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# DIAGNOSTIC SIGNIFICANCE OF COIL PLANET CENTRIFUGATION IN OBSTRUCTIVE JAUNDICE

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## Abstract

**Deviation of hemolysis patterns of coil planet centrifugation (CPC) were observed sequentially at a week interval for more than three weeks in 28 cases of obstructive jaundice (cholelithiasis 21, malignant biliary obstruction 5, primary biliary cirrhosis 1 and primary sclerosing cholantitis 1). (1) As already pointed out by various investigators, the deviation of hemolysis end point (HEP) to lower osmolar side is characteristic of biliary obstruction (HEP was 63.5 mOsm in benign biliary obstruction, while it was 41.2 mOsm in malignant biliary obstruction on the average). (2) Shift of hemolysis starting point (HSP) should also be observed with attention, because it often deviates to hyperosmolar side in benign obstruction, especially in its recovery stage. (3) In general, HEP and HSP shift to lower osmolar side in malignant obstruction. At the same time the hemolysis curves mostly assume a T type pattern. However, in aggravation, they are of R type pattern. Therefore, observation of hemolysis curves is valuable for diagnostic purpose. (4) In primary biliary cirrhosis or primary sclerosing cholangitis the CPC patterns remain within the normal range despite the presence of overt signs of biliary obstruction.**

## INTRODUCTION

Coil planet centrifugation (CPC) was invented in this country as a new method for measuring osmotic fragility of erythrocytes[1] and introduced not only to hematology but also to hepatology as a useful diagnostic tool[2,3,4]. Yamada[5,6] will be one of the first investigators who pointed out that the hemolysis end point (HEP) of the hemolysis band observed by CPC shifted to hypoosmolar side in liver cirrhosis and liver cancer. He classified the hemolysis curves into four category and noticed the specific changes of their shapes

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in individual liver diseases. We examined 28 cases of obstructive jaundice and could obtain interesting results about the changes of the hemolysis patterns.

## MATERIALS AND METHODS

Twenty eight patients with obstructive jaundice were chosen for examination, in which 21 cases of cholelithiasis, 5 of malignant obstruction and each one of primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). The diagnosis of biliary obstruction was confirmed by cholangiography (DIC, PTC, ERCP) or by surgical operation. Examination of HEP and HSP were achieved by the standard technique already described by Shibata *et al.*[7]. The densitograms of the hemolysis bands were classified into four types according to their shapes with special reference to the position of their hemolysis peaks; type L (left sided), M (middle), T (table-like plateau) and R (right sided[5]).

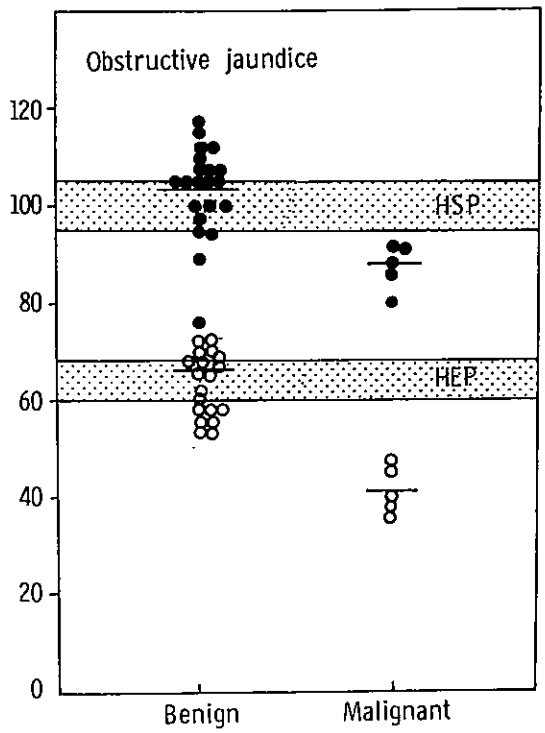


Fig. 1. Hemolysis end point (HEP) and hemolysis starting point (HSP) in benign and malignant biliary obstruction.

## RESULTS

1) HEP and HSP in obstructive jaundice

HEP and HSP in obstructive jaundice were shown in Fig. 1. In benign obstruction HEP was 63.5 ± 6.13 mOsm and HSP was 102.9 ± 9.01 mOsm, while in malignant biliary obstruction HEP and HSP were 41.2 ± 4.71 mOsm and 87.6 ± 4.45 mOsm, respectively. Statistical differences of HEP and HSP between benign and malignant biliary obstruction were evident ($p < 0.001$ and $p < 0.01$, respectively).

2) Serial alterations of HEP and HSP in obstructive jaundice

Changes of CPC hemolysis pattern in obstructive jaundice were examined periodically once a week for at least six weeks. Fig. 2 shows the alterations of HEP and HSP in benign obstruction, in which HEP remained always in normal range, but HSP were below the normal range in the early stage but

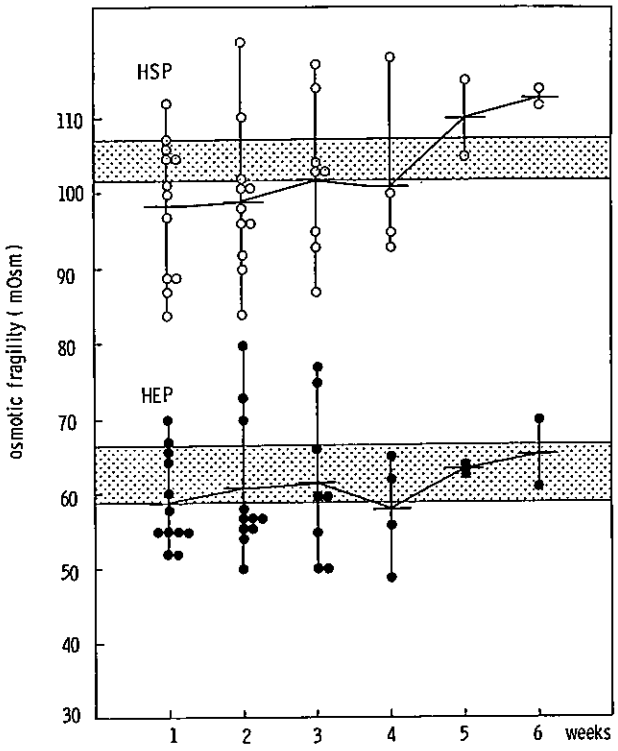


Fig. 2. Weekly changes of HEP and HSP in benign biliary obstruction. Note the hyperosmolar deviation of HSP in the recovery stage.

gradually deviated to the left (hyperosmolar) side and tended to trespass on the left range outside of the normal HSP limit in recovery stage. In malignant obstruction HEP and HSP shifted rightwards (to the hypoosmolar side) and deviated extremely to lower osmolar side in some cases (Fig. 3).

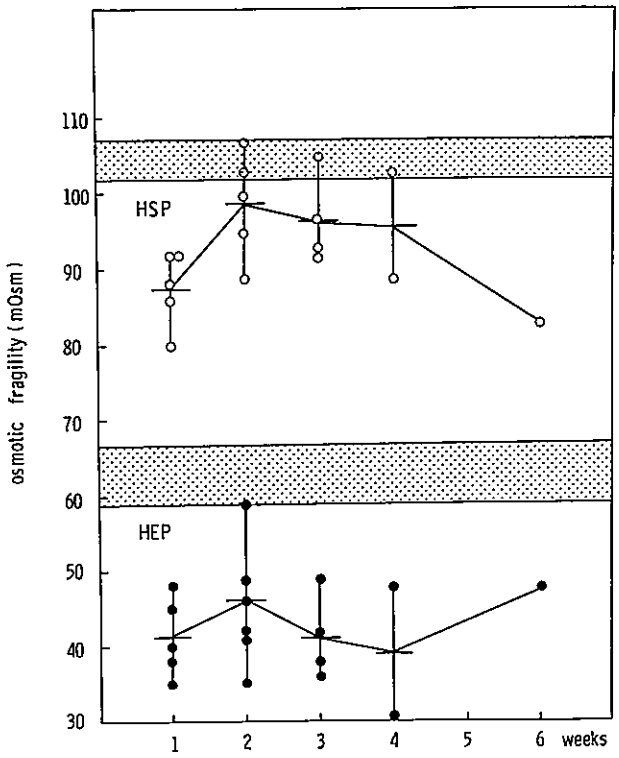


Fig. 3. Weekly changes of HEP and HSP in malignant biliary obstruction. Both HEP and HSP remain in the hypoosmolar range.

3) Serial changes of CPC in various biliary obstruction

The case shown in Fig. 4 was a 60 year old female with cholelithiasis, who complained of right hypochondralgia on April 8, 1978, and was hospitalized on April 11 because of swelling of the gallbladder. ERCP revealed numerous stones within the gallbladder with dilatation of common bile duct. Laboratory examinations on admission were WBC 7800, serum bilirubin 0.5 mg/dl, GPT 13 and GOT 14 I.U./L. The patient was operated on and 50 stones were removed from the gallbladder. HEP varied from 69, 70, 75 mOsm and HSP reached 112 mOsm. Hemolysis patterns remained L throughout.

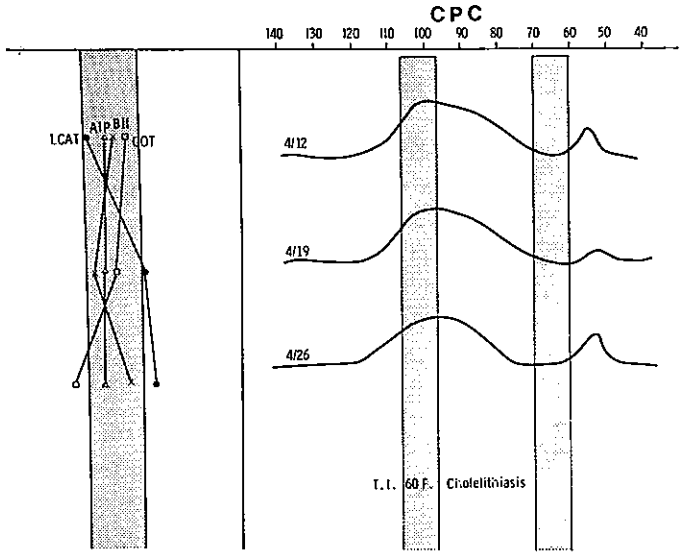


Fig. 4. Serial alterations of hemolysis band in cholelithiasis.

Fig. 5 is the hemolysis patterns of a case of acute obstructive suppurative cholangitis. The patient was a 63 year old female and she had high fever

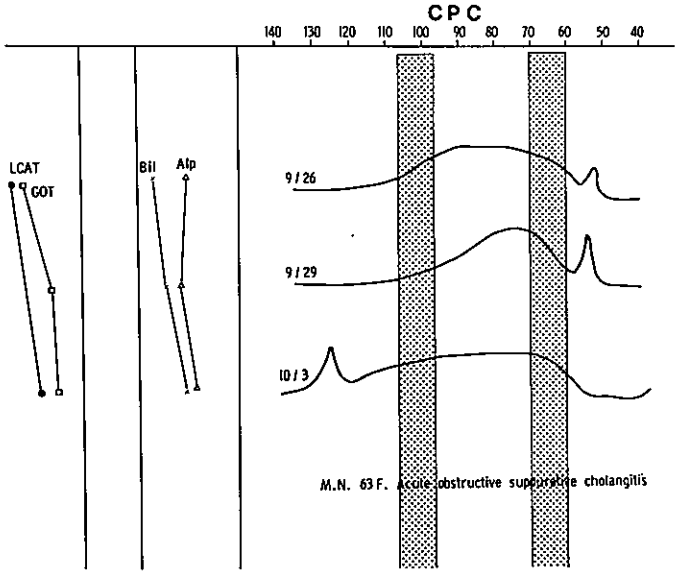


Fig. 5. Serial alterations of hemolysis band in acute obstructive suppurative cholangitis.

(40°C) on September 16, 1977 and was admitted to the hospital on September 19. Laboratory data showed that WBC was 12400, serum bilirubin 11.5 mg/dl, alkaline phosphatase 252 I.U./L, GPT 34 and GOT 49 I.U./L. After admission remittent fever continued and she fell into septic shock on the 7th hospital day and WBC increased to 70000. Blood culture was positive for Klebsiella. The patient was dead on October 5 because of renal failure. HEP was as low (shifted to the hypoosmolar side) as 50–56 mOsm and hemolysis patterns changed from T type to R type in accordance with aggravation. As seen in this case CPC hemolysis patterns of R type was suggestive of poor prognosis.

Changes of CPC hemolysis patterns in pancreas head cancer[8] are shown in Fig. 6. The patient was a 78 year old female who was hospitalized on October, 1975, with the complaint of jaundice. PTC and HDG suggested cancer of the head of the pancreas. The patient was dead on November 16 because of hepatic coma. Autopsy established the diagnosis of adenocarcinoma of the head of the pancreas. HEP was shifted toward extremely low range, even as low as 36 mOsm on October 20. The hemolysis patterns were T to R types.

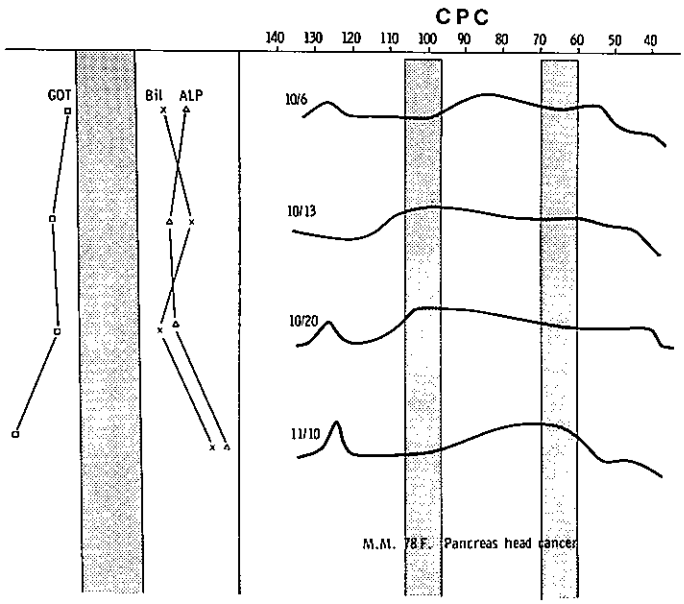


Fig. 6. Serial alterations of hemolysis band in maligant obstruction due to cancer of the head of the pancreas.

Fig. 7 illustrates the CPC patterns of a 44 year old female with primary biliary cirrhosis[9]. The patient noticed slight jaundice in May, 1976, and was admitted on July 4. Physical examination revealed hepatomegaly, xanthoma on the upper palpebrae, and skin pigmentation. Laboratory data showed serum bilirubin 4.8 mg/dl, IgM 848 mg/dl and antimitochondrial antibody strongly positive. CPC patterns were of T or LT type during icteric stage, but changed to L type on November 1, when jaundice was decreased in intensity and HSP was shifted to 112 mOsm.

The case shown in Fig. 8 was a 72 year old male of primary sclerosing cholangitis[10]. He became aware of jaundice in May, 1976, and was admitted on the 6th of the same month. PTC revealed localized stenosis of the common bile duct and surgical operation revealed generalized thickening of the extrahepatic bile duct. CPC patterns were of MT or T type without association of little changes of HSP and HEP throughout the whole course.

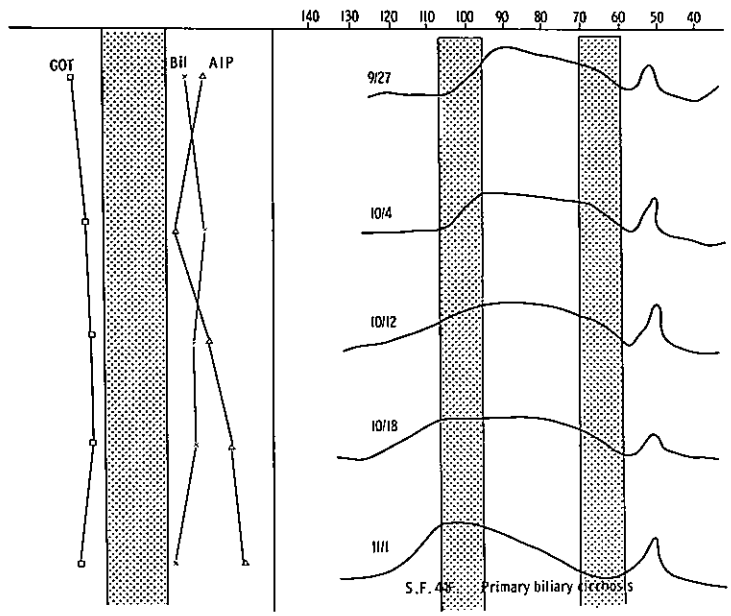


Fig. 7. Serial alterations of hemolysis band in primary biliary cirrhosis.

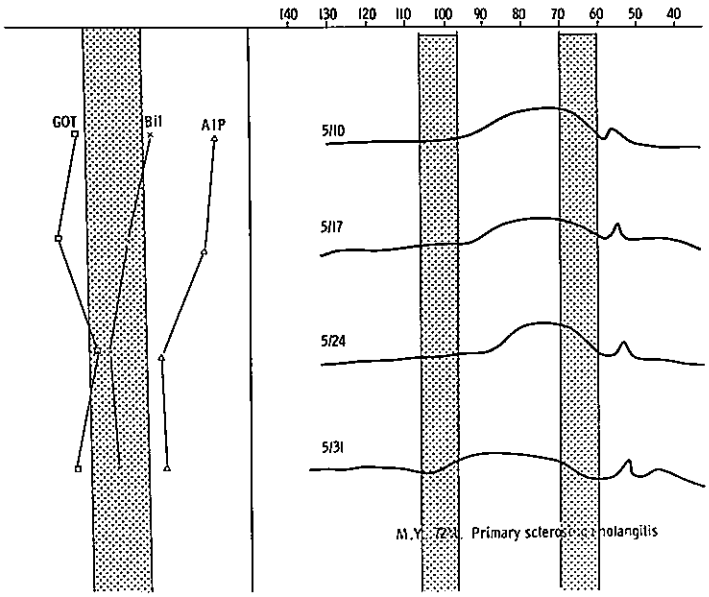


Fig. 8. Serial alterations of hemolysis band in primary sclerosing cholangitis.

## DISCUSSION

Application of CPC to the diagnosis of hepatobiliary disorders is becoming increasingly popular since the pioneering work made by Kitazima *et al.*[2] and its usefulness has been confirmed by many authors[3,4,6,11,12], However, these previous reports are chiefly interested in the deviation of HEP of the hemolysis band. As shown in the results which have been described in the preceding section there is a marked difference in hemolysis band (HSP and HEP) and hemolysis patterns between benign and malignant obstructions. The HEP was 63.5 mOsm in benign biliary obstruction, being within the normal range, whereas it was as low as 41.2 mOsm. The HSP showed the same tendency. As to the osmolar value of HEP in obstructive jaundice Kitazima *et al.*[2] reported 43 mOsm, Ando *et al.*[3] showed 61.0 mOsm in benign obstruction and 44.2 mOsm in malignant obstruction. The present authors[4] have already reported 48.7 mOsm of HEP for obstructive jaundice. Sasagawa *et al.*[11] advocated that HEP and HSP were within the normal range in the anicteric cases of cholelithiasis or cholecystitis but they were deviated to the lower somolar side with the appearance of jaundice. Our data which have been mentioned above are in agreement with these reports. The more the jaundice became severe, the more the HEP deviates to the lower osmolar side and the osmotic fragility of erythrocytes became decreased. Therefore, we could re-

affirm the data already reported by Kitazima *et al.*[2] so far as the HEP was concerned.

The mechanism of decreased osmotic fragility of erythrocytes has hitherto been explained as follows. In biliary obstruction bile acids regurgitate from bile cancliculi to the circulating blood and they rise to a considerably high level which will be able to inactivate LCAT (lecithin cholesterol acyltransferase) activity. This results in stagnation of free cholesterol in plasma and the free cholesterol thus stagnated passes into erythrocytes and fortifies its membrane in a way that it becomes resistant to hypoosmolar stress[2,13,14,15,16]. In contrast, there is another opinion that lipoprotein x, a globulin fraction which produces a complex substance with albumin, cholesterol and phospholipid, appears in the blood plasma of the patient with obstructive jaundice and it adheres to the erythrocytes bringing about the increment of cholesterol content of their membranes[3]. We have noticed marked decrease of LACT activity in malignant biliary obstruction[17].

One point that we want to emphasize is that we should pay attention not only to the HEP alone but also to the HSP because in benign obstruction HSP often diviates to hyperosmolar side, especially in convalescence and the tendency of HEP to move toward the hypoosmolar side is negated, and thus both HSP and HEP are prone to shift to the hyperosmolar side. The mechanism of this phenomenon remains to be elucidated, but it is obviously an interesting fact.

In a case of acute obstructive suppurative cholangitis which was shown in Fig. 5 the CPC hemolysis patterns took R type and the HEP deviated to the hypoosmolar side before death. Comparing these fatal cases accompanied by severe infection with the cases of simple cholelithiasis of good prognosis, it may be germane to say that the disease remains " benign " so long as the hyperosmolar deviation of HSP coexists with normal HEP.

In cases of malignant biliary obstruction presented in this paper marked deviations of HSP and HEP to the lower osmolar side associated with T type hemolysis patterns ultimately transforming into R type shortly before death were unanimously observed. It is supposed that in malignant obstruction not only the inhibition of LACT activity by bile acids or bilirubin due to severe jaundice but also the secondary hepatocellular impairment may accelerate the decrease of LCAT activity intensively, to induce extreme increment of cholesterol content of erythrocyte membranes resulting in deviation of HEP to the hypoosmolar side.

Finally we want to mention that there were no particular changes of hemolysis bands of CPC in primary biliary cirrhosis and primary sclerosing

cholangitis. No significant shift of hemolysis bands were noticed in spite of obvious evidence of biliary obstruction. It is therefore interpreted that the possibility of the rare diseases of this kind should be recalled in the absence of significant change of hemolysis patterns by CPC which contradicts the apparent sign of biliary obstruction demonstrated by the other hepatic tests.

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