

THE CLINICAL ASSOCIATION OF JAUNDICE AND RENAL FAILURE.

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Several authors⁽¹⁻⁴⁾ have found that there is little evidence for the existence of a specific hepatorenal syndrome, and yet there is evidence in animals⁽⁵⁾ that jaundice makes the kidney more sensitive to anoxic damage. We should like to analyse our experience of renal failure in association with jaundice during the years 1956-1964 at Hammersmith Hospital.

During this period 384 patients have required dialysis treatment for acute or acute on chronic renal failure, and of these 81, or 21% have been jaundiced, defined as a serum bilirubin over 1.5 mg. %. A further five patients were reported to be clinically icteric, but as the serum bilirubin was not measured they have not been included. We have omitted from consideration all patients with renal failure who recovered on conservative management alone, all patients who died of their primary disease before dialysis was considered necessary, or who died before dialysis could be undertaken. Thus we are only considering here a group of patients with severe renal failure whose blood ureas all exceeded 350 mg. % at some point in their illness.

The 81 patients have been subdivided into 12 groups depending on the predominant aetiology of the jaundice (Table I). There is some degree of overlap in the groups as there may be mild haemolysis in some obstetric patients, and infection was obviously present in some patients with obstructive jaundice.

RESULTS

Haemolytic anaemias

In 6 patients haemolysis was sufficiently severe to cause acute renal failure (maximum serum bilirubin ranged from 1.5-11.5 mg. %). Only 2 patients died in this group, one from a haemolytic anaemia complicating chronic lymphatic leukaemia, and one from a severe sensitivity reaction to sulphonamides. In 2 patients hypotension played a part in the development of the acute renal failure.

Leptospirosis

Seven patients were proven to have this disease by means of positive agglutination reactions. Only 2 patients, the youngest, both aged 34 years, survived after periods of 5 and 7 days oliguria. One other patient recovered from renal failure only to die of a *Pseudomonas pyocyaneus* septicaemia, and 4 patients were significantly hypotensive. The maximum serum bilirubin range was 2.9-38 mg. % .

Hepatitis

Eight patients suffered clinically from acute hepatitis and 4 have died. The maximum serum bilirubin ranged from 4.2-32 mg. %. None of these patients had a demonstrable septicaemia. In 2 patients the diagnosis was proven by biopsy, and 2 at autopsy. A fifth patient had a Zahn infarct of liver at autopsy. Only 2 patients were hypotensive in this group.

Common bile duct obstruction

There are six patients in this group, and all are dead. This is not surprising, as none were considered fit for surgery. Five out of the 6 patients were hypotensive, and two had proven septicaemias. The obstruction was due to stone in four cases, and to malignant obstruction in 2. Five out of the 6 patients had abscess formation at death, either in lung, liver or subphrenic space. The maximum serum bilirubin in this group was 2.0-24 mg. % .

Pancreatitis

Four patients had acute pancreatitis and 2 had undergone laparotomy. Two of the patients died, but only one was noted to have been hypotensive, and none had proven septicaemias. The maximum serum bilirubin range was 2. 5-21 mg. % .

Biliary surgery

Eight patients underwent biliary or pancreatic surgery, but all are dead. In none of these patients was the surgery uncomplicated, in that 4 patients developed post-operative pancreatitis, one had a subphrenic abscess, one had biliary peritonitis, and 3 patients had septicaemias due to *Staph. pyogenes*. Six out of the 8 patients were significantly hypotensive. The maximum serum bilirubin ranged from 3.3-34 mg. % ..

Other surgery

Eleven patients developed jaundice following other forms of surgery (Table II). Four of these patients had proven septicaemias, and 7 had periods of hypotensivn. The mortality in this group was 74% as compared with 64% in a similar group of surgical patients without jaundice. The maximum serum bilirubin in this group ranged from 2. 4-30 mg. % .

Trauma

Three patients had multiple injuries, and one had severe burns, the latter patient having also a staphylococcal pneumonia. The maximum serum bilirubin in this group was 4. 8-10. 5 mg. % and the jaundice was presumably related to absorption of blood from haematoma sites. All 3 patients with multiple injuries were hypotensive.

Obstetric causes.

There are 13 patients in this group, 5 with induced abortions and 8 with toxæmic complications of late pregnancy. Nine of the patients in this group were significantly hypotensive, but only 2 patients died, one due to infective complications of abortion, and one patient with zonal hepatic necrosis from toxæmia. The maximum serum bilirubin in this group ranged from 3. 2-20. 4 mg. % .

Infection

In 5 patients septicaemia seemed to be the only link between jaundice and renal failure. Three patients had infection due to *Staph. pyogenes*, one due to *Strep. viridans* and one due to *B. coli*. Three patients in this group died, and the maximum serum bilirubin ranged from 2. 6-10 mg. % .

Poisons and Drugs

Four patients had taken poisons or drugs and became jaundiced and developed renal failure. In only 2 of these patients was the noxious agent

identified, in one case being carbon tetrachloride, and in the other phenindione but both these patients survived. The maximum bilirubin ranged from 1.6-20.5 mg. % .

Others

Two patients had polyarteritis nodosa, one had acute glomerulonephritis, one had an infiltrating reticulum cell sarcoma of liver, and one patient developed jaundice following a halothane anaesthetic for carcinoma of prostate.

In conclusion, it is our experience that virtually any cause of jaundice may be associated with renal failure. In 47% of cases there was significant hypotension, and in 17% a septicaemia was demonstrated. The overall mortality in the group was 58% as compared with a mortality rate in the non-jaundiced patients of 59% . In each jaundice group there does not appear to be any correlation between the degree of jaundice and the eventual outcome, and it would appear that mortality is related more to the nature of the primary disease process. It had been our impression before analysing our results that jaundice and renal failure was a lethal combination, but clearly the poor prognosis in the surgical group is balanced by the better outlook in patients with obstetric troubles.

REFERENCES

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TABLE I
CAUSES OF JAUNDICE

| | Total Patients | Dead |
|----------------------------|----------------|-----------|
| Haemolytic anaemia | 6 | 2 |
| Leptospirosis | 7 | 5 |
| Hepatitis | 8 | 4 |
| Bile duct obstruction | 6 | 6 |
| Acute pancreatitis | 4 | 2 |
| Biliary/pancreatic surgery | 8 | 8 |
| Other surgery | 11 | 7 |
| Trauma | 4 | 2 |
| Obstetric causes | 13 | 2 |
| Infection | 5 | 3 |
| Poisons and drugs | 4 | 2 |
| Others | 5 | 4 |
| Total | <u>81</u> | <u>47</u> |

TABLE II
SURGICAL OPERATIONS

Pulmonary valvotomy.
 Anterior resection of rectum and cystectomy.
 Nephrectomy for carcinoma.
 Repair of ruptured cirrhotic liver.
 Colostomy for perforated colonic diverticulum.
 Hysterectomy with cardiac arrest.
 Repair of aortic aneurysm. Intestinal obstruction.
 Hysterectomy in polycystic renal and liver disease.
 Drainage of pyonephrosis with amyloidosis.
 Gastrotomy for haematemesis with amyloidosis.

THE CHAIRMAN, W. J.KOLFF, Cleveland: Is there anybody who would like to make a comment or to ask a question? We will give Dr. Pringle an opportunity to rebut afterwards.

G. M. BERLYNE (Manchester): I should like to know what the histological lesions were in the kidneys of your patients.

A.PRINGLE (London): For various reasons we have not, in fact, got accurate histology in all our patients, but there has not been anything very significant. Sometimes they have shown what has been called tubular necrosis and sometimes they have had bile stained casts, but there has not been anything specific.

N.ALWALL (Lund): I think it would have been very interesting to know the average mortality rate in your heterogeneous groups.What I should like to know is the total mortality rate in each group and the mortality rate of the jaundiced patients.

A.PRINGLE (London): The mortality in tbc comparable series who were not jaundiced was 59% and the ones with jaundice 58% .

J. L. FUNCK-BRENTANO (Paris): Je voudrais demander au Mr. Pringle s'il pense que le fait d'être jaune a une influence directe sur la fonction rénale et s'il attribue à la jaunisse la même signification qu'elle soit due à une hémolyse aigue, à une obstruction de la voie biliaire ou à une insuffisance hépatique.

THE CHAIRMAN: Which is worse, to have anuria on the basis of haemolysis, or renal failure on the basis of hepatic failure?

A. PRINGLE (London): On my figures it would be far better to have haemolytic jaundice, but it depends what your haemolysis is due to.

J.SCHIRMEISTER (Freiburg): Have the patients with hepatitis been in coma hepaticum?

A. PRINGLE (London): No, none of them was in hepatic coma at all.

THE CHAIRMAN: None of your patients was in coma. I have seen one or two patients that were in coma where the coma was actually relieved by the dialysis. It was believed that that was due to high ammonia content. At one time dialysis was the only thing that could do something about ammonia intoxication but the fun has been spoiled there too, because now you can give arginine etc.

J.SCHIRMEISTER (Freiburg): We have had one twenty year old patient with coma hepaticum and have dialyzed her three times during six days. She came back and is still alive, but we do not know whether the dialysis, or something else, is the reason for her being alive.

THE CHAIRMAN: Have you deduced from this magnificent series of patients any general rules from which you can predict what is going to happen in patients with jaundice and renal failure?

A. PRINGLE (London): The answer to that is, 'No, we have not'.

THE CHAIRMAN: We have had the impression, which is perhaps not

very helpful, that in cases of jaundice where the jaundice is getting better, after some time, the renal failure will always recover. However, if the jaundice, for some reason or another, does not get better, no matter how long you keep them alive with the artificial kidney you will lose your patients anyway. So it is worth your while to look with great intensity at whether or not you can do something about the jaundice.

A. PRINGLE (London): I would agree in general terms with what you have said; our experience has been the same.