs. It was contracted to about a half after administering the yolk, and the contrast medium was faintly seen in the bowels. The contrast medium was also seen in the urinary bladder.

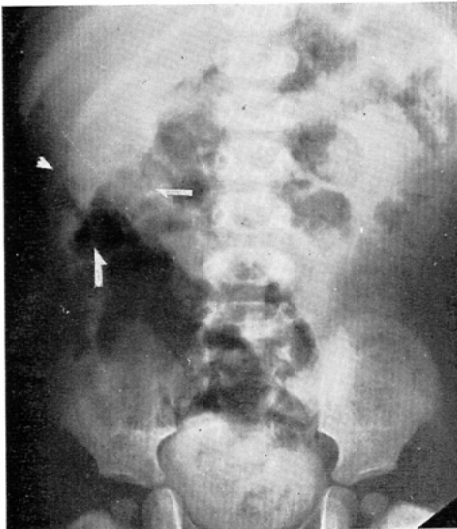
1st hr.



2nd hr.



3rd hr.



30 min. after the yolk



Fig. 2. Case of Cong. biliary atresia. Injecting 8.2ml of Biligrafin, the radiograms were taken at the end of 1st, 2nd and 3rd hour. The gall bladder was not imaged. The contrast medium was seen in the urinary tract demonstrating the pyelogram and cystogram, No contrast medium was seen in the bowels.

1st hr.



2nd hr.



3rd hr.



and the urinary bladder was seen in 12 cases at the end of 1st, 2nd and 3rd hour. Generally the intestinal gas shadows seemed to increase when the time passed after injecting Biligrafin and the gall bladders, therefore, were sometimes partially obscured. (Table 1 and Fig. 1)

## 2) Infantile jaundice.

The cholegraphic examination was performed for 20 infants with a chief complaint of jaundice (10 males and 10 females, of 2 to 13 months). Two out of 20 cases were established clinically the diagnosis of virus hepatitis and eighteen cases were biliary atresia. The common bile ducts and gall bladders were not seen in all cases on the radiograms taken at the end of 1st, 2nd and 3rd hour. And no contrast medium was seen in the intestinal tract. On the other hand the contrast medium was seen in the urinary system in all radiograms. That is, the urinary pelvis were shown at the end of 1st hour in 9 to 20 cases and the urinary bladders were demonstrated almost in all radiograms. (Table 2 and Fig. 2)

Five out of 18 cases of congenital biliary atresia were confirmed by the operation: The first cases showed the marked dilatation of the cystic duct due to stenosis in the lower portion of the common bile duct, the second case was due to band-like malformation of the biliary tract and the other three cases were due to absence of the biliary system.

## Side effects

No side reactions such as urticaria, diarrhea and vomiting were observed. Even in cases of infantile jaundice no case was shown the increase of liver damage by Biligrafin.

## Discussion

Pseudo-cholera infantum (Hakuri)<sup>14)15)</sup> affects preferably the infants of the weaning time and appears mostly in late autumn and early winter. It has never been made clear the genesis of milky-white stool which is a characteristic sign of this disease. In order to make clear the genesis of this milky-white stool, the author considered significant to compare the cholegraphic findings in these cases with that of infantile jaundice apparently being due to biliary stenosis.

It has been reported about the trials of cholegraphy in infancy<sup>2)10)</sup>, being difficult and visualizing below 50% of the gall bladder<sup>1)</sup>.

Biligrafin, a new contrast medium, however, is disodium salt of N·N'-adipyl-bis-(3-amino-2·4·6-triiodo)-benzoic acid containing 6 molecules of iodine being 64.6%, that is, the iodine content is higher and the excretion from the liver after the intravenous injection is faster with higher density than that of the oral contrast media.

It is reported that the rate of visualizing the gall bladder in infants with Biligrafin is favourable and is successful about 80 to 90%<sup>4)5)6)7)</sup>.

In the adults the 90% of this contrast medium is excreted in the feces and only 10% is excreted from the kidney. But the oral contrast medium Priodax (Bilisektan),

is excreted 20 to 30% in the feces and 60 to 80% from the kidney. In this point of view, it is considered the Biligrafin is superior than the oral contrast medium and is suitable for the infantile use<sup>8)9)12)</sup>.

The radiograms are taken 3 times, that is, at the end of 1st, 2nd and 3rd hour after the injection, because most of the gall bladders are visualized during this time<sup>7)</sup>.

In all cases of pseudo-cholera infantum the gall bladders were well visualized with no evidence of abnormal dilatation. Therefore the evidence of liver damage of any origin was not concluded from this cholegraphic findings. And the contraction of the gall bladder was well functioned. As the contrast medium was shown in the intestinal tract, the obstruction of the biliary tract cannot be suspected. These findings were completely confirmed with that studied by the autopsy<sup>14)15)</sup>.

On the other hand in all cases of infantile jaundice the gall bladders were not visualized and the contrast medium was not detected in the intestinal tract. This findings can be concluded with the presence of obstructive lesion in the biliary tract. It can be explained by the experiments<sup>11)</sup> on dog's in which after ligation of the common bile duct only exceedingly small amounts of Biligrafin reached the bowel, and even after removal of the kidneys only 0.5 per cent of the dose was chemically demonstrable in the bowels 8 hours after intravenous injection.

If the contrast medium is not seen in the bowels and in the gall bladder<sup>7)</sup>, it is, therefore, strongly suspected the presence of biliary atresia. This was agreed with our five cases of the obstructive lesion of the biliary tract confirmed by the surgical operation. And thus the thirteen remaining cases diagnosed as biliary atresia will be probably supported as correct by those operation.

However, two cases out of 20 infantile jaundice were virus hepatitis and their gall bladders were not visualized. Because of this, the definite differential diagnosis of biliary atresia from jaundice of the other origin seems to be difficult to be concluded from the cholegraphy. As there is no other better pre-operative diagnostic method at present, and there is observed no any unfavorable side effect such as increasing liver damage, this examination, however, should be recommended to perform at least once before the treatment mode is decided.

In our experience the excretion of the Biligrafin from the urinary system was higher than that reported in the adults. This is estimated probably due to immaturity of the liver in its activity even in normal infants excreting a larger amounts of the contrast medium from the kidney when compared with that of the adults.

In cases of infantile jaundice the liver damage is more or less present and therefore this phenomenon is more dominant. It is characteristic for infantile jaundice that the contrast medium is excreted only from the urinary system and nothing is visualized in the bowels. That can be why no harmful reaction is noted after injecting the Biligrafin in the cases of infantile jaundice.



### Conclusion

1) The cholegraphy was performed by administration of one and a half ml of 30% Biligradin per kilogram (about 10 ml per case) intravenously in cases of pseudo-cholera infantum (14 cases) and infantile jaundice (20 cases) below 13 months of age. The radiograms were taken at the end of 1st, 2nd and 3rd hour injecting the Biligradin.

2) In all cases of Hakuri, the gall bladders were well visualized without abnormal dilatation and were contracted well after fatty meal. There was no evidence of disturbance of passage of the biliary tract.

3) However, in all cases of infantile jaundice the gall bladders were not visualized. Accordingly, it was suggested the presence of stenosis of the biliary tract. Five cases out of 20 infantile jaundice cases were confirmed the stenosis by the operation.

Two cases were suffered from virus hepatitis and their gall bladders were not demonstrated as those of the other case. Because of this the differential diagnosis of congenital biliary atresia from jaundice of the other origin can not be concluded definitely from the cholegraphy.

Even though the results were described above, the cholegraphy can be considered useful as a supplemental diagnostic tool in the case of congenital biliary atresia, if the clinical findings and the clinical course of the disease are referred besides the cholegraphic graphic findings.

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