Canad. Med. Ass. J.
June 12, 1965, vol. 92

Pruritus and Jaundice

N. T. McPHEDRAN, M.D., F.R.C.S.[C]* and R. D. HENDERSON, M.D.,†
Toronto

ABSTRACT

The records of 147 patients who had pruritus and jaundice (11% of a series of 1262 patients with jaundice) were reviewed in an effort to delineate more clearly the etiology of jaundice associated with pruritus.

Fifty-two had obstructive jaundice caused by neoplasm, 51 had obstructive jaundice not caused by neoplasm, 42 had pruritus associated with hepatogenous jaundice, and two had jaundice and pruritus associated with a lymphoma.

Pruritus occurred in 17% of all patients with non-neoplastic obstructive jaundice and in 45% of patients with neoplastic obstructive jaundice. Hepatogenous jaundice was the cause of pruritus in almost one-third of the patients in this series—occurring in 20% of patients with infectious hepatitis and in 7% of patients with cirrhosis.

This large series confirms the clinical impression that pruritus occurs most often in association with extrahepatic biliary obstruction, and as well re-emphasizes the common association of pruritus with hepatogenous jaundice.

SOMMAIRE

Les auteurs passé en revue les fiches cliniques de 147 malades qui présentaient un ictère et du prurit (11% d'un groupe de 1262 ictériques) dans une tentative de préciser l'étiologie du prurit qui accompagne la jaunisse.

Chez 52 malades, on constatait un ictère par rétention d'origine néoplasique, chez 51 un ictère par occlusion non néoplasique, 42 souffraient de prurit accompagnant un ictère hépatogène et deux autres avaient une jaunisse et du prurit accompagnant un lymphome.

Le prurit s'est manifesté chez 17% de tous les malades qui avaient un ictère par retention qui n'était pas d'origine néoplasique et chez 45% des malades ayant un ictère d'origine néoplasique. L'ictère hépatogène était la cause du prurit chez près d'un tiers des malades de ce groupe—soit chez 20% des malades souffrant d'hépatite infectieuse et chez 7% des cirrhotiques.

Ce vaste groupe de malades confirme l'impression clinique que le prurit se manifeste plus souvent chez les malades qui présentent une occlusion biliaire extrahépatique et la constatation d'une association courante de prurit et d'ictère hépatogène.

AS LONG ago as the second century A.D., Aretaeus the Cappadocian[1] described pruritus as a symptom of jaundice. As recently as 1949 Thorek[2] stated that pruritus was almost diagnostic of obstructive jaundice, yet others have reported pruritus in 46% of cases of infectious hepatitis[3] and 18% of cases of hepatic cirrhosis.[4] Contradictions such as these, which are characteristic of the rather sparse literature on pruritus, led us to a study of this problem in our own patients.

This communication is based on the findings in a review of the records of 147 patients who had pruritus and jaundice. These patients comprise 11% of a series of 1262 patients with serum bilirubin levels above 1 mg. %, who were admitted to the Toronto General Hospital between 1953 and 1957. One hundred and three of the 147 had obstructive jaundice; 42 had hepatogenous jaundice; two had pruritus and jaundice with a lymphoma. No patient had pruritus with hemolytic jaundice.

Obstructive Jaundice (103 cases)

Obstructive jaundice and pruritus were caused by neoplasm in 52 patients. The causative lesions in these cases were: carcinoma of the head of the pancreas, 23; secondary carcinoma of the porta hepatis, 17; carcinoma of the bile ducts, seven; carcinoma of the gallbladder, four; and carcinoma of the ampulla of Vater, one.

In 51 patients obstructive jaundice and pruritus were not due to neoplasm. Causes of obstruction in these cases were as follows: choledocholithiasis in 26 cases; strictures of the common bile duct in 11; cholecystitis without recorded choledocholithiasis in eight; acute pancreatitis in two; chronic pancreatitis in two; choledochus cyst in one; and in one the cause of the obstruction was not determined.

Hepatogenous Jaundice (42 cases)

Hepatogenous jaundice accounted for almost one-third (42) of the cases of pruritus associated with jaundice. Twenty-one of these patients had infectious or serum hepatitis, 13 had cirrhosis (seven portal and six biliary), three had reactions to chlorpromazine, three had extensive secondary carcinoma of the liver, and two had other forms of hepatitis.

*Assistant Surgeon, Toronto General Hospital.
†Medical Research Council Research Fellow, Department of Surgery, University of Toronto, and Toronto General Hospital.

Relationship of Serum Bilirubin to Pruritus

Pruritus was associated with a serum bilirubin above 5 mg. % in 122 patients, of whom 97 had a serum bilirubin level above 10 mg. %.

DISCUSSION

Pruritus associated with obstructive jaundice is common, and the intensity of pruritus is usually proportional to the degree and duration of obstruction. However, the etiology and pathogenesis of the pruritus is not clear. Elevated cholesterol levels, disturbed porphyrin metabolism, release of histamine, failure of "detoxification",[6] and vitamin A deficiency[7] have all been suggested as the cause, but for the most part these theories have been rejected because of the good evidence that retention of bile salts is responsible.[8] Improved methods of blood cholate estimation have led to the demonstration of high cholate levels in most patients with pruritus, yet this relationship is not linear.[9] Blood cholate levels do not always correspond with the intensity of the pruritus, and in some patients administration of bile salts does not increase—in fact it may actually ameliorate—the pruritus. Other constituents of bile may yet prove to be responsible for the production of pruritus.

TABLE I.—NON-NEOPLASTIC OBSTRUCTIVE JAUNDICE

	Number of patients with pruritus	*Total number of cases*	*Incidence of pruritus*
(a) Choledocholithiasis	26	105	25%
(b) Cholecystitis and cholelithiasis	8	168	5%
(c) Stricture of common bile duct	11	17	65%
(d) Other causes	6	37	16%
Total	51	327	15.6%

Pruritus occurred in 51 of 327 (16%) patients with non-neoplastic obstructive jaundice (Table I), and in 52 of 116 (45%) with neoplastic obstructive jaundice (Table II). Obstructive jaundice as the result of choledocholithiasis caused pruritus in 25%; that secondary to carcinoma of the pancreas caused pruritus in 42%; while obstructive jaundice secondary to strictures of the common bile duct caused pruritus in 65% of cases. These figures correspond with those reported by Meyer and Steigmann[10] (21% with non-neoplastic obstructive jaundice and 41% with neoplastic obstructive jaundice), but are at variance with those of Snell and Keys[5] who reported that 60% of a series of patients with non-neoplastic obstructive jaundice and 75% of those with neoplastic obstructive jaundice had pruritus. No explanation for this wide variation is apparent.

TABLE II.—NEOPLASTIC OBSTRUCTIVE JAUNDICE

	Number of patients with pruritus	*Total number of cases*	*Incidence of pruritus*
(a) Carcinoma of head of pancreas	23	55	42%
(b) Carcinoma of the ampulla of Vater	1	3	33%
(c) Carcinoma of the bile ducts	7	18	37%
(d) Carcinoma of the gallbladder	4	5	80%
(e) Secondary carcinoma, porta hepatis	17	35	49%
Total	52	116	45%

Carcinoma of the head of the pancreas is a well-known cause of pruritus, and in Ransom's[11] series 44.6% of patients with this neoplasm had pruritus. Probably this is due to the duration of complete biliary tract obstruction in such cases.

TABLE III.—HEPATOGENOUS JAUNDICE

	Number of patients with pruritus	*Total number of cases*	*Incidence of pruritus*
(a) Infectious and serum hepatitis	21	106	20%
(b) Cirrhosis	13	179	7%
(c) Other causes	8	163	5%
Total	42	448	9%

Hepatogenous jaundice leads to pruritus less often than does extrahepatic obstructive jaundice, but because this condition is common, it led to pruritus in almost one-third of all patients in our series. Pruritus occurred in 20% of patients with infectious or serum hepatitis, and in 7% of patients with cirrhosis (Table III). These figures correspond closely with those reported by Colbert,[13] but they do not support the assertion of Thorek[2] that pruritus is very rare in jaundice not caused by biliary tract obstruction, or the opposing view of Hoagland and Shank[3] who reported a 46% incidence of pruritus in patients with cirrhosis. Obviously the symptom of pruritus may occur with either obstructive or hepatogenous jaundice, but it occurs most commonly with obstructive jaundice.

Authorities agree that there is a relationship between pruritus and high serum bilirubin levels, but there is little agreement about diseases which are most often associated with pruritus and low serum bilirubin levels. On the one hand, Reisman[14] and Crile[12] stated that preicteric pruritus is strongly suggestive of carcinomatous biliary obstruction, while on the other hand McVicar and Weir[15] reported that preicteric pruritus suggests cirrhosis. In our series there were 22 patients with pruritus associated with serum bilirubin levels below 5 mg. %. Ten of these had cholecystitis and cholelithiasis; four had infectious hepatitis; three had cirrhosis; and one each had lymphoma, secondary carcinoma, chlorpromazine poisoning, common duct stricture, and an unidentified obstruction. There were no cases of carcinoma of the head of the pancreas in this group. Consideration of the wide variety of

conditions that lead to pruritus in association with a low serum bilirubin makes it apparent that preicteric pruritus is not a reliable symptom upon which to base a diagnosis.

SUMMARY

Pruritus occurred in 147 patients (11%) of a series of 1262 patients with serum bilirubin levels of 1 mg. % or more.

Fifty-one patients had obstructive jaundice not caused by neoplasm: 26 of these had choledocholithiasis, 11 had stricture of the common bile duct, eight had cholecystitis and cholelithiasis, and six had "other" causes of obstruction (e.g. choledochus cyst, acute or chronic pancreatitis).

Fifty-two patients had obstructive jaundice caused by neoplasm: 23 of these had carcinoma of the head of the pancreas, and 29 had other forms of neoplastic obstruction of the biliary system.

Forty-two patients had pruritus associated with hepatogenous jaundice: 21 of these had infectious or serum hepatitis, seven had portal cirrhosis, six had biliary cirrhosis, and eight had miscellaneous liver damage.

Two patients had jaundice and pruritus associated with a lymphoma.

Twenty patients had pruritus and a serum bilirubin level below 5 mg. %, but no relationship could be demonstrated between low serum bilirubin with pruritus and any particular disease.

REFERENCES

1. ADAMS, F., editor: The extant works of Aretaeus the Cappadocian, Sydenham Society, London, 1856.
2. THOREK, P.: *J. A. M. A.*, **141**: 767, 1949.
3. HOAGLAND, C. L. AND SHANK, R. E.: *Ibid.*, **130**: 615, 1946.
4. EPPINGER, H.: *Ibid.*, **85**: 1573, 1925 (abstract).
5. SNELL, A. M. AND KEYS, H. C.: *Med. Clin. N. Amer.*, **16**: 1455, 1933.
6. LICHTMAN, S. S.: Diseases of the liver, gall bladder and bile ducts, 3rd ed., Lea & Febiger, Philadelphia, 1953, p. 197.
7. SEN GUPTA, B. R. AND KONAR, N. R.: *J. Indian Med. Ass.*, **38**: 583, 1962.
8. WOOTTON, I. D. P., DASILVA, L. C. AND SHERLOCK, S.: *Lancet*, **2**: 1049, 1959.
9. SHERLOCK, S.: Diseases of the liver and biliary system, 2nd ed., Blackwell Scientific Publications, Oxford, 1958, p. 377.
10. MEYER, K. A. AND STEIGMANN, F.: *Surg. Gynec. Obstet.*, **67**: 640, 1938.
11. RANSOM, H. K.: *Amer. J. Surg.*, **40**: 264, 1938.
12. CRILE, G., JR.: *Ibid.*, **47**: 87, 1940.
13. COLBERT, J. W.: *Bull. U.S. Army Med. Dept.*, **8**: 954, 1948.
14. REISMAN, D.: *Amer. Med. (Phila.)*, **2**: 77, 1907.
15. MCVICAR, C. S. AND WEIR, J. F.: *Med. Clin. N. Amer.*, **10**: 499, 1926.