Liver General

MEDICAL GRAND ROUNDS

January 13, 1977

JAUNDICE

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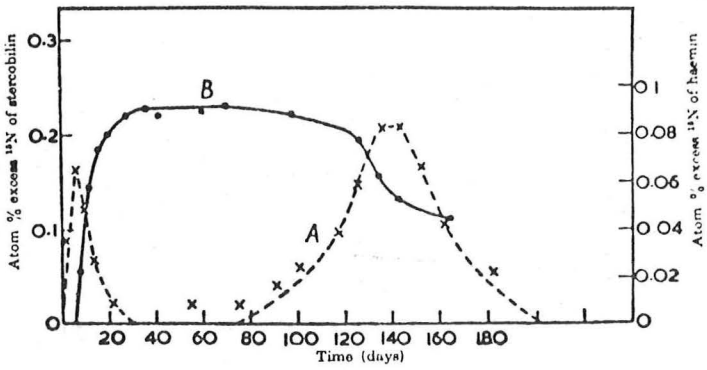
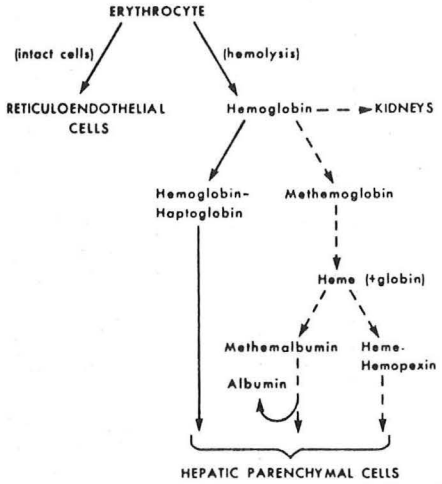
SOURCES OF BILE PIGMENT



. ^{15}N content of hemin samples (line *B*) and of stercobilin (line *A*) at various times after administration of glycine (12 gm) containing 31.65 atoms per cent excess ^{15}N to normal subjects.

from Gray et al., Biochem. J. 47:87, 1950.

Provides evidence that erythrocytes and shunt pathways serve as sources of bile pigments.

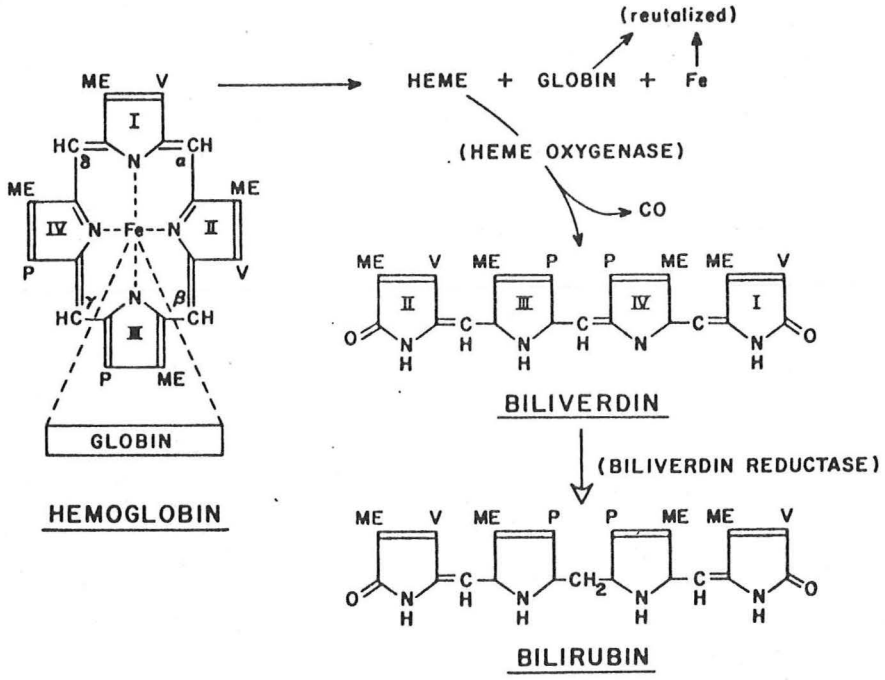


Routes of erythrocyte disposal. Postulated routes are indicated for physiological (*solid arrows*) or pathological (*dashed arrows*) catabolism of red blood cells.

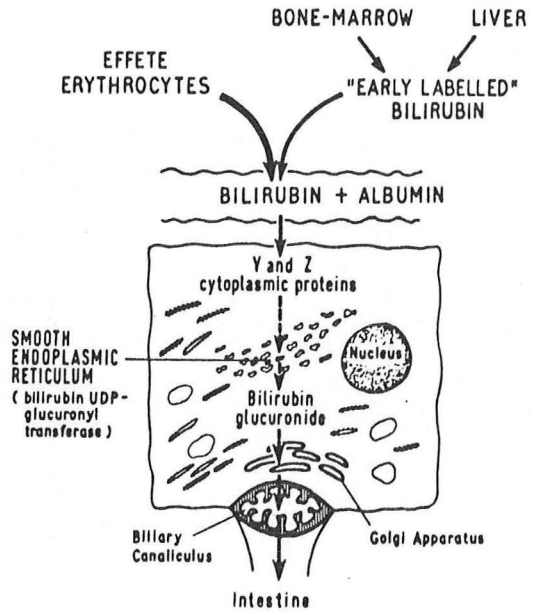
from D.M. Bissell, Gastroenterology 69:519, 1975.

Heme in erythrocytes can be converted to bilirubin in reticuloendothelial or hepatic parenchymal cells.

PATHWAY OF HEME DEGRADATION



DISPOSITION OF BILIRUBIN



BILIRUBIN METABOLISM

Reviews

Bissell, D. M.: Progress in Gastroenterology. Formation and elimination of bilirubin. Gastroenterology 69:519-538, 1975.

Lester, R. and Troxler, R. F. Progress in Gastroenterology. Recent Advances in bile pigment metabolism. Gastroenterology 56:143-169, 1969.

Jansen, F. H. and Devriendt, A. Recent advances in bilirubin metabolism. Medikon 1:269-278, 1972.

Elder, G., Gray, C. H. and Nicholson, D. C. Bile pigment fate in gastrointestinal tract. Seminars in Hematology 9:71-88, 1972.

With, Torben K. Bile Pigments: Chemical, Biological, and Clinical Aspects. Academic Press, New York, 1968.

BILIRUBIN PRODUCTION AND TURNOVER

Barrett, P.V.D., Berk, P. D., Menken, M. and Berlin, N. I. Bilirubin turnover studies in normal and pathologic states using bilirubin-^{14}C. Ann. Int. Med. 68:355-377, 1968.

Berk, P. D., Howe, R. B., Bloomer, J. R. and Berlin, N. I. Studies of bilirubin kinetics in normal adults. J. Clin. Invest. 48:2176-2190, 1969.

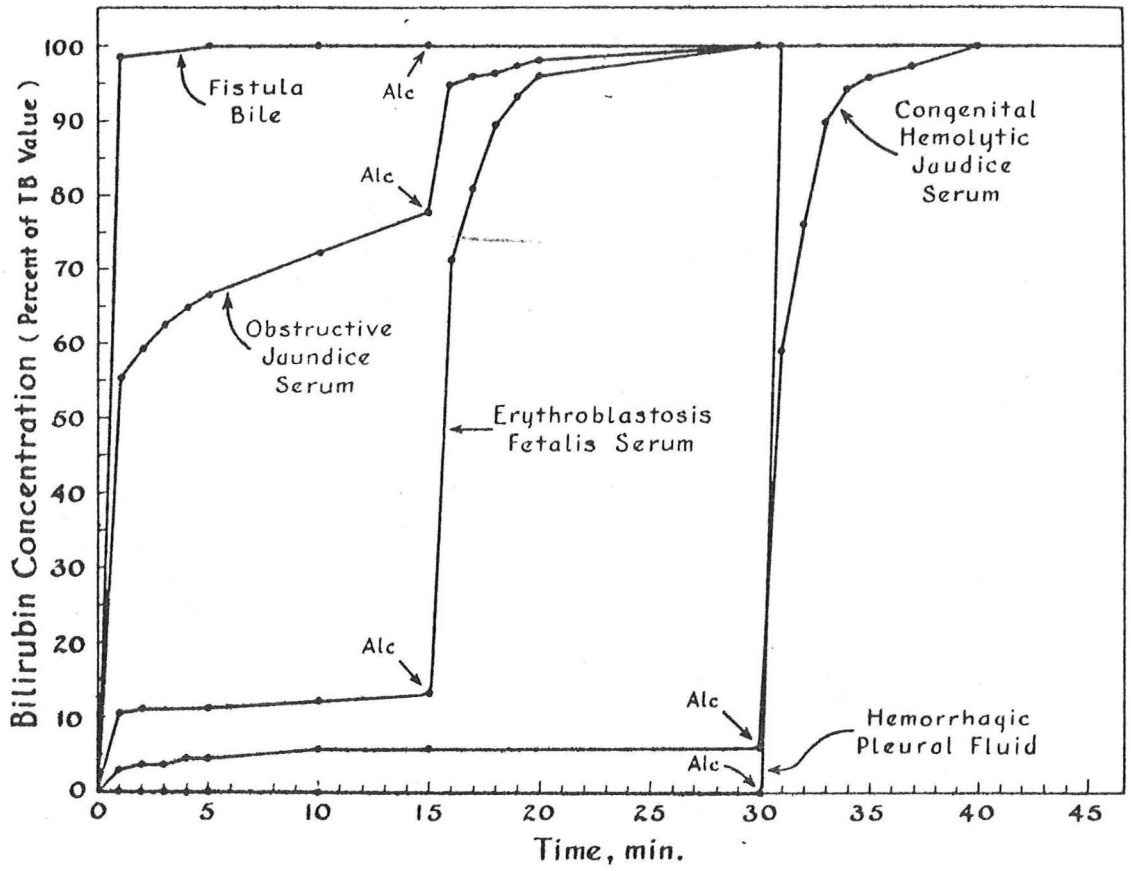
Bloomer, J. R., Berk, P. D., Howe, R. B., Waggoner, J. G. and Berlin, N. I. Comparison of fecal urobilinogen excretion with bilirubin production in normal volunteers and patients with increased bilirubin production. Clin. Chim. Acta 29:463-471, 1970.

Bloomer, J. R., Berk, P. D., Howe, R. B. and Berlin, N. I. Interpretation of plasma bilirubin levels based on studies with radioactive bilirubin. J.A.M.A. 218:216-220, 1971.

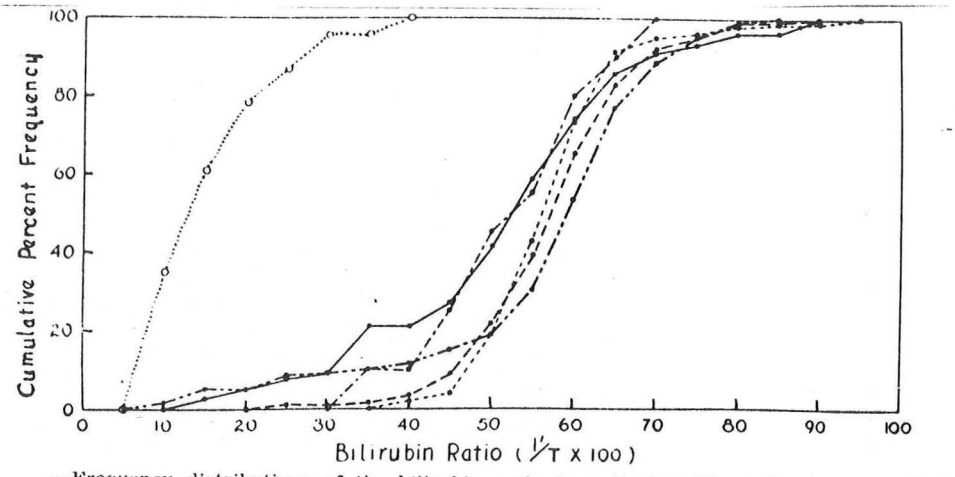
Berk, P. D., Bloomer, J. R., Howe, R. B., Blaschke, T. F. and Berlin, N. I. Bilirubin production as a measure of red cell life span. J. Lab. Clin. Med. 79:364-378, 1972.

Berk, P. D., Rodkey, F. L., Blaschke, T. F., Collison, H. A. and Waggoner, J. G. Comparison of plasma bilirubin turnover and carbon monoxide production in man. J. Lab. Clin. Med. 83:29-37, 1974.

Adaptation of the van den Bergh reaction to differential diagnosis of hyperbilirubinemia.



—Color development time curves of direct and indirect reacting bilirubin in fistula bile, hemorrhagic pleural fluid, hemolytic jaundice serum, and obstructive jaundice serum.

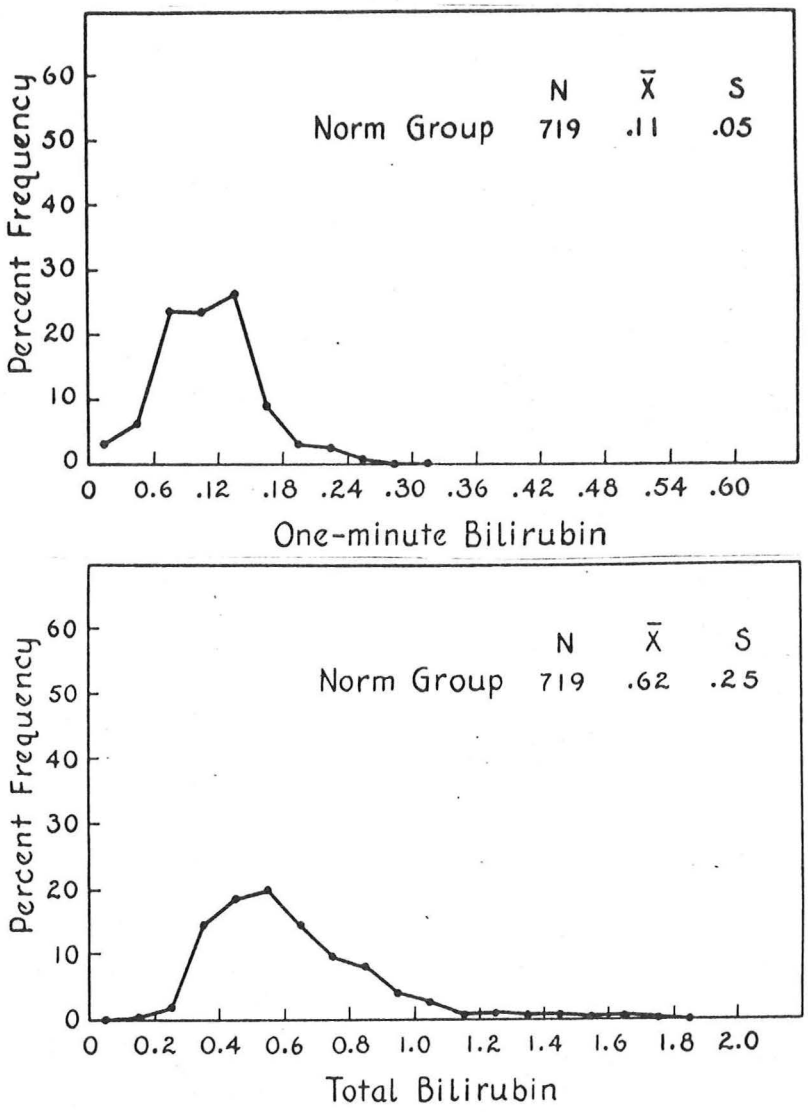


All Cases TB >2.0	N	X	S
Cirrhosis	77	51	16
Hepatitis	101	57	8
Obstr. Jaundice	138	57	10
Cong. Failure	20	52	10
Misc. Reg. J.	60	56	15
Hemolytic J.	23	15	8

—Frequency distributions of the bilirubin ratio in patients with moderate or marked jaundice, by disease type.

from Zieve et al., J. Lab. Clin. Med. 38:446, 1951.

Normal values for one-minute and total bilirubin



from Zieve et al., J. Lab. Clin. Med. 38:446, 1951.

UNCONJUGATED HYPERBILIRUBINEMIA

Characterization by determination of direct and total bilirubin

Zieve, L., Hill, E., Hanson, M. Falcone, A. B. and Watson, C. J. Normal and abnormal variations and clinical significance of the one-minute and total serum bilirubin determinations. J. Lab. Clin. Med. 38:446-469, 1951.

Watson, C. J. The importance of the fractional serum bilirubin determination in clinical medicine. Ann. Int. Med. 45:351-368, 1956.

Tisdale, W. A., Klatskin, G. and Kinsella, E. D. The significance of the direct-reacting fraction of serum bilirubin in hemolytic jaundice. Am. J. Med. 26:214-227, 1959.

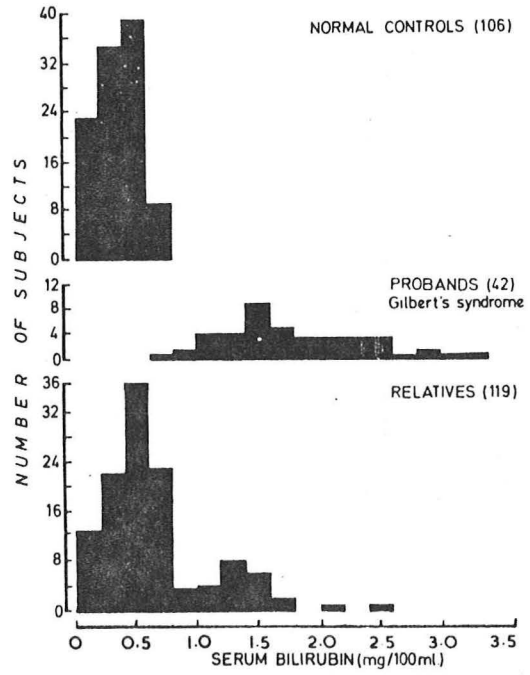
Levine, R. A. and Klatskin, G. Unconjugated hyperbilirubinemia in the absence of overt hemolysis. Am. J. Med. 36:541-552, 1964.

Schalm, L and Weber, A. Ph. Jaundice with conjugated bilirubin in hyperhaemolysis. Acta Med. Scand. 176:549-553, 1964.

Causes of Unconjugated Hyperbilirubinemia

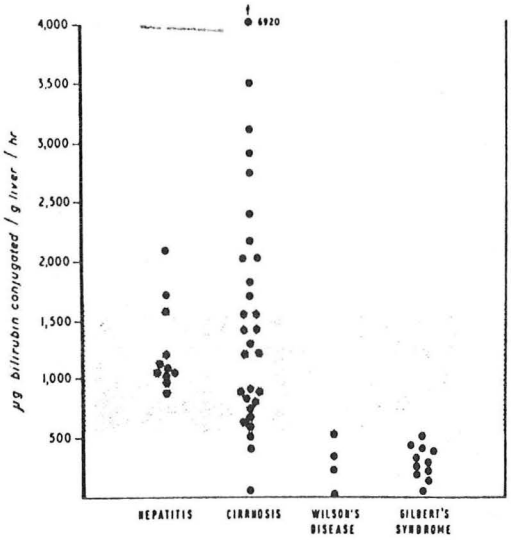
SYNDROMES	MECHANISMS
Pediatric	
Physiologic jaundice	Immaturity of bilirubin conjugating system;? Immaturity of bilirubin uptake
Crigler-Najjar syndrome	Inborn or acquired impairment of hepatic bilirubin conjugating system
Breast milk jaundice	
Lucey-Driscoll syndrome	
Pediatric and Adult	
Intravascular hemolysis	Overproduction of bilirubin
"Shunt" hyperbilirubinemia	
Constitutional hepatic dysfunction (Gilbert's disease)	Impaired uptake and conjugation of bilirubin
Posthepatitic hyperbilirubinemia	Unknown – ? impaired uptake
Miscellaneous (cardiac, hepatobiliary disease, etc.)	Unknown

Gilbert's syndrome is characterized by unconjugated hyperbilirubinemia with values of total serum bilirubin up to 3-4 mg%. The syndrome probably contains a diverse group of underlying defects. The syndrome is frequently familial.



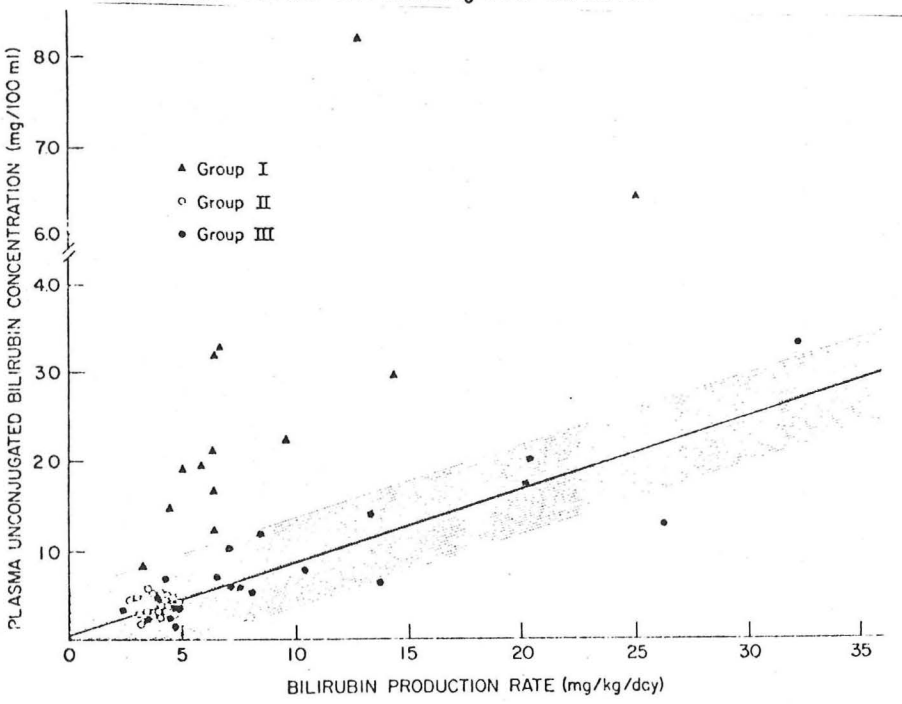
from Powell et al., N. Engl. J. Med. 227:1108, 1967.

Assessment of bilirubin kinetics utilizing injected radioactive bilirubin has revealed a defect in hepatic uptake of bilirubin. Bilirubin glucuronyl transferase activity in liver is also low. It is uncertain to what extent this contributes to impaired hepatic uptake of bilirubin.



from Black and Billing, N. Engl. J. Med. 280:1266, 1969.

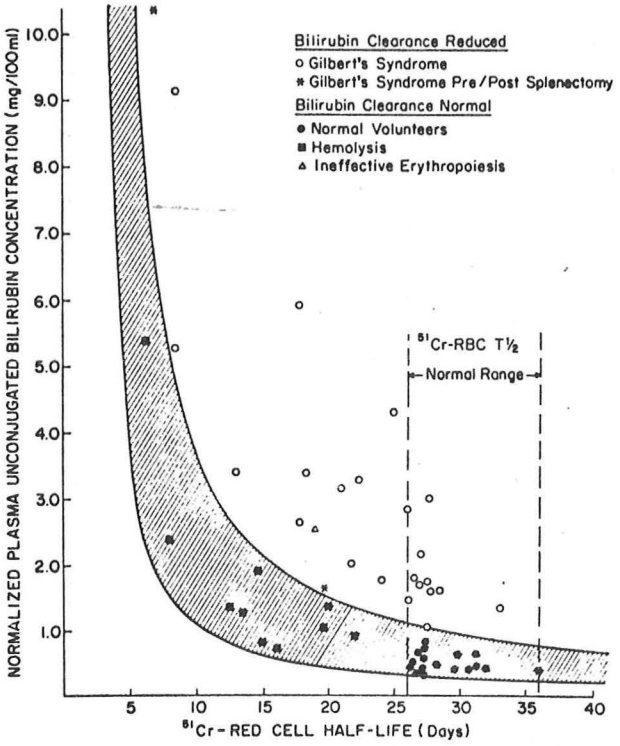
Red cell life span is shortened in up to 50% of cases studied in various series. Nevertheless, serum bilirubin is higher than would be expected even with increased bilirubin production rates, as for example in patients with various forms of hemolytic anemia.



Plasma unconjugated bilirubin concentration as a function of bilirubin production rate. A given rate of bilirubin production results in a higher plasma unconjugated bilirubin concentration in patients with Gilbert's syndrome (group I) than in normal subjects (group II) or patients with anemia and/or increased bilirubin production and normal liver function (group III). The solid line and stippled area represent a regression line ± 95 per cent confidence limits for the forty studies in groups II and III (subjects with normal liver function).

from Berk et al, Amer. J. Med. 49:296, 1970.

Bilirubin production is a function of red cell life span. Measurement of ^{51}Cr-labeled red cell half-life will permit an assessment of whether serum bilirubin is appropriate for the degree of hemolysis.



Normalized values for the plasma concentration of unconjugated bilirubin, plotted as a function of the ^{51}Cr-labeled red cell half-life ($^{51}Cr\text{-}RBCT_{1/2}$). Shaded area represents the normal range for these values, as defined by equation 8 in the text, for individuals with normal hepatic bilirubin clearance. In patients with reduced hepatic bilirubin clearance, as occurs in Gilbert's syndrome, the normalized value exceeds the upper limit of normal at any ^{51}Cr-labeled red cell half-life. The normalized values may also be elevated in patients with ineffective erythropoiesis.

from Berk and Blaschke, Ann Int. Med. 77:527, 1972.

GILBERT'S SYNDROME

Foulk, W. T., Butt, H. R., Owen, C. A. Jr., Whitcomb, F. Jr. and Mason, H. L. Constitutional hepatic dysfunction (Gilbert's Disease): Its natural history and related syndromes. Medicine 38:25-46, 1959.

Alwall, N., Laurell, C. B. and Nilsby, I. Studies on heredity in cases of non-hemolytic bilirubinemia without direct van den Bergh reaction (hereditary, non-hemolytic bilirubinemia). Acta Med. Scand. 124:114-125, 1946.

Powell, L. W., Hemingway, E., Billing, B. H. and Sherlock, S. Idiopathic unconjugated hyperbilirubinemia (Gilbert's Syndrome). A study of 42 families. N. Engl. J. Med. 277:1108-1112, 1967.

Metge, W. R., Owen, C. A. Jr., Foulk, W. T. and Hoffman, H. N. Bilirubin glucuronyl transferase activity in liver disease. J. Lab. Clin. Med. 64:89-98, 1964.

Black, M. and Billing, B. H. Hepatic bilirubin UDP-glucuronyl transferase activity in liver disease and Gilbert's Syndrome. N. Engl. J. Med. 280:1266-1271, 1969.

Felsher, B. F., Craig, J. R. and Carpio, N. Hepatic bilirubin glucuronidation in Gilbert's syndrome. J. Lab. Clin. Med. 81:829-837, 1973.

Billing, B. H., Williams, R. and Richards, T. G. Defects in hepatic transport of bilirubin in congenital hyperbilirubinaemia: An analysis of plasma bilirubin disappearance curves. Clin. Sci. 27:245-257, 1964.

Berk, P. D., Bloomer, J. R., Howe, R. B. and Berlin, N. I. Constitutional hepatic dysfunction (Gilbert's syndrome). A new definition based on kinetic studies with unconjugated radiobilirubin. Am. J. Med. 49:296-305, 1970.

Powell, L. W., Billing, B. H. and Williams, H. S. An assessment of red cell survival in idiopathic unconjugated hyperbilirubinaemia (Gilbert's syndrome) by the use of radioactive diisopropylfluorophosphate and chromium. Aust. Ann. Med. 16:221-225, 1967.

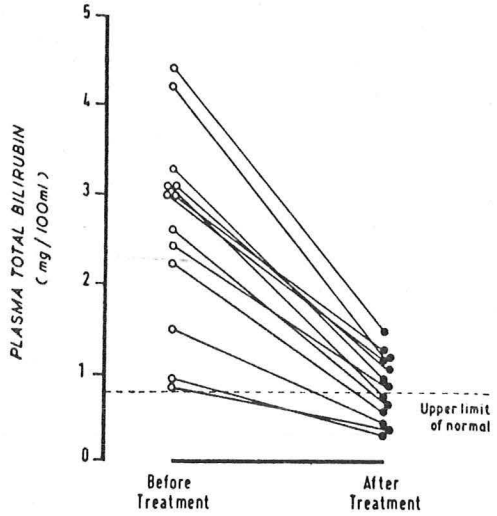
Berk, P. D. and Blaschke, T. F. Detection of Gilbert's syndrome in patients with hemolysis. A method using radioactive chromium. Ann. Int. Med. 77:527-531, 1972.

Berk, P. D., Glaschke, T. F. and Waggoner, J. G. Defective bromosulfophthalein clearance in patients with constitutional hepatic dysfunction (Gilbert's syndrome). Gastroenterology 63:472-481, 1972.

Martin, J. F., Vierling, J. M., Wolkoff, A. W., Scharschmidt, B. F., Vergalla, J., Waggoner, J. G. and Berk, P. D. Abnormal hepatic transport of indocyanine green in Gilbert's syndrome. Gastroenterology 70: 385-391, 1976.

Barth, R. F., Grimley, P. M., Berk, P. D., Bloomer, J. R. and Howe, R. B. Excess lipofuscin accumulation in constitutional hepatic dysfunction (Gilbert's syndrome). Arch. Path. 91:41-47, 1971.

Serum bilirubin is influenced by drugs such as phenobarbital (bilirubin concentration falls) as well as by food.



—Effect of phenobarbitone (180 mg. daily for 2 weeks) on plasma-bilirubin levels in Gilbert's syndrome.

from Black and Sherlock, Lancet i: 1359, 1970.

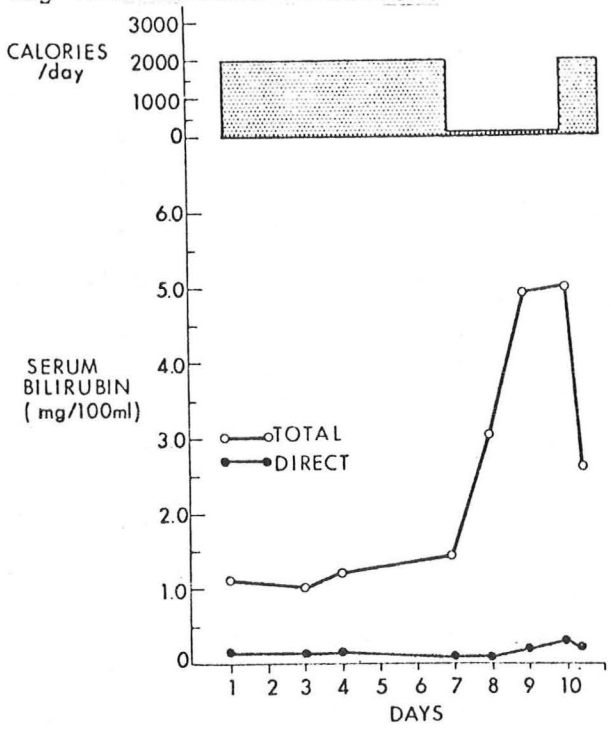
EFFECT OF PHENOBARBITAL ON HYPERBILIRUBINEMIA

Black, M. and Sherlock, S. Treatment of Gilbert's syndrome with phenobarbitone. Lancet i:1359-1362, 1970.

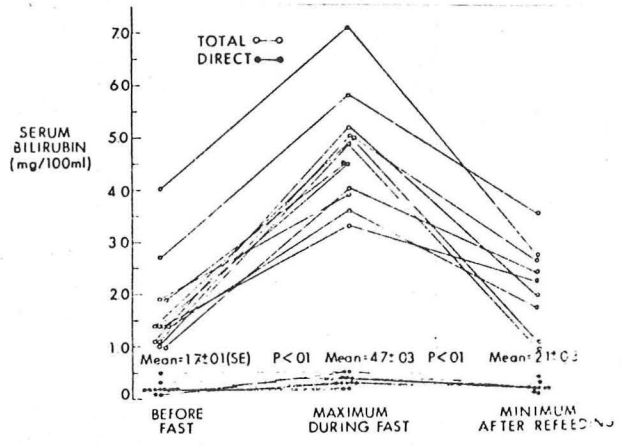
Blaschke, T. F., Berk, P. D., Rodkey, F. L., Scharschmidt, B. F., Collison, H. A. and Waggoner, J. G. Drugs and the Liver-I. Effects of glutethimide and phenobarbital on hepatic bilirubin clearance, plasma bilirubin turnover and carbon monoxide production in man. Biochem. Pharmacol. 23:2795-2806, 1974.

Black, M., Fevery, J, Parker, D., Jacobson, J., Billing, B. H. and Carson, E. R. Effect of phenobarbitone on plasma [^{14}C]bilirubin clearance in patients with unconjugated hyperbilirubinaemia. Clin. Sci. Mol. Med. 46:1-17, 1974.

Fasting undoubtedly provides one major explanation for the exaggeration of jaundice during intercurrent infection.



. Results of One Diet Study in Case 1.
The diet on days seven, eight, and nine consisted of only 30 calories. The decrease in serum bilirubin on day 10 occurred after three meals over a 12-hour period.

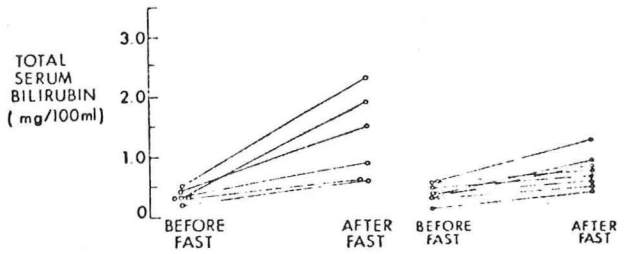


Results of 12 Diet Studies in Seven Patients with Gilbert's Syndrome.

from Felsher et al., New Engl. J. Med. 283:170, 1970

The mechanism involves further impairment of hepatic uptake of bilirubin. Measurements of glucuronyl transferase activity in liver reveal no significant change in enzyme activity. Moreover, fasting hyperbilirubinemia can be induced even when glucuronyl transferase activity is absent. Bilirubin production has been found to be increased, decreased, or not to change in various fasting studies.

Serum bilirubin also increases in normal persons with fasting. Of interest, it increased relatively more in nonicteric relatives of a patient with Gilbert's syndrome.



. Changes in Serum Bilirubin during a Fast of 24 to 48 Hours in Six Nonicteric Relatives of Case 1 (Left) and in Eight Normal Control Subjects (Right).

from Felsher et al., N. Engl. J. Med. 283:170, 1970

EFFECT OF FASTING ON HYPERBILIRUBINEMIA

Felsher, B. F., Rickard, D. and Redeker, A. G. The reciprocal relation between caloric intake and the degree of hyperbilirubinemia in Gilbert's syndrome. N. Engl. J. Med. 283:170-172, 1970.

Bensinger, T. A., Maisels, M. J., Carlson, D. E. and Conrad, M. E. Effect of low caloric diet on endogenous carbon monoxide production: Normal adults and Gilbert's syndrome. Proc. Soc. Exp. Biol. Med. 144: 417-419, 1973.

Kirshenbaum, G., Shames, D. M. and Schmid, R. An expanded model of bilirubin kinetics: effect of feeding, fasting, and phenobarbital in Gilbert's syndrome. J. Pharmacokin. Biopharm. 4:115-155, 1976.

Barrett, P. V. D. Hyperbilirubinemia of fasting. J.A.M.A. 217:1349-1353, 1971.

Barrett, P. V. D. The effect of diet and fasting on the serum bilirubin concentration in the rat. Gastroenterology 60:572-576, 1971.

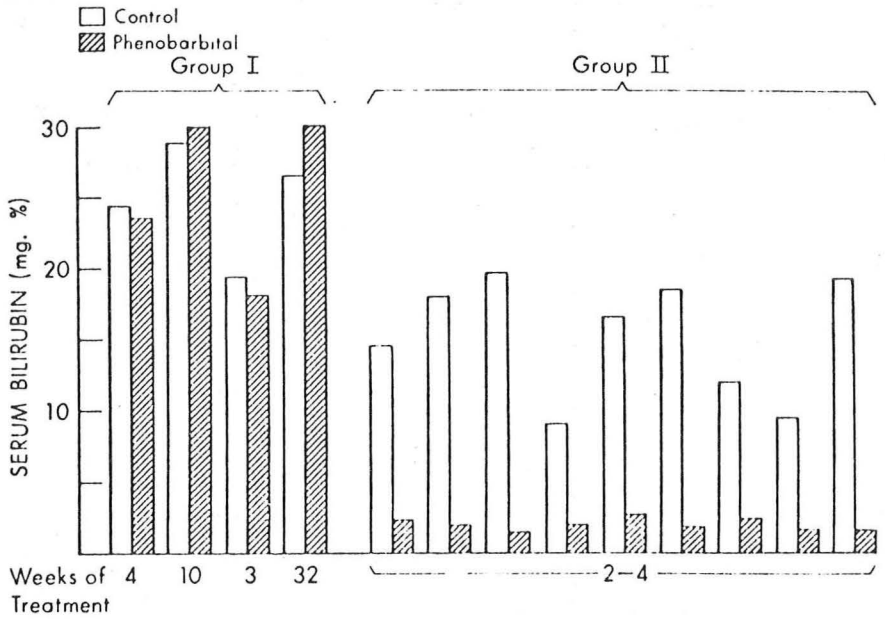
Bloomer, J. R., Barrett, P. V., Rodkey, F. L. and Berlin, N. I. Studies on the mechanism of fasting hyperbilirubinemia. Gastroenterology 61:479-487, 1971.

Barrett, P. V. D. Effects of caloric and noncaloric materials in fasting hyperbilirubinemia. Gastroenterology 68:361-369, 1975.

Rosental, E. and Thaler, M. M. Nutrient type, amount, and route of administration in reversal of fasting hyperbilirubinemia (FH). Gastroenterology 71:927, 1976 (abstract).

Bradley, E. M., Bellamy, H. M., Knudsen, K. B. and Lecocq, F. R. Impairment of biliary transport as a cause of sulfobromophthalein retention in fasting men. Metabolism 18:675-683, 1969.

The Crigler-Najjar syndrome is characterized by more profound unconjugated hyperbilirubinemia, and virtual absence of bilirubin glucuronyl transferase activity. Two types have been differentiated by the response of serum bilirubin to administration of phenobarbital. In Type I, inherited as an autosomal recessive disorder, serum bilirubin does not change. In Type II, inherited as an autosomal dominant, serum bilirubin falls significantly when phenobarbital is administered.



The effect of phenobarbital administration on serum bilirubin concentrations in four patients (Cases 1 through 4) in group I and nine patients (Cases 6 through 14) in group II.

from Arias et al., Am. J. Med. 47:395, 1969.

CRIGLER-NAJJAR SYNDROME

Arias, I. M., Gartner, L. M., Cohen, M. Ezzer, J. B. and Levi, A. J. Chronic nonhemolytic unconjugated hyperbilirubinemia with glucuronyl transferase deficiency. Am. J. Med. 47:395-409, 1969.

Crigler, J. S. and Najjar, V. A. Congenital familial non hemolytic jaundice with kernicterus. Pediatrics 10:169, 1962.

Childs, B. and Najjar, V. A. Familial non-hemolytic jaundice with Kernicterus. Pediatrics 18:369, 1956.

Kreek, M. J. and Sleisenger, M. H. Reduction of serum-unconjugated-bilirubin with phenobarbitone in adult congenital non-haemolytic unconjugated hyperbilirubinaemia. Lancet ii:73-77, 1968.

Bloomer, J. R., Berk, P. D., Howe, R. B. and Berlin, N. I. Bilirubin metabolism in congenital nonhemolytic jaundice. Pediat. Res. 5:256-264, 1971.

Blaschke, T. F., Berk, P. D., Scharschmidt, B. F., Guyther, J. R., Vergalla, J. M. and Waggoner, J. G. Crigler-Najjar Syndrome: An unusual course with development of neurologic damage at age eighteen. Pediat. Res. 8:573-590, 1974.

Gollan, J. L., Huang, S. N., Billing, B., and Sherlock, S. Prolonged survival in three brothers with severe type 2 Crigler-Najjar syndrome. Ultrastructural and metabolic studies. Gastroenterology 68:1543-1555, 1975.

Gordon, E. R., Shaffer, E. A., and Sass-Kortsak, A. Bilirubin secretion and conjugation in the Crigler-Najjar syndrome type II. Gastroenterology 70:761-765, 1976.

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Hyperbilirubinemia in rare instances may be due to hypertrophy of the "shunt pathway."

SHUNT HYPERBILIRUBINEMIA

Israels, L. G., Suderman, H. J., Ritzmann, S. E. Hyperbilirubinemia due to an alternate path of bilirubin production. Am. J. Med. 27:693-702, 1959.

Watson, C. J. The continuing challenge of hemoglobin and bile pigment metabolism. Ann. Intern. Med. 63:931-944, 1965.

Robinson, S., Vanier, T., Desforges, J. F. and Schmid, R. Jaundice in thalassemia minor. A consequence of "ineffective erythropoiesis." N. Engl. J. Med. 267:523-529, 1962.

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There are two distinct forms of inheritable conjugated hyperbilirubinemia referred to as the Dubin-Johnson and Rotor Syndromes.

Inheritable Conjugated Hyperbilirubinemia

	Dubin-Johnson	Rotor
Other liver tests	Normal	Normal
Bile acid metabolism	Normal	Normal
Visualization of biliary tract	-	+
Pigment in liver cells	+	-
Mode of inheritance	Autosomal Recessive	Autosomal Recessive
Transport defect(s)	Excretory	Uptake and Excretory

They have distinguishable transport defects and differences in urinary coproporphyrin excretion. Urinary coproporphyrin studies have also helped define their modes of inheritance.

BSP Disposition in Dubin-Johnson and Rotor's Syndromes

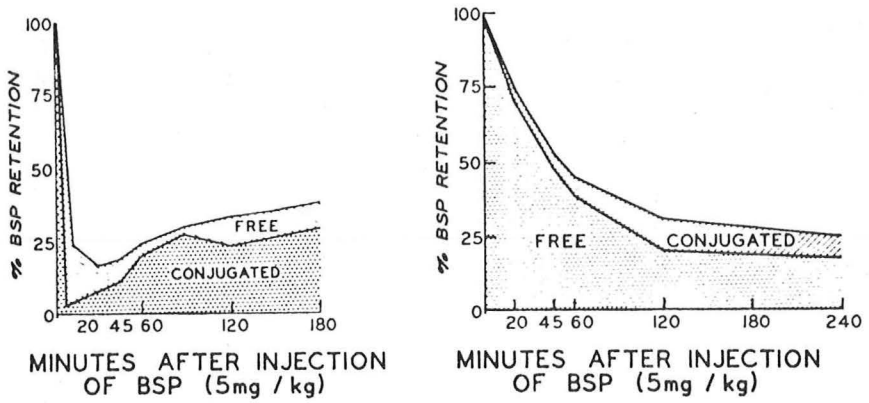


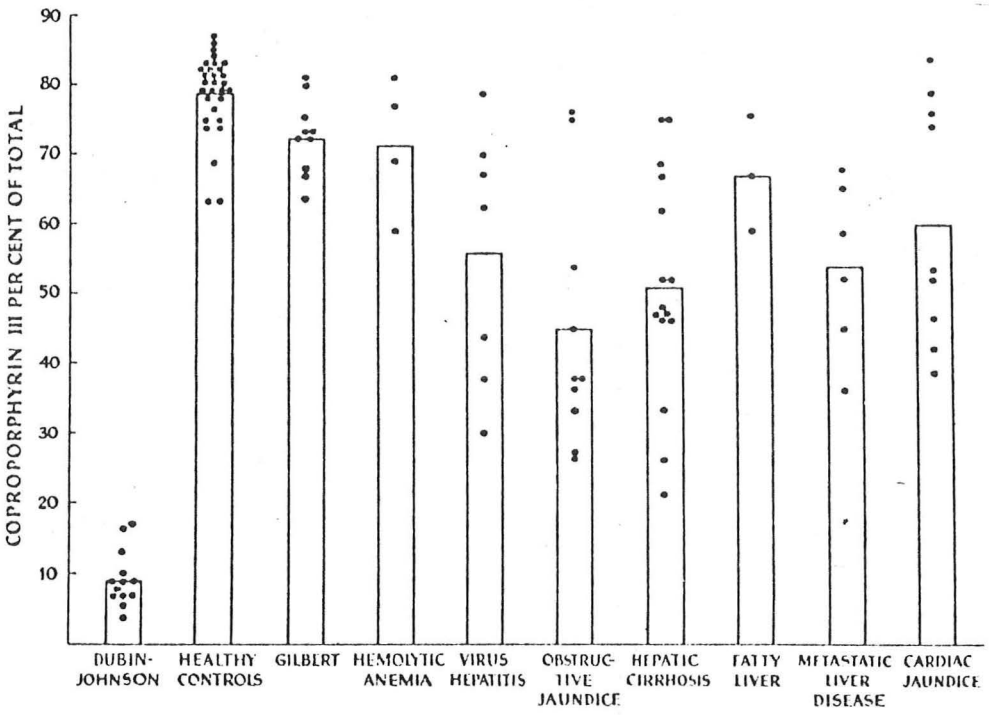
Fig. · (*left*). Bromsulfalein (BSP) excretion test in patient with Dubin-Johnson syndrome, showing conjugated and unconjugated serum BSP levels following I.V. injection of 5 mg./kg. BSP. A late rise in serum BSP is observed beginning 30 min. after injection. **Fig.** · (*right*). Bromsulfalein (BSP) excretion test in patient with Rotor's syndrome, showing conjugated and unconjugated serum BSP levels following I.V. injection of 5 mg./kg. BSP. No late rise in serum BSP is observed.

from Dollinger and Brandborg, Am. J. Dig. Dis. 12:415, 1967.

BSP Disposition in Rotor's and Dubin-Johnson's Syndrome

	S (storage) mg/mg/100ml	Tm (maximal transport) mg/min
Normal Controls	67.8 ± 17.9	8.0 ± 0.4
Dubin-Johnson	68.8 ± 15.9	0.4 ± 0.2
Rotor	7.7 ± 1.5	4.4 ± 0.8

Coproporphyrin Excretion in Dubin-Johnson and Rotor's Syndromes



Urinary coproporphyrin Isomer III content in Dubin-Johnson syndrome and other states.

from Koskelo et al., Clin. Chem. 13:1006, 1967.

Urinary coproporphyrin isomer I content, expressed as percentage of total coproporphyrin[a]

Subjects	*No. of subjects*	*Mean relative content of isomer I* (%)	*Isomer III* (μg/g creatinine)[c]
Controls	73	27	43.9 ± 25.3
DJS patients	56	88	11.5 ± 6.2
First degree relatives	151	47[b]	25.5 ± 17.3[b]
Other relatives	63	38[b]	29.8 ± 23.0[b]

[a] Results of examinations of single samples.
[b] Significantly different from normal controls and from DJS patients ($P < 0.001$).
[c] Values are means ± SD.

from Ben-Ezzer et al., Isr. J. Med. Sci. 9:1531, 1973.

Urinary Coproporphyrin Excretion in
Rotor's and Dubin-Johnson's Syndrome

(From Woekoff et al., Am. J. Med. 60:173, 1976)

	Urinary Coproporphyrin 1 % of Total Coproporphyrin
Normal Controls	24.8 ± 1.3
Dubin-Johnson	88.9 ± 1.3
Rotor's - patients	64.8 ± 2.5
obligate heterozygotes	42.9 ± 5.4

DUBIN-JOHNSON SYNDROME

Dubin, I. N. and Johnson, F. B. Chronic idiopathic jaundice with unidentified pigment in liver cells: A new clinico pathologic entity with a report of 12 cases. Medicine 33:155-196, 1954.

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* *

Laboratory Profile of Obstructive Jaundice

Bilirubin	5-20 mg %
Alkaline Phosphatase	3X or > normal
SGOT	< 300-400
Prothrombin time	Normal or responds rapidly to Vitamin K
Serum proteins	Usually well preserved

Non-surgical Causes of Obstructive Jaundice

1. Drugs - history

   A. Hormones - methyl testosterone
                 estrogens
                 progestogens

      1. Underlying liver disease
      2. Predisposition - pruritus or jaundice of pregnancy

   B. Unpredictable

      Phenothiazines
      Sulfonamides
      Ilosone
      Propylthiouracil
      Tapazole
      Phenylbutazone
      Chlorpropamide
      Many others

2. Viral hepatitis - HB_sAg

3. Alcohol - history

4. Primary Biliary Cirrhosis - antimitochondrial antibody

5. Inflammatory bowel disease

      Pericholangitis
      Sclerosing cholangitis

6. Hodgkin's disease

7. Severe infection

8. Sarcoidosis

9. Benign recurrent cholestasis

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* *

Non-invasive Cholecystography and Cholangiography

Relationship Between Serum Bilirubin Level and the Likelihood of Common Bile Duct Visualization*

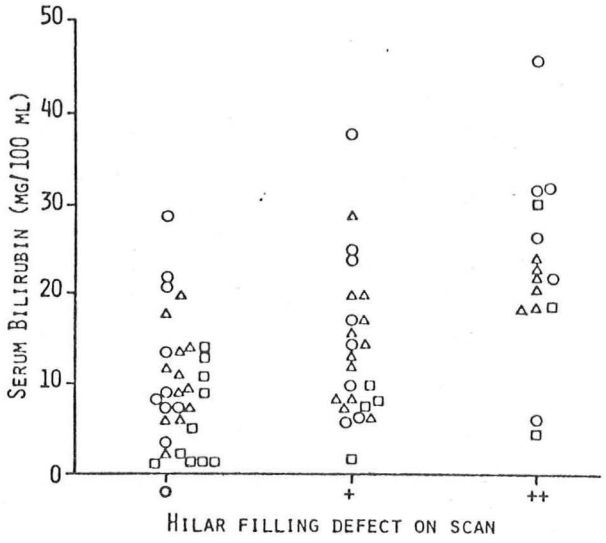
SERUM BILIRUBIN (mg/100ml)	PERCENT OF VISUALIZATION
0-1.0	92.5
1.0-2.0	81.7
2.0-3.0	40.0
3.0-4.0	31.8
4.0+	9.3

*Modified from Wise RE: Intravenous Cholangiography. Springfield, Ill., Charles C. Thomas, 1962, p. 25.

* *

Liver Scans in Obstructive Jaundice

Approximately half of the liver scans in extrahepatic obstruction showed a filling defect in the hilar region of the liver. Present in 80 per cent of patients with a serum bilirubin greater than 15 mg/100 ml.



Relationship between depth of jaundice and reports of hilar defect on liver scan (○—Duct carcinoma, △—carcinoma of the pancreas, □—non-malignant obstructive jaundice).

0 = no defect; + = moderate
++ = severe defect

from Agnew et al., Br. J. Radiol. 48:190, 1975

LIVER SCANNING

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Liver Biopsy in Obstructive Jaundice

LIVER BIOPSY IN LARGE BILE DUCT OBSTRUCTION
(Morris et al. Gastroenterology 68:750, 1975
Royal Free Hospital-London)

Number biopsies performed	127	
Number failure	2	
Biopsy compatible with large bile duct obstruction	103	(81%)
Cholestasis sole histologic abnormality	16	(13%)
Biopsy - not helpful or misleading	6	(5%)

COMPLICATIONS OF LIVER BIOPSY IN LARGE BILE DUCT OBSTRUCTION

(Morris et al. Gastroenterology 68:750, 1975)

Number biopsies performed	127	
Complications	8	
Bile peritonitis		1
Sepsis		2
Pleural effusion		1
RUQ pain, severe		3
Blood stained ascites found at surgery one week later		1

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High SGOT in Extrahepatic Obstruction

EAH, 26 ♀, PMH # 50-59-53.

12-17-74 underwent cholecystectomy for cholelithiasis and cholecystitis. No common duct exploration. Received no blood. Experienced recurrent episodes of pain resembling those she had prior to surgery.

Admitted to PMH on 5-20-75. Received demerol in emergency room, and 3x during week prior to admission.

	5/20	5/21	5/22	5/28
Bilirubin	7.2	5.5	3.8	2.4
Alk. Ptase-KA		25.6	28.4	16.0
SGOT	2070	172	91	34
Amylase	<320			
Hb_sAg	neg.			

5-23 Liver biopsy #75-4439
Edematous portal tracts with mixed inflammatory infiltrate

5-24 Common duct exploration - 12 mm duct
2 calcium bilirubinate stones at level of Ampulla of Vater

SGOT >500 with Cholelithiasis

Patient		Highest SGOT	Highest Bilirubin	Pain	Narcotics
EAH	26 ♀	2070	7.2	+	+
HW	44 ♀	>500(2x)	2.0	+	+
ME	33 ♀	781	2.4	+	-
CB	21 ♀	>500(2x)	5.1	+	-

All HB_sAg-; multiple amylases < 320

MISLEADING SGOT RESULTS IN EXTRAHEPATIC OBSTRUCTION

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Ultrasound and Invasive Cholangiography in Obstructive Jaundice

GRD 36 ♂ PMH # 55-33-48

Onset jaundice, dark urine, light stools, pruritus in early September 1976. Hospitalized elsewhere. No definite diagnosis.

Admitted to PMH October 1976. Denied abdominal pain, exposure to toxins, use of drugs or alcohol, exposure to hepatitis, any gastrointestinal symptoms. Physical examination revealed icterus, excoriations, 14 cm liver span.

10-8 Liver scan normal

10-9 Ultrasonography - normal gallbladder. Liver normal without evidence of dilated bile ducts

10-12 UGI series normal

10-14 Transhepatic cholangiogram - normal ducts and gallbladder.

10-15 Liver biopsy - marked centrilobular cholestasis with marked Kupffer cell hyperplasia. Minimal chronic portal inflammation. Minimal individual cell necrosis.

Patient was started on cholestyramine - one month following discharge, pruritus was markedly improved, bilirubin had fallen, but SGOT and alkaline phosphatase were higher.

Diagnosis - Intrahepatic cholestasis, etiology unknown.

	NCM Hospital			PMH				
1976	9/15	9/20	9/23	10/4	10/8	10/13	10/18	11/18
Bilirubin	15.6	11.2	8.8	13.1	12.2	14.0	13.0	2.5
Alk Ptase	390	260	250	265	17.0 KA	30.0	29.4	500
SGOT	48	37	37	93	60	64	59	344
Amylase				<320	<320	<320		
HB$_S$Ag	neg.				neg.		neg.	
Antimitochondrial antibody		neg			neg.			
Liver scan		normal			normal			
UGI		normal				normal		
Hypotonic duodenography		normal						
IVP		normal						
α-fetoprotein	<20 mg/ml							

RW 53 ♂ PMH # 53-33-56.

10/75 Suprapubic cystotomy for bladder stone.
2-3 units of blood for post-op bleeding.

12/75 Jaundice. Impression: post transfusion hepatitis, non B.
(see laboratory data).

3/30/76 Admitted to PMH because of persistent jaundice. Denied abdominal pain or any GI symptoms other than anorexia. No alcohol intake for 7 years. 30 pound weight loss.
Physical exam: jaundice. 6 x 6 cm mass in epigastrium to right of midline. No hepatosplenomegaly.

3/30 Ultrasonography: round cystic mass in region of head of pancreas, 6 x 10 cm. Dilated ducts in liver. Gallbladder normal.

4/1 Liver Scan: decreased activity lower right lobe anteriorly, most likely due to external compression.

4/2 UGI series: diffuse calcification in region of pancreas. Extrinsic compression of duodenum.

4/8 Transhepatic cholangiogram: Common hepatic and common bile ducts dilated to approximate midportion of the common bile duct. Smooth concentric narrowing of common bile duct with posterior displacement of duct. Compatible with pancreatitis or pseudocyst.

Preoperative diagnosis: Pseudocyst of pancreas

4/8 Surgery: Cystojejunostomy
No gallstones

Diagnosis: Chronic pancreatitis
Pseudocyst of pancreas
Common bile duct obstruction.

					PMH						
1976	1/6	1/13	1/30	2/25	3/30	4/1	4/8	4/13	4/19	4/21	4/27
Bilirubin	>12	9.8	9.5	6.7	5.1	5.3	5.8	2.5	1.7	1.9	1.3
Alk Ptase	>80	200	280	145	>700	140 KA	112KA	60	57	59	83
SGOT	>200	1750	350	158	350	175	156	27		32	93
Amylase					<320		<320	<320			
HB_sAg	neg.										

KS 40 ♂ PMH # 53-33-69

First admission 3-31-76

Bartender, chronic alcohol consumption characterized by binges of 2-3 weeks duration. Most recent binge ended 3-23.

3-27 Dark urine, light stools
No GI or flu-like symptoms
No pruritus.
Physical exam - icteric, dark skin with erythematous flush of neck and upper chest. Scars on neck. No hepatosplenomegaly or ascites. No spiders.

4-1 Liver scan normal

4-8 Ultrasonography - normal gallbladder. No pancreatic abnormality. No focal liver defects.

Pt. refused liver biopsy.

4-10 Discharged with diagnoses

1. Alcoholic liver disease
2. Porphyria cutanea tarda

Second admission 5-6-76

Remained off alcohol. Jaundice increased. Developed pruritus.

Physical examination - unchanged, but more icteric.

5-10 Antimitochondrial antibody negative

5-11 Liver scan - patchy hepatic uptake with enlargement of left lobe. No discrete filling defects.

5-12 Ultrasonography - dilated intrahepatic ducts.

In retrospect, this was present but less obvious on initial examination. Sonolucent structure 2 x 5 cm, overlying inferior vena cava in region of the head of the pancreas. Gallbladder not enlarged.

5-13 UGI series normal.

5-19 Transhepatic cholangiogram - impacted common duct stone in the region of the ampulla of Vater with markedly dilated common bile duct superior to this.

5-19 Cholecystectomy, common duct exploration with removal of stones. Insertion of T-tube.

1976	1st Admission				2nd Admission					
	4/1	4/5	4/7	4/9	5/6	5/10	5/16	5/19	5/25	6/4
Bilirubin	15.4		15.8		23.2	26.4	19.5	15.0	9.8	3.8
Alk Ptase KA	30	32	15.7		42.8	35	43		25.5	
SGOT	166	99	96		72	64	79		118	
Amylase	<302	<320			<320	<320	<320			
Protein										
Total	7.8	7.1								
Albumin	4.1	4.1								
HB_sAg		neg.								
WBC	11.5			12.3	20.8	11.7				

BE 19 ♀ PMH # 49-52-33
10-23-75 Term delivery (G4, P4).

1-8-76 Admitted to PMH with history of intermittent nausea, vomiting and abdominal pain. Symptoms began during latter part of recent pregnancy. Was being followed in clinic as probable viral hepatitis.

No drugs prior to development of abnormal liver tests. Gantrisin for 1 week prior to admission.

Physical exam - no fever, jaundiced, excoriations of arms and legs. Abdomen - normal.

1-9 Liver scan normal
IVP normal

1-12 Ultrasound - normal gallbladder. Head of pancreas slightly prominent but probably normal. Probable dilation of intra-hepatic bile ducts.

1-15 UGI series normal.

Intermittent nausea, vomiting and upper abdominal pain in hospital. No fever and WBC normal.

1-19 Transhepatic cholangiogram - large stone in the common bile duct.

1975	10/23*	12/5*	12/12*	1976	1/9	1/14	1/20	1/23	2/3	3/22*
Bilirubin	0.7	8.6	11.8		11.4	12.6	15.2	5.4	2.1	0.5
Alk Ptase	145	332	358		108	95	144		5.5	103
SGOT	42		184		126	109	117		64	48
Amylase						<320	<320			
HB_sAg						neg.				
	↑ term delivery									

* SMA

Results of Grey-Scale Ultrasonography
(Mitcell et al., Gut 17:814, 1976, Abstract)

Patients with clinical features of biliary obstruction	53
Unsuccessful test	7

Subsequent clinical course		Dilated ducts	No dilated ducts
Biliary obstruction excluded	24	2	22
Biliary obstruction confirmed	22	18	4

ULTRASOUND EVALUATION OF THE BILIARY TRACT

Taylor, K.J.W., Carpenter, D. A., McCready, V. R. Gray scale echography in the diagnosis of intrahepatic disease. J. Clin. Ultrasound 1:284, 1973.

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Invasive Cholangiography

Success Rates of Conventional and Fine Needle Transhepatic Cholangiography

Technique and Reference	Overall No.	Overall %	Dilated No.	Dilated %	Not Dilated No.	Not Dilated %
Conventional:						
Evans [4]	150/200	75	...	92	...	50
Hines et al. [5]	80/102	78	68/73	93	7/23	30
Fine needle:						
Okuda et al. [1]	268/314	85	95/95	100	54/80	67
Redeker et al. [2]	32/40	80	20/20	100	12/20	60
Present report	46/50	92	33/33	100	14/17	82

from Ferrucci et al., Am. J. Roentgenol.127:403, 1976.

Comparison of Transhepatic and Endoscopic Retrograde Cholangiography

The success rate for both procedures according to whether cholestasis was intrahepatic or extrahepatic

Type of cholangiography	No. of patients	Successful	Failed	% success
Extrahepatic cholestasis (29 patients)				
Retrograde	21	13	8	62
Percutaneous	20	19	1	95
Intrahepatic cholestasis (31 patients)				
Retrograde	25	19	6	76
Percutaneous	24	6	18	25

from Elias et al., Gastroenterology 71:439, 1976

Comparative Features of Direct Cholangiography

Feature	Endoscopic Retrograde Cholangiography	Fine Needle Transhepatic Cholangiography
Success Rate of bile duct opacification (%)	70	90
Time required (min)	90	45
Total cost ($)	400	100
Operator skill required	Considerable	Modest
Complications:		
Bacteremia (%)	1–2	5–10
Other	...	...

from Ferrucci et al., Am. J. Roentgenol. 127:403, 1976.

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