similar accuracy to these physicians. However, the groups of patients may not have been exactly comparable.

The results of the sequential model are somewhat better than those of our previous non-sequential model using 172 patients,¹ in whom the accuracy of diagnosis as between nine diseases was 43% using ^{99m}Tc scintiscan indicants alone, 58% using laboratory indicants alone, 65% using clinical indicants alone, and only marginally better using all three combined. The figures for a medical v. surgical decision were 75%, 80%, and 82% respectively. Our present model achieves an 89% accuracy for a medical v. surgical decision.

There are two main reasons for incorrect diagnoses made by the model. Firstly, although more information is obtained from the history than from the physical examination, laboratory tests, or ^{99m}Tc scintiscan, history-taking is the least accurate source of information. This was shown by an observer error study performed by one of us (R.B.S.) on 25 of the new patients in which each patient answered a self-administered questionnaire as well as the standard form. When using indicants from the history alone the diagnoses reached by the model using indicants from the doctor's form and then from the patient's questionnaire agreed in only two of the 25 patients.

Secondly, the past experience of the model is still relatively small, and there are a few atypical cases that have not been seen sufficiently often to be recognized as a separate diagnostic category. For example, two errors were due to the fact that the model regarded a prolonged prothrombin time and small liver on ^{99m}Tc scintiscan as favouring fulminant hepatic failure rather than cirrhosis, and one error was due to regarding a long history as favouring carcinoma of the biliary tree rather than atypical viral hepatitis. These errors will become fewer in the future, since the model's past experience is enlarged and updated every time 50 further new patients are seen. As these numbers increase, both hepatic failure in association with cirrhosis and hepatitis with prolonged cholestasis will be regarded as additional distinct diagnostic categories by the model. Improvement in the accuracy of a Bayesian model with increasing numbers of patients has

been shown to occur in the diagnosis of acute abdominal pain,¹³ and in the present study accuracy improved from 74% using 220 patients to 89% when 309 patients were available for past experience.

If in the future it could be decided which indicants are most often redundant in reaching a sequential diagnosis a great saving in cost and time could be made in obtaining information. The model is being developed so that given the cost of obtaining each indicant the cost of reaching a diagnosis can be minimized. This has been shown to be possible for thyroid disease.¹⁴

The help and advice of Professor W. I. Card is gratefully acknowledged. We thank D. Teather for help with statistical methods and Mary Nicholson for computer programming. R.P.K.-J. was in receipt of a grant from the Medical Research Council, R.B.S. a Bernard Sunley Anniversary Research Fellowship from the Royal College of Physicians, and R.P.H.T. a Medical Research Council Clinical Research Fellowship.

References

- 1 Knill-Jones, R., Maxwell, D. M., Thompson, R. P. H., and Williams, R., *Gut*, 1970, 11, 1062.
- 2 Card, W. I., and Good, I. J., *Methods of Information in Medicine*, 1971, 10, 176.
- 3 Bayes, T., *Philosophical Transactions of the Royal Society of London*, 1763, 3, 370.
- 4 Bailey, N. T. J., *Proceedings of Medical Research Council Conference on Mathematics and Computer Science in Biology*, No. 103. London, H.M.S.O., 1965.
- 5 Bailey, N. T. J., *Mathematical Approach to Biology and Medicine*, chapt. 11. London, Wiley, 1967.
- 6 Trey, C., and Davidson, C. S., *Progress in Liver Disease*, ed. H. Popper and F. Schaffner, vol. 3, chapt. 11, p. 282. London, Heinemann, 1970.
- 7 Burbank, F., *American Journal of Medicine*, 1969, 46, 401.
- 8 Bégon, F., and Dhumeaux, D., *Minnesota Medicine*, 1971, 54, 101.
- 9 Vishnevsky, A. A., et al., *Eksperimental'naya Khirurgiya*, 1964, 4, 22.
- 10 Cattaneo, A. D., Luchelli, P. E., Rocca, E., Mattioli, F., and Becchi, G., *Abdominal Surgery*, 1972, 14, 71.
- 11 Martin, W. B., Apostolakis, P. C., and Roazon, H., *American Journal of Medical Sciences*, 1960, 240, 571.
- 12 Schenker, S., Balint, J., and Schiff, L., *American Journal of Digestive Diseases*, 1962, 7, 499.
- 13 de Dombal, F. T., Lesper, D. J., Staniland, J. R., McCann, A. P., and Horrocks, J., *British Medical Journal*, 1972, 2, 9.
- 14 Taylor, T. R., Shields, S., and Black, R., *Lancet*, 1972, 2, 79.

Pitfalls in the Diagnosis of Jaundice due to Carcinoma of the Pancreas or Biliary Tree

R. B. STERN, R. P. KNILL-JONES, ROGER WILLIAMS

British Medical Journal, 1973, 1, 533-534

Summary

Analysis of 56 patients with obstructive jaundice due to carcinoma of the pancreas or extrahepatic biliary tree showed that unexpected features were present in 25%. Presentation with painless jaundice was uncommon, and the symptoms were more often non-specific, with malaise, anorexia, and vomiting. Abdominal pain was frequent, and the condition

was found in young patients. One-fifth presented with serum alkaline phosphatase levels of less than 30 K.A. units. Some had high serum aspartate aminotransferase levels, more characteristic of hepatocellular jaundice. A mathematical model may be helpful in correctly weighting these various criteria.

Introduction

During the past five years we have been using a computer-assisted mathematical model based on Bayesian probability theory for the diagnosis of patients with jaundice.¹ Data have been collected from 286 patients, so the validity of accepted diagnostic criteria can be analysed with some certainty. This paper is concerned with certain anomalies of the presenting symptoms, signs, and laboratory investigations of patients with obstructive jaundice due to carcinomata. These have been described before²⁻⁷ but they are not widely appreciated

King's College Hospital and Medical School, London SE5 9RS

R. B. STERN, M.B., M.R.C.P., Research Fellow, Liver Unit

ROGER WILLIAMS, M.D., F.R.C.P., Consultant Physician and Director of Liver Unit

Department of Medicine in Relation to Mathematics and Computing, University of Glasgow, Glasgow W2

R. P. KNILL-JONES, M.Sc., M.R.C.P., Research Fellow

and may be partly responsible for the delay in making a diagnosis in many cases.

Findings

Fifty-six jaundiced patients seen between January 1968 and January 1972 were proved to have extrahepatic biliary obstruction due to carcinoma. The tumour arose in the right or left hepatic duct or at their junction in eight instances and in the common bile duct in eight. Forty patients had a carcinoma of the pancreas, including some in whom it originated in the ampulla. None of these sites was especially likely to give rise to "unusual" findings.

Only 10 patients (17.9%) presented with painless jaundice, and in over a quarter the presentation was with non-specific features, such as malaise, anorexia, nausea, vomiting, or diarrhoea. In just over half (31 patients) abdominal pain was present at some stage during the illness, and the frequency of pain as the first symptom was about the same as in 25 patients admitted over the same period with obstructive jaundice due to gall stones (table I).

TABLE I—First Symptoms of 56 Patients with Carcinoma of the Pancreas or Biliary Tree compared with 25 Patients with Gall Stones

	Carcinoma		Gall Stones	
	No.	%	No.	%
Abdominal pain	15	26.8	6	24
Jaundice	10	17.9	1	4
Diarrhoea	7	12.5	0	0
Anorexia	7	12.5	4	16
Malaise	4	7.1	4	16
Nausea and vomiting ..	3	5.4	1	4
Pruritus	1	1.8	0	0
Other	9	16.1	9	36

The mean duration of symptoms to the time of diagnosis was 14 weeks, but in eight patients the history was six months or longer and in two a year or more, the longest being a two-year history of nausea and epigastric pain radiating into the back in a 23-year-old man. Overall five patients were aged 40 or less at the time of diagnosis, although the mean age was 61.2 years.

At the time of presentation the serum alkaline phosphatase level was less than 30 K.A. units (normal < 13) in 11 cases (19.6%) (table II). The depth of jaundice varied considerably, with the serum bilirubin levels ranging from 2 to 35 mg/100 ml. Four patients had levels below 5 mg/100 ml. No correlations could be detected between the depth of jaundice and the duration of symptoms, serum alkaline phosphatase, or serum aspartate aminotransferase levels. There was also a considerable range in the serum aspartate aminotransferase levels, the highest being 1,000 IU/100 ml (normal < 40). Eight patients had values greater than 200 IU/100 ml.

TABLE II—Serum Alkaline Phosphatase Levels in the Carcinoma and Gall Stone Groups

Alkaline Phosphatase (K.A. Units)	Carcinoma		Gall Stones	
	No.	%	No.	%
<13	0	0	1	4
13-30	11	19.6	14	56
>30	45	80.4	10	40

Discussion

It is clear from our findings and from other reports^{2, 5, 6} that progressive, painless jaundice is the exception rather than the rule in carcinoma of the pancreas or biliary tree. In view

of the frequency with which anorexia, nausea, or vomiting is the first symptom it is perhaps not surprising that difficulties in differentiating the disease from infectious hepatitis arise when the patient subsequently becomes jaundiced. The mean duration of symptoms before diagnosis in these patients was 17 weeks, which emphasizes that an underlying carcinoma of the biliary tree or pancreas should always be considered in patients with such persistent, often ill-defined gastrointestinal symptoms. In the present series diarrhoea was common at some point in the illness, and this was also noted by Sherlock.⁹ Although in some cases the cause may be maldigestion due to lack of bile salts or pancreatic juice in the intestine six of the patients with this symptom had tumours not involving the pancreatic duct, and the jaundice in these patients was no deeper than in those without diarrhoea.

Another feature of these tumours that may lead to a delay in diagnosis is their occasional occurrence in young people. Schiff and Billing¹⁰ reported several cases between the ages of 30 and 40 years, and one patient with a pancreatic carcinoma presented at 24. The case of a 17-year-old patient with a bile-duct carcinoma was reported by Ham and McKenzie⁶—the youngest in the literature at that time. At the first laparotomy in our 23-year-old patient it was felt that the pancreatic mass could not be a carcinoma because of his age, and by the time of the second laparotomy the growth had metastasized to the liver.

The results of the liver function tests in the present series show that a serum alkaline phosphatase level of 30 K.A. units is unreliable in distinguishing hepatocellular jaundice from obstructive jaundice due to carcinoma, and even more so from gall stones (as in 60% of our patients). Popper and Schaffner's¹¹ series of patients with obstructive jaundice included a similar proportion (24%) with values below this level, and in 3% of their patients the values were within normal limits. In some of our patients, however, the serum alkaline phosphatase did rise to a more expected level after admission. The impression that the serum aspartate aminotransferase level is only moderately raised in obstructive jaundice is equally misleading. High levels may be due to hepatocellular damage from increased intrabiliary pressure, but no correlation was found between serum aspartate aminotransferase levels and the serum bilirubin or alkaline phosphatase levels.

Although all these features make the assessment of an individual patient difficult for the clinician they are less of a problem to a computerized model, since this enables the correct weight of evidence to be placed on each piece of information based on past experience.¹ Indeed, using this model we were able to distinguish between a "medical" and a "surgical" cause of jaundice in over 93% of patients.

We are grateful to Professor W. I. Card and Dr. R. P. H. Thompson for their advice. The computer assisted diagnostic model for jaundice is being supported by the Royal College of Physicians, London. R.B.S. is in receipt of a Bernard Sunley Anniversary Fellowship. The support of the Medical Research Council is also acknowledged.

References

- 1 Knill-Jones, R. P., *et al.*, *British Medical Journal*, 1973, 1, 530.
- 2 Arkin, A., and Weisberg, S. W., *Gastroenterology*, 1949, 13, 118.
- 3 Bouchier, I. A. D., *British Medical Journal*, 1968, 3, 169.
- 4 Gullick, H. D., *Medicine*, 1959, 38, 47.
- 5 Halpert, B., Makk, L., and Jordan, G. L., *Surgery, Gynecology and Obstetrics*, 1965, 121, 91.
- 6 Ham, J. M., and McKenzie, D. C., *Surgery, Gynecology and Obstetrics*, 1964, 118, 977.
- 7 White, R. J., *Annals of Surgery*, 1959, 149, 762.
- 8 Glenn, F., and Thorbjarnarson, B., *Annals of Surgery*, 1964, 159, 945.
- 9 Sherlock, S., *Diseases of the Liver and Biliary System*, 3rd edn. Oxford, Blackwell, 1963.
- 10 Schiff and Billing, *Diseases of the Liver*, ed. L. Schiff, p. 256. Philadelphia, J. B. Lippincott, 1969.
- 11 Popper, H., and Schaffner, F., *Liver, Structure and Function*. New York, McGraw-Hill, 1957.