dilution due to water retention caused by salicylates. In none of the cases was there any evidence of haemolysis.

Treatment followed the usual lines: the offending drug was withheld and aspirin alone was given to relieve any slight pain; constipation was relieved by enemata and liquid paraffin; severe purgatives were avoided lest hyperaemia of the intestinal mucosa facilitate absorption of hydrogen sulphide and perpetuate the sulphaemoglobinaemia. Blood transfusion was required for Case 4 because of anoxia, and appeared almost life-saving. No specific treatment is of any avail. Treatment of the concomitant diseases was not altered by the presence of sulphaemoglobin, and no sequelae attributable to sulphaemoglobin were noticed.

Summary

Five cases of sulphaemoglobinaemia are described. One case followed the administration of magnesium sulphate as an aperient and the other four cases were due to analgesic preparations containing phenacetin. The presence of caffeine in such preparations is thought to induce habituation, particularly in neurotic personalities. Anaemia was present in four of the cases, but was not attributable to sulphaemoglobinaemia. The principles of treatment are enumerated.

REFERENCES

- Brandenburg, R. O., and Smith, H. L. (1951). *Amer. Heart J.*, 42, 582.
Campbell, D., and Morgan, T. N. (1939). *Lancet*, 2, 123.
Finch, C. A. (1948). *New Engl. J. Med.*, 239, 470.
Lazarus, S. (1945). *British Medical Journal*, 2, 565.
Morgan, T. N., and Anderson, A. G. (1940). *Ibid.*, 2, 187.

RISE OF SEDIMENTATION RATE AT LOW LABORATORY TEMPERATURE

ITS VALUE AS A LIVER-FUNCTION TEST

BY

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Most authors believe that a high laboratory temperature increases and a low one decreases the erythrocytic sedimentation rate (E.S.R.). Temperature, however, has been shown to exert an inconstant effect on the E.S.R., and in many cases a higher fall is recorded at a lower temperature when the test is performed simultaneously in hot and cold atmospheres (Weingarten, 1946; Buttaro and Tosti, 1946). It was also observed by Weingarten that a greater fall at lower temperature occurred in those cases which had some hepatic damage. Gupta (1954) proved that the higher fall at a lower temperature is due to a qualitative change in the euglobulin fraction of the plasma proteins. Since most of the flocculation reactions that test the liver function depend on the euglobulin fraction of the plasma proteins (Dyke, 1947), it was thought worth while to investigate if such a simple observation could be used to determine the liver damage.

Material and Method

Cases having definite liver damage were selected for investigation. These included cases of cirrhosis and cancer of the liver, infective and amoebic hepatitis, and chronic malaria and kala-azar. Most of the malaria patients had an enlarged liver, and all had an enlarged spleen and fever for more than three months.

Blood was collected in the morning, the patient having been kept fasting overnight. The E.S.R. was carried out by the Westergren method at temperatures of 99 and 44° F. (37.2 and 6.7° C.) in an incubator and a refrigerator respectively. The readings were taken every ten minutes for a

period of one hour. If the E.S.R. was found more than 10% higher at 44° F. (6.7° C.) it was adjusted to be a higher fall in the cold—that is, a positive reaction for liver damage—while a greater fall at 99° F. (37.2° C.) was regarded as a negative reaction; and if the difference between the two readings was less than 10% the reaction was regarded as indeterminate.

After having observed a fairly large number of cases a comparative study was made with a number of well-established liver-function tests as controls. The control reactions were the Takata-Ara, thymol turbidity, hippuric acid synthesis, blood proteins, and the Weltmann. The tests were performed in 17 cases of cirrhosis, 10 cases each of infective and amoebic hepatitis, 12 cases of chronic malaria, and 4 cases of cancer of the liver.

The Takata-Ara, thymol turbidity, and intravenous hippuric acid tests were performed according to the technique described by Dyke (1947), and the Weltmann test as described by Tyagi (1947). Proteins were estimated in the beginning of our series by the biuret reaction (Harrison, 1947), but later on the "lumetron" photoelectric colorimeter was substituted.

Observation and Results

The results of the cases studied by the fractional estimation of the E.S.R. in the hot and cold chambers are given in Table I and those of the comparative study in Table II.

TABLE I.—Results of E.S.R. in Hot and Cold Temperatures

	No. of Cases	Positive	Negative
Cirrhosis	71	51 (72%)	20
Infective hepatitis ..	12	0	12
Cancer of liver ..	10	7 (70%)	2
Amoebic hepatitis ..	14	9 (64%)	5
Kala-azar	2	2 (100%)	0
Chronic malaria ..	19	15 (79%)	4

TABLE II.—Percentage of Positives with Various Tests

	No. of Cases	Thymol Turbidity	Takata-Ara	Weltmann Reaction	Hippuric Acid	Blood Protein	E.S.R. Hot and Cold
Cirrhosis	17	76%	82%	76%	88%	71%	76%
Infective hepatitis	10	90%	70%	50%	0%	50%	0%
Cancer liver	4	25%	100%	100%	50%	75%	75%
Amoebic hepatitis	10	50%	50%	50%	50%	25%	60%
Chronic malaria	12	66%	75%	83%	58%	75%	58%

It will be seen that 51 out of 71 (72%) cases of cirrhosis of the liver gave a positive result. Cases which showed a negative reaction were usually of long standing, some of five years' duration; and it could be concluded that in many of them the activity of the disease had come to an end. In 10 out of 20 cases which showed a negative reaction, the E.S.R. at the end of one hour was less than 20 mm., while the remainder showed a tendency towards a declining E.S.R., indicating that the activity of the lesion was waning. The positive results with other tests varied between 70 and 84%. It is of interest to quote the observations of Ernst and Dotti (1948), who while doing the thymol turbidity test on 33 cirrhotics found positive results in 22 (67%). They concluded that the compensated cirrhotics in whom there is considerable fibrosis with abdominal ascites, but in whom the remaining liver parenchyma is functioning adequately for bodily needs, do not show a rise of thymol turbidity. When, however, the remaining cells are damaged by an infection, or by a toxin, or by anoxia, then the thymol reaction becomes positive. The only three cases of alcoholic cirrhosis met with in our series gave completely negative results. It is interesting to note that Kunkel (1948) also got similar findings with the thymol turbidity and the cephalin-cholesterol flocculation tests, and in a large percentage of cases a negative reaction was consistently obtained with the two tests.

In amoebic hepatitis and abscess a high percentage of positives was obtained. Out of five cases which showed a negative

reaction four had a well-formed abscess, and the E.S.R. in the fifth was only 10 mm. It may be possible that as abscess formation took place the localization of the disease allowed other liver cells to recover and to function normally. Other tests gave positive results in about 50% of the cases. In the hands of Gminder (1939) the Takata-Ara test gave 71.4% positive, while the serum colloidal test gave completely negative results (MacLagan, 1944). In four cases of amoebic hepatitis Wahi (1946) found 100% positive results with the hippuric acid excretion test.

A negative reaction in the presence of definite carcinoma of the liver remains unexplained. In the present series 2 cases out of 10 showed a negative reaction, and in a third it was indeterminate. Ernst and Dotti (1948) also observed that in several cases of carcinoma of the stomach with extensive metastasis in the liver the thymol turbidity was not raised. He also found that primary carcinoma of the liver very often gave negative results. The thymol turbidity and colloidal gold tests gave positive results in 40% (Ernst and Dotti, 1948) and 12.5% (Cates, 1941) cases respectively.

The cases of infective hepatitis showed a general slowing of the E.S.R. This is in accord with the reports of Miles (1945) and Boveri *et al.* (1947). The one-hour reading never exceeded 20 mm. in any of them. Sedimentation in the cold chamber was, however, still lower in all; so that all the patients gave a negative reaction. The general slowing of the E.S.R. was assumed to be due to the presence of bile salts. Damodaran (1948) found that in infective hepatitis concentration of the bile salts in the blood may reach 1 in 500. According to our investigations with the same concentration of bile salts *in vitro*, the E.S.R. came to a standstill. The presence of bile salts therefore considerably handicapped the evaluation of the effect of temperature on the E.S.R. Positive results from 66% (Watson *et al.*, 1945) to 99% (Wahi, 1946) have been reported with the thymol turbidity test. Serum colloidal gives 93% positives (MacLagan, 1944), while the Takata-Ara test gives 84% positives (Wahi, 1946).

From time to time workers have reported dysfunction of liver in malaria. As reported by Carter and MacLagan (1946), the thymol turbidity test gave positive results in 80% of the cases and serum colloidal gold in 94% of them. The E.S.R. was positive in 79% of the cases of malaria and in 100% of the cases of kala-azar.

Discussion

It is seen that the percentage of positives with individual tests differs in different diseases. Tests like hippuric acid synthesis, and plasma proteins, depend on the actively functioning liver tissue, and would be positive only if a sufficient amount of the liver tissue was destroyed. Other tests which appear to depend on the quantitative and qualitative variations of globulin fraction would give a negative reaction so long as the abnormal fraction is absent or present in only small amounts.

The common flocculation tests depend on the euglobulin fraction of the plasma proteins (Dyke, 1947). A closer link between the Takata-Ara test and the higher fall of E.S.R. in the cold chamber becomes evident from the observations of Baur (1948). He observed that in many cases of parenchymal disease of the liver verified at necropsy the Takata-Ara reaction was occasionally negative when done at room temperature, but became positive when done in a refrigerator. Furthermore, in cases of hepatic damage the cold Takata-Ara reaction becomes positive sooner and remains so longer than if the test is done at room temperature.

The flocculation in the Takata-Ara test is originated by mercuric chloride and sodium carbonate, and this flocculation is enhanced when exposed to refrigerator temperature, an observation very much akin to the present one, in which rouleaux formation is influenced favourably by low temperature.

It could be said that a higher fall of the E.S.R. at low laboratory temperature will in the large majority of cases indicate liver damage. The uniformly negative results in

infective hepatitis, however, cannot be adequately explained, and this is a drawback of the procedure. The general slowing of the E.S.R. in these cases was proved to depend on bile salts, yet all the cases showed a higher fall in the hot atmosphere—that is, a negative reaction.

The basis of the test is the euglobulin fraction of the plasma proteins (Gupta, 1955). The decrease of albumin and fibrinogen and the rise of euglobulin appear to be characteristic of failing liver function. It would be supposed that the diseased liver cells would not be capable of producing a special protein fraction in more than the normal quantities, and it is justifiable to assume that the euglobulin arises from extrahepatic sources, possibly the reticulo-endothelial system.

Summary

The general consensus of opinion is that the sedimentation rate of red cells increases with the increase of laboratory temperature, and vice versa. In a particular group of cases the E.S.R. is higher in a cold than in a warm temperature and (1) the accelerated E.S.R. in the cold is indicative of parenchymal liver damage; (2) the results are comparable with those obtained with other flocculation tests in general use except that the cases of infective hepatitis gave uniformly negative results; and (3) the reaction is an elaboration of a test already in universal clinical use and can be easily performed without any additional equipment: it also does not require any experience with more complicated methods, which remain the preserve of the clinical pathologist.

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REFERENCES

- Baur, H. (1948). *Helv. med. Acta*, **15**, 285.
 Boveri, R. M., Waterfield, R. L., and Newman, T. H. (1947). *Lancet*, **2**, 831.
 Buttaró, C. A., and Tosti, A. (1946). *Minerva med. (Torino)*, **37**, 155.
 Carter, A. B., and MacLagan, N. F. (1946). *British Medical Journal*, **2**, 80.
 Cates, H. B. (1941). *Ann. Intern. Med.*, **15**, 244.
 Damodaran, K. (1948). *British Medical Journal*, **1**, 1079.
 Dyke, S. C. (1947). *Recent Advances in Clinical Pathology*, p. 146. Churchill, London.
 Ernst, R. G., and Dotti, L. B. (1948). *Amer. J. med. Sci.*, **216**, 316.
 Gminder, E. (1939). *Arch. Schiffs- u. Tropenhyg.*, **43**, 215.
 Gupta, K. D. (1954). *J. Lab. clin. Med.*, **44**, 885.
 Harrison, G. A. (1947). *Chemical Methods in Clinical Medicine*, p. 382. Churchill, London.
 Kunkel, H. G. (1948). *Amer. J. Med.*, **4**, 201.
 MacLagan, N. F. (1944). *British Medical Journal*, **2**, 363.
 Miles, J. A. R. (1945). *Ibid.*, **1**, 767.
 Tyagi, N. (1947). *J. Indian med. Ass.*, **16**, 373.
 Wahi, P. N. (1946). *Indian med. Gaz.*, **81**, 521.
 Watson, C. J., Rappaport, E. M., Hawkinson, V., and Giebenhain, M. (1945). *J. Lab. clin. Med.*, **30**, 983.
 Weingarten, R. J. (1945). *Lancet*, **2**, 526.

The Institute of Psychiatry of the University of London, located at Maudsley Hospital, is the only university school in Britain devoted wholly to postgraduate education in psychiatry. The report from mid-1953 to mid-1954 states that the number of postgraduate students, including registrars, who received training during the year was 230, not including case workers who have spent varying periods in one or other of the departments. Students from abroad came from 25 countries. Rather more than two years ago the Guy's-Maudsley neurosurgical research unit was opened, and this has extended the clinical facilities of the Institute for teaching and research, and a number of collaborative investigations are in progress. The wider experience of temporal lobectomy for the relief of epilepsy has provided much more material than has been available hitherto, and studies to elucidate the relationship between the site of epileptic foci, the site and nature of associated lesions, the seizures, and the psychological changes have been started. In the teaching carried on at the Institute, although systematic instruction has to be given, particularly to those preparing for the D.P.M., the emphasis is on free discussion, related to reading and clinical experience.