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BLOOD SPECTRUM, A SYSTEM OF GRAPHICAL REPRESENTATION OF TWELVE CHEMICAL CONSTITUENTS OF BLOOD FOR THE PURPOSE OF CLINICAL DIAGNOSIS*

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Progress in the technics of clinical biochemistry of the last two decades which culminated in the advent of the microtechnics by means of a photoelectric colorimeter and a flame photometer has enabled the concurrent performance of the determination of various chemical constituents on a small amount of blood within a short period of time even with the significant level of accuracy that is required for clinical purposes. At present as little as eight milliliters of blood are, for instance, sufficient for the simultaneous estimation of twelve kinds of blood ingredients which are contained in Tables I and II. In our laboratory an attempt has been made for the past several years to establish a system of graphical representation of the chemical constituents of blood which were determined routinely, in the hope that clinical biochemistry might be used for diagnosis more directly and with better efficiency than it had been.

TABLE I

Procedures employed [1]

		Blood (ml.)	Serum (ml.)	
1.	Hemoglobin (Hb)	0.05		Cyanhemiglobin method (Stadie) [2]
2.	Serum Protein (SP)		1 drop	Hitachi's protein-meter (Yoshikawa) [3]
3.	Albumin to Globulin Ratio (A/G)		0.5	Sodium-sulfate-salting-out method adapted to biuret reagent [4]
4.	Blood Sugar (BS)		0.2	Alkaline-copper-sulfate-arsenomolybdate method (Somogyi-Nelson) [5]

A required volume of venous blood (8 ml.) was withdrawn with a completely dried aseptic syringe from each patient assigned for the biochemical examination, and it was transferred into a glass vial con-

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TABLE II

Procedures employed

		Serum (ml.)	
1.	Icteric index (Ii)	0	Comparator colorimetry with potassium-dichromate-cobaltous-sulfate solutions as standard series [7]
2.	Bilirubin (Bil) One-min. Bil. (1-Bil)	0.60	Methanol-diazo method (Malloy-Evelyn) [8]
3.	Cephalin cholesterol flocculation test (CCF)	0.20	Sumitomokagaku's Hanger antigen (Hanger) [9]
4.	Cholinesterase (ChE)	0.10	Phenol-red-comparator method [10]
5.	Alkaline phosphatase (Alk P)	0.40	Modified Shinowara's glycerophosphate method [1]
6.	Cholesterol (Chol)	0.20	Modified Bloor's method [11]
7.	Phenol turbidity test (Ph t)	0.20	Kunkel's method [12]
8.	Non-protein nitrogen (NPN)	0.30	Trichloroacetic acid filtrate of serum, digested with Hg-containing sulfuric acid, followed by Nesslerization. [13]

taining dried oxalate mixture (about 1 ml.) and a centrifuge tube (about 7 ml.) in order to be sent to the laboratory. Blood constituents including hemoglobin in blood, protein, albumin, globulin, glucose, icteric index, cephalin cholesterol flocculation test, cholinesterase, alkaline phosphatase, cholesterol, phenol turbidity test and non-protein nitrogen in serum were determined, and they were plotted on a special graph for their clinical interpretation which was concerned with the appraisal of the general condition and organ dysfunction of the relevant patient.

The purpose of this paper is to present the results of our attempt at formulation of a system of graphic representation of blood chemistry as well as to portray its clinical significance in a summarized form.

APPRAISAL OF GENERAL CONDITION

Three milliliters of blood were sufficient for determination of hemoglobin in blood (Hb), total protein (SP), albumin to globulin ratio (A/G) and glucose in serum (BS), when the procedures listed in Table I were employed. If the determinations of the constituents are plotted on a graph (Figure 1), and the points thus obtained are connected, a chart, such as depicted in Figure 2, will be the result. In this figure the graduated horizontal lines on which the constituents are plotted individually are arranged for the purpose of easy visualization in a manner that the upper and lower limits of their normal ranges stand separately on two assumed lines which are supposed to cross the graduated lines perpendicularly, circumscribing a rectangle which connotes normal

area. A healthy person gave, of course, an approximately vertical line which remained within the normal area (pattern N or normal). In a diseased person the connection line presented a variety of shapes which are different from that of normal individuals (Figure 2); it assumed L-shape when albumin to globulin ratio was subnorml (pattern L), and

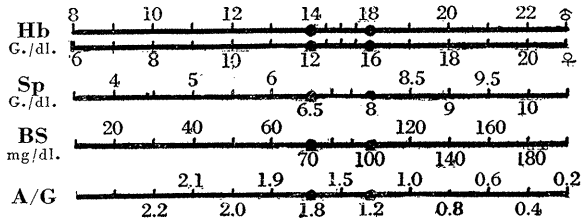


Fig. 1 Graph A for the appraisal of general condition.

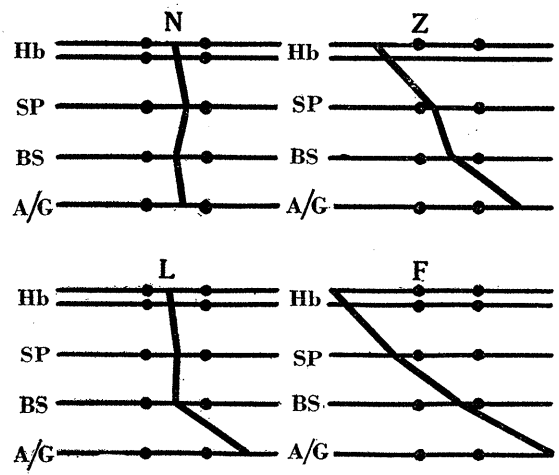


Fig. 2 The patterns of the connection line. N: normal, L: L-shaped, Z: Z-shaped and F: falling-sideways.

mimicked Z when anemia was in combination with the low albumin to globulin ratio (pattern Z). When hypoproteinemia was present in addition to anemia and subnormal albumin to globulin ratio, the connection line fell sideways from upper left to lower right (pattern F). These were apparently a few examples, but an extensive examination with a great number of patients revealed that the connection lines were divided into four main types, each of which was represented by N, L, Z or F pattern with its relevant subtypes (Table III)

TABLE III

PATTERNS encountered (493 cases)

1. N	N	**77**	3. Z	Z	**130**
	N·	27		Z.	30
	·N	27		Z·	19
	·N.	17		Others	9
	Others	35	4. F	.....	**49**
2. L	L	**74**			
	L.	19			
	L·	20			
	Others	19			

←Decr. Incr.→

Hb ·		· Hb
Sp ·		· Sp
BS .		· BS

Example: ·N = N+anemia
L. = L+hyperglycemia

Then, what is really the clinical significance of these connection lines? Figure 3 presents the comparison of the connection lines with the extension of pulmonary lesion which was examined radiologically on 121 cases of pulmonary tuberculosis without any complication of tuberculous process in the extrapulmonic tissues.[6] Inspection of this figure discloses that the incidence of pattern N and its subpatterns descends, whereas the occurrence of patterns Z and F comprising their subpatterns ascends in proportion to the increase in the extension of

Fig. 3 Comparison of the connection lines with the extension of pulmonary lesion in pulmonary tuberculosis.

pulmonary lesion, suggesting the presence of a certain correlation between the connection lines and the pulmonary lesion (coefficient of contingency : + 0.600). Patterns Z and F were likewise predominat over patterns N and L, as shown in Figure 4, when 53 cases of chronically and severely ill patients, who died within two weeks after they had happened to receive the examination of blood chemistry, were observed. Inasmuch as these observations seemed to provide support for the supposition that the general conditions, graded as slightly, moderately and severely impaired,

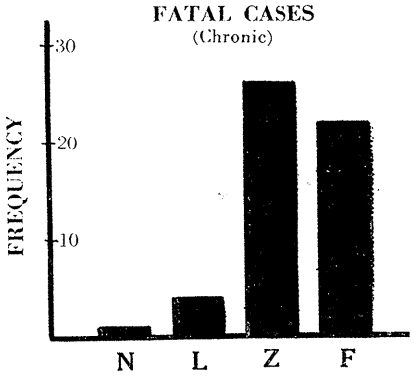


Fig. 4 Patterns encountered in the fetal cases of chronic diseases.

might be approximately related to the patterns L, Z and F, respectively, a comparative study was undertaken between the general conditions assessed by the clinical experts and the patterns of the connection line on 752 patients with surgical as well as medical diseases. The results are listed in Table IV, which reveals an approximate coincidence of the slightly impaired with patterns N and L, of the moderately impaired with patterns L and Z, and of the severely impaired with patterns Z and F, respectively. A coefficient of contigency of + 0.500 was obtained between the general conditions and the pattern. The determination of blood hemoglobin, serum protein, albumin to globulin ratio and blood sugar will accordingly be thought to afford a clinico-biohemical measure to appraise the general conditions of patients, because Table IV justifies that the patterns N, L, Z and F in blood chemistry are interpreted as the slightly, moderately and severely ill states in general conditions, respectively, with a certain degree of agreement which does not contradict the purely clinical sense. Unlimited application of this interpretation obviously jeopardizes the pertinent appraisal, however. Acute diseases were, for instance, hardly assessed for general conditions in this way, because their blood chemistry was rarely altered to an appreciable extent; it was also the case with some of the chronic diseases, such as listed in

Table V, since deviation of the pattern (to the favorable side) which obscured the interpretation was common in these conditions. But the opportunity of application of connection line was not reduced appreciably, since the majority of patients admitted to our hospital belonged to chronic cases which were especially suited to this kind of examination.

TABLE IV

Correlation between the patterns and the clinically assessed general condition.

		PATTERN			
		N	L	Z	F
GENERAL CONDITION impaired	Slightly	**170**	**72**	51	4
	Moderately	66	**91**	150	22
	Severely	5	12	**73**	**36**

(752 cases in all, excluding acute illness)
Contingency Coefficient 0.500

TABLE V

Pattern deviation encountered in 1620 cases of various diseases.

PATTERN DEVIATION

1. Acute Cond.
   - Dehydration ..... dysentery, acute diarrhea diabetes mellitus, pyloric stenosis, etc. 12
   - Biliary obstr. (acute attack) ..... cholelithiasis, cholecystitis, etc. 11
   - Other conditions 21
2. Chronic Cond.
   - Dehydration ..... liver cirrhosis (ascites) 3
   - Neoplasma 8
   - Other conditions 8

3.9 % 63/1620

APPRAISAL OF HEPATIC FUNCTION [14]

Five milliliters of blood in addition to the three milliliters which have been mentioned enabled the expansion of the framework of the examination to the extent that was listed in Table II. Twelve kinds of determinations or tests were thus feasible simultaneously on eight milliliters of blood, in total amount, for every patient when procedures described in this table were employed.

It was demonstrated by the comparison with the results of the liver biopsy [15] (on 159 patients, including hepatobiliary as well as non-hepato-

biliary diseases) that, among the determinations and tests, cephalin cholesterol flocculation test (CCF), serum cholinesterase (ChE), albumin (Alb) and globulin (Glob) indicated the damage to hepatic parenchyma, while total serum bilirubin (Bil), alkaline phosphatase (Alk P), cholesterol (Chol) and phenol turbidity test (Pht) mirrored the obstruction to biliary tract. Table VI and Figure 5 are presented in order to show their sensitivity and specificity for the respective hepatobiliary disturbances. A graph, like that shown in Figure 6 was constructed by the tests which were thus classified

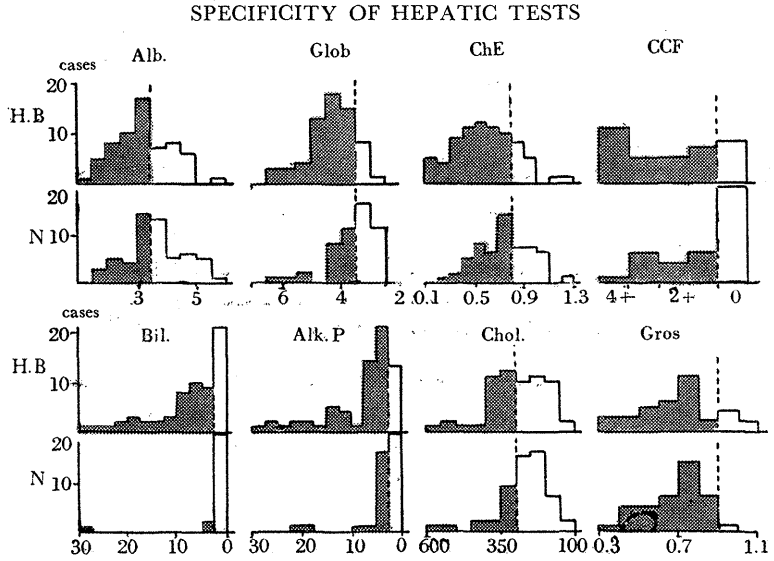


Fig. 5 Specificity of hepatic tests. H.B: hepatobiliary diseases, N: without hepatobiliary diseses. Units on the abscissa are as follows: Albumin and globunin in g./dl; bilirubin and cholesterol in mg/dl; alkaline phosphatase in Bodansky unit; Cholinesterase in pH; Gros' reaction test in ml. of Hayem's solution consumed; cephalin cholesterol flocculation test in 0 to 4+. White column represent the cases of normal test and the black column the cases of positive or pathological test.

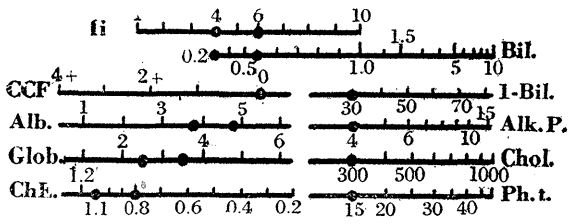


Fig. 6 Graph B (left) for the detection of the damage to hepatic parenchyma, and graph C (right) for the appraisal of the degree of biliary obstruction.

into the indicators of parenchymatous damage and those of the biliary stasis. In this graph the limits of normal range are denoted by nodules on the graduated lines, and these are arranged in a way that a normal person gives two connection lines, one of which is straight and oblique from upper right to lower left in the realm of the indicators of parenchymatous damage (the left half) and the other of which passes vertically from top to bottom to the left of nodules (upper limits of normal range) in the area of the indicators of biliary stasis (the right half). Patients with hepatobiliary diseases gave, of course, straight or variously bent lines which were different from those of normal. The lines of parenchymatous damage were assorted into patterns N, n, d and D according as the relevant tests deviating from normal range were zero or one, two, three and four in number, respectively (Figure 7). Lines of biliary stasis were also

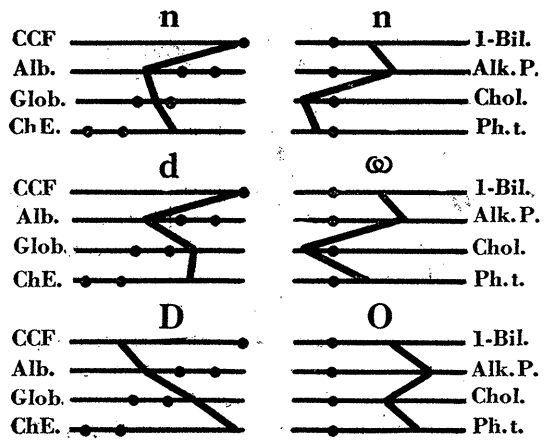


Fig. 7 Various pathologcal patterns of graph B (left) and graph C (right).

classified similarly into patterns N, n, ω, and O, and it was assumed from the comparative study of hepatic tests and liver biopsy (Table VI) that the disturbance in the hepatic parenchyma or biliary outflow might be increasingly profound as the patterns advanced in the order $N \rightarrow n \rightarrow d \rightarrow D$ or $N \rightarrow n \rightarrow \omega \rightarrow O$. The application of the graph to the diagnosis of hepatitis and liver cirrhosis is presented in Figure 8, where scattering of dots shows the determination of individual cases, and the strips represent the confidence limits ($\alpha = 0.05$) of the mean connection line. It is apparent from this figure that the connection line of hepatic damage gives pattern d for hepatitis and pattern D for liver cirrhosis, while that of biliary stasis exhibits pattern ω and pattern n for hepatitis and liver cirrhosis,

TABLE VI

Correlation between the hepatic tests and hepatic histology (159 cases including hepatobiliary as well as non-hepatobiliary diseases)

	Cases	Singnif. coeff* of correlat.	Hepat. tissue** damage	(A) Liver cell damage	(B) Inflam-mation	(C) Scarring	(D) Biliary stasis
1. Protein	142	0.165	+0.098	−0.061	+0.108	+0.113	+0.114
2. Albumin	142	0.165	−0.355	−0.138	−0.311	−0.234	−0.141
3. Globulin	142	0.165	+0.471	+0.096	+0.318	+0.553	+0.340
4. Alb. to glob. ratio	142	0.165	−0.528	−0.220	−0.322	−0.424	−0.343
5. Non-protein nitrogen	86	0.212	+0.072	+0.172	+0.124	+0.304	−0.098
6. Glucose	99	0.198	−0.042	−0.075	−0.060	+0.040	+0.152
7. Bilirubin	153	0.159	+0.556	+0.103	+0.214	+0.276	+0.499
8. Cholesterol	115	0.183	+0.031	−0.129	+0.158	+0.006	+0.344
9. Alk. phosphatase	129	0.173	+0.367	−0.158	+0.046	+0.165	+0.341
10. Cholinesterase	157	0.158	−0.461	−0.295	−0.361	−0.449	−0.214
11. C C F T***	76	0.228	+0.548	+0.381	+0.485	+0.329	−0.002
12. Gros' reaction	76	0.228	−0.202	−0.096	−0.225	−0.311	+0.121
13. Zinc sulfate t. t.	50	0.276	+0.395	+0.160	+0.314	+0.283	−0.006
14. Thymol turbid. t.	50	0.276	+0.154	+0.169	−0.187	+0.186	−0.038
15. $(NH_4)_2$ SO_4–NaCl t. t. ****	51	0.275	+0.103	+0.117	+0.171	+0.065	−0.165
16. Phenol turbid. t.	130	0.173	−0.061	−0.107	+0.128	−0.038	+0.205

* Level of significance ($\alpha = 0.05$) for the coefficients of correlation.
** The damage to the liver tissue considered as a whole or the summation of the individual alterations in hepatic histology.
*** Cephalin cholesterol flocculation test (Hanger)
**** Ammonium sulfate-sodium chloride turbidity test (De La Huerga and Popper)

respectively, mirroring the contrast which exists between hepatitis (relatively slight hepatic damage with marked biliary stasis) and liver cirrhosis (profound hepatic damage and slight biliary stasis). The contrast becomes more evident when the determination of individual constituents are observed with respect to their extent of deviation from normal range. Liver cirrhosis distinctly surpasses hepatitis in the degree of hyperglobulinemia as well as in the extent of reduction in albumin and cholinesterase. The clinical observation which maintains that severe damage to hepatic tissue

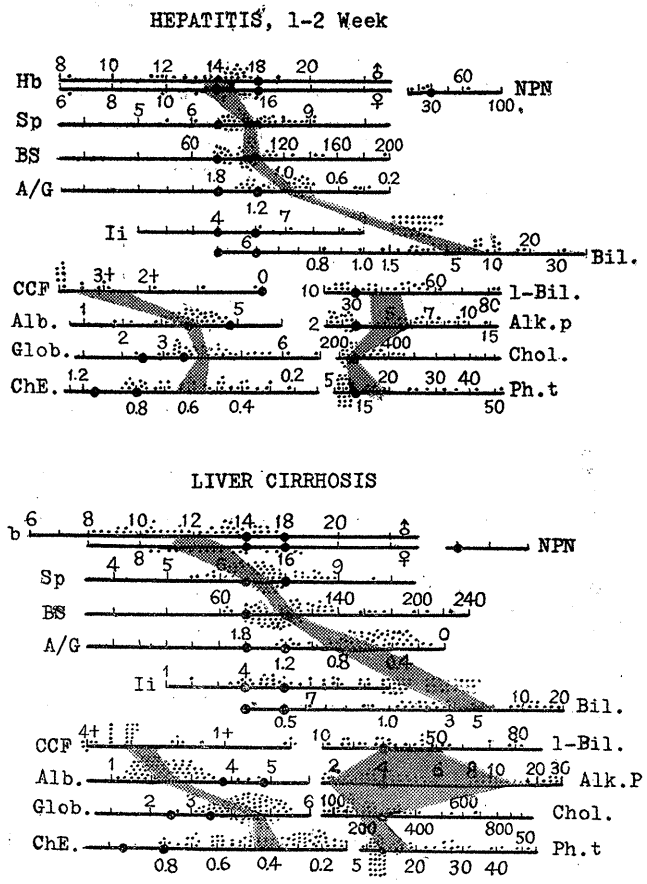


Fig. 8 Blood spectra of hepatitis and liver cirrhosis.

is more common in liver cirrhosis than in hepatitis is thus substantiated more vividly. It will therefore be obvious that for the exact appraisal of hepatobiliary disorder not only the pattern but also the deviation of connection line should be taken into consideration. Incidentally an additional remark is made about the fact that, as is revealed by the clinical observation, blood chemistry indicates more severe depletion in liver cirrhosis than in hepatitis, because the connection line for the appraisal of general condition bears pattern Z in the former against pattern L in the latter This will afford further proof for the usefulness of the connection line, although indirectly.

Application of the graph to the diagnosis of biliary stasis is exemplified by the case which is illustrated in Figure 9. A cursory glance at the figure

reveals a depleted patient (connection line of general conditions: Z pattern) with considerable jaundice (icteric index over 10; the serum bilirubin 13.5 mg/dl); and the scrutiny of the connection lines shows without any reference to the record of morbid history that the patient had distinct obstruction to biliary tract, since the line of biliary stasis bears 0 pattern. No doubt, it was accompanied by a moderate degree of damage to hepatic tissue (connection line: pattern d), but the negative reaction in cephalin cholesterol flocculation test pointed to the fact that the damage ensued from biliary obstruction rather than from primary hepatic destruction. The patient, a house wife aged 40, entered the Hospital of the Yamaguchi Medical College

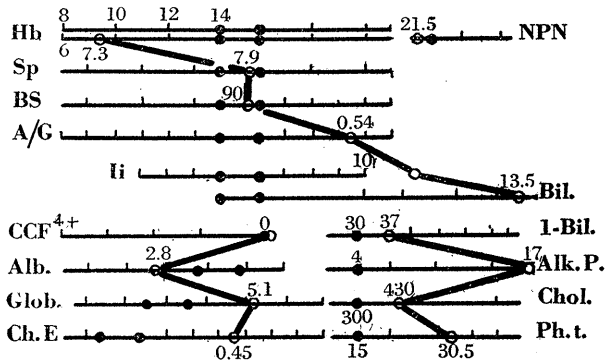


Fig. 9 Blood spectum of a case of cholelithiasis.

on 15 October 1953 because of severe epigastric pain, noted jaundice five days later, received internal treatment, and was discharged with alleviation of symptoms on 19 December of the same year. She re-entered the hospital on the first day after discharge, because she had recurrence of pain, and was examined for blood chemistry. Figure 9 which has been given repre-

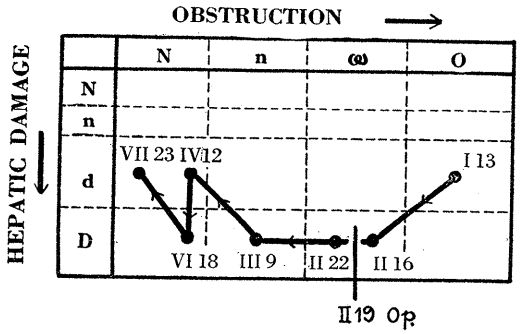


Fig. 10 A summary of clinical course of the patient presented in Fig. 9, as examined by blood spectrum. I 13, II 16, II 22, III 9, VI 18, and VII 23 indicate the date of examinations carried out on January 13, February 16, February 22, March 9, April 12, June 18 and July 23, 1953. The patient was operated on on February 19 (II 19).

sents its result. Vagostigmine test for the obstruction to pancreatic duct was negative, and X-ray examination failed to disclose gall stones even though Telepak was used to contrast the biliary tract. Laparotomy was done, however, since blood chemistry strongly pointed to biliary obstruction, cholelithiasis especially. A gall stone was found, as was expected, in the common bile duct which was dilated to the thickness of a thumb. The subsequent course was successively traced by blood chemistry. Figure 10 summarizes the results in tabular form, where the disappearance of the sign of biliary obstruction in proportion to the lapse of time after surgical operation is clearly visualized (Biliary obstruction: pattern 0 → pattern N). The same figure seems to show also that improvement in hepatic damage was not so remarkable during the whole course of observation (pattern D

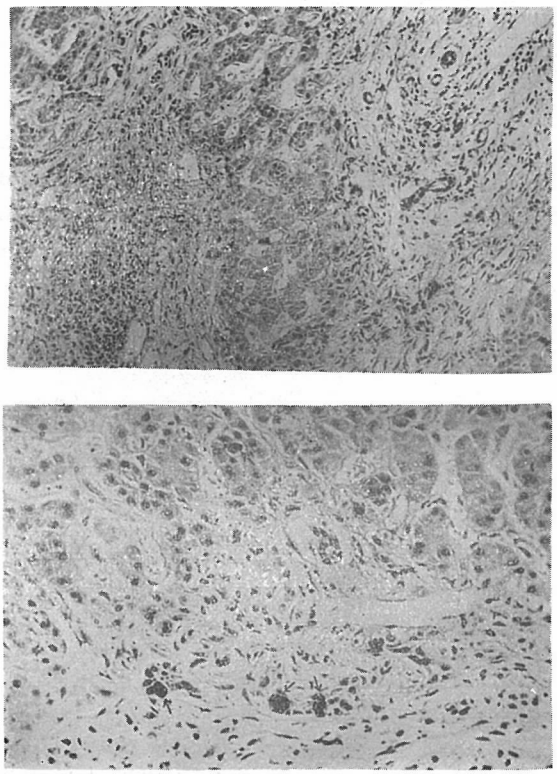


Fig. 11 Photomicrograph of the liver obtained by surgical operation from the case presented in Fig. 9. Top: Proliferation of the connective tissue in the portal space with invasion of round cells. Bottom: Scattered bile thrombi in the lobule and in the bile ducts (indicated by arrows) associated with the proliferation of Kupffer's cells which engulf bile pigment granules. (Magnification: top 100× and bottom 200×)

→ pattern d) in spite of the removal of biliary obstruction, connoting a damage which advanced so far that the liver could not be repaired in the comparatively short period of time. The conjecture was corroborated by the histological picture of the liver which was excised at the operation. Besides the bile thrombi there was a considerable increase in the connective tissue and the section of bile and pseudo bile ducts of the portal space (Figure 11)

It will now be apparent from the illustration given above that the connection lines are helpful for the diagnosis of hepato biliary disorder, and that the scrutiny thereof enables the conjecture of the character of clinical conditions, both present and future, with a satisfactory degree of reliability.

Appraisal of Renal Function

Unfortunately no sensitive blood-chemical indicator has hitherto been obtained for the detection of renal disturbance. Non-protein nitrogen study was therefore resorted to, although it was well known that it had much to be desired in sensitivity as well as in specificity as a renal test (Table VII).

Table VII

Diseases which cause azotemia
(exceeding 40 mg./dl. of serum NPN level)

Cholelithiasis	9	Nephrosis	7
Gall bladder carcinoma	2	Nephrosclerosis	8
Subacute yellow atrophy of the liver	3	Bladder cancer	1
Liver abscess	1	Nephrolithiasis	1
Liver cancer	2	Renal tuberculosis	3
Pulmonary cancer	2	Intoxication	9
Pneumonia	1	Gastric cancer	12
Circulatory failure	2	Gastroduodenal ulcer	4
Rheumatism	1	Pancreatitis	3
Acute peritonitis	2	Diabetes mellitus	1
Ileus	1	Meningoencephalitis	3
Dysentery	10	Neurologic diseases	5
Glomerulonephritis	8	Others	3
		Total	104

cases out of 1620 cases examined.

The blood chemistry proved useful, however, for the diagnosis of renal diseases when all of the twelve constituents of blood were examined graphically, including non-protein nitrogen as a part. The diffuse bilateral renal diseases gave three different types of graph: Group (1) in which serum protein, cholesterol and phenol turbidity exhibited the nearly normal values.

while the serum cholinesterase activity was decreased slightly (top of Figure 12), group (2) in which profound reduction in the serum protein and albumin formed a striking contrast with the marked increase in cholesterol, phenol turbidity and serum cholinesterase activity (bottom of Figure 12), and group

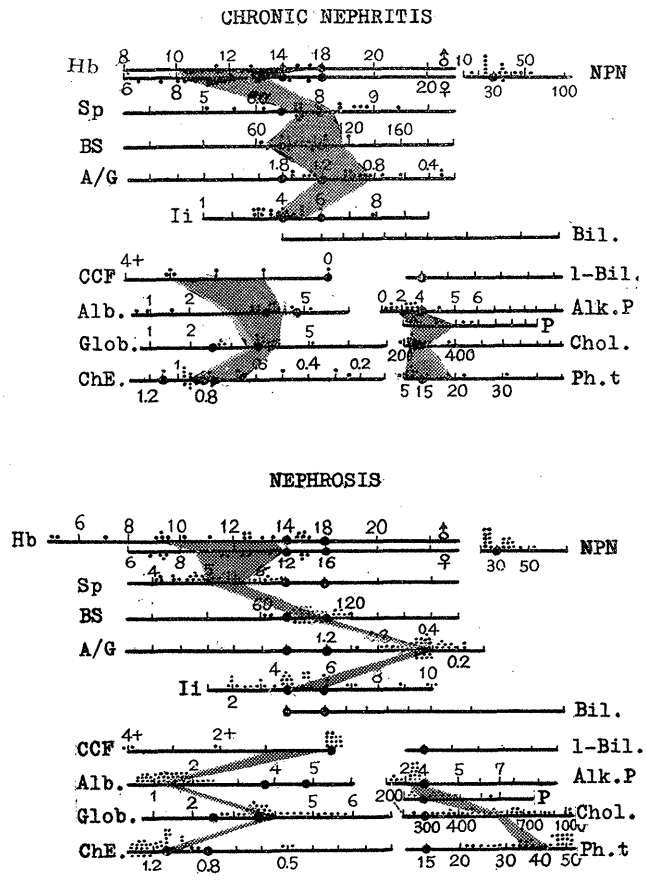


Fig. 12 Blood spectra of renal diseases.

(3) which showed a distinct rise in non-protein nitrogen accompanied by the decrease in hemoglobin, albumin and cholinesterase as well as by the increase in blood sugar and serum inorganic phosphorus (Figure 15). Of these three patterns the group (2) was most characteristic. Its connection line was so pathognomonic of renal diseases that they were easily diagnosed from the graph without any aid of the description of morbid history and urine examination. Detailed collation of the morbid history and the result

of kidney function tests with the classification of renal diseases which has recently been advocated by Ellis, Evans and Wilson[16] led to the conclusion that the group (1) corresponds to the type 1 Nephritis (acute and chronic glomerulonephritis) and group (2) to the type 2 Nephritis (nephrosis). Group (3) was uremia. The chronic cases of glomerulonephritis alone were presented in Figure 12 for the purpose of clarity, but acute glomerulonephritis, of course, belonged to the pattern depicted in this figure. Acute glomerulonephritis was distinguished from the chronic only by the absence of appreciable anemia (Figure 13). The significance of the graph for the diagnosis of nephrosis which has been mentioned may deserve emphasis, because no diseases, except nephrosis, have ever given the group (2) pattern.

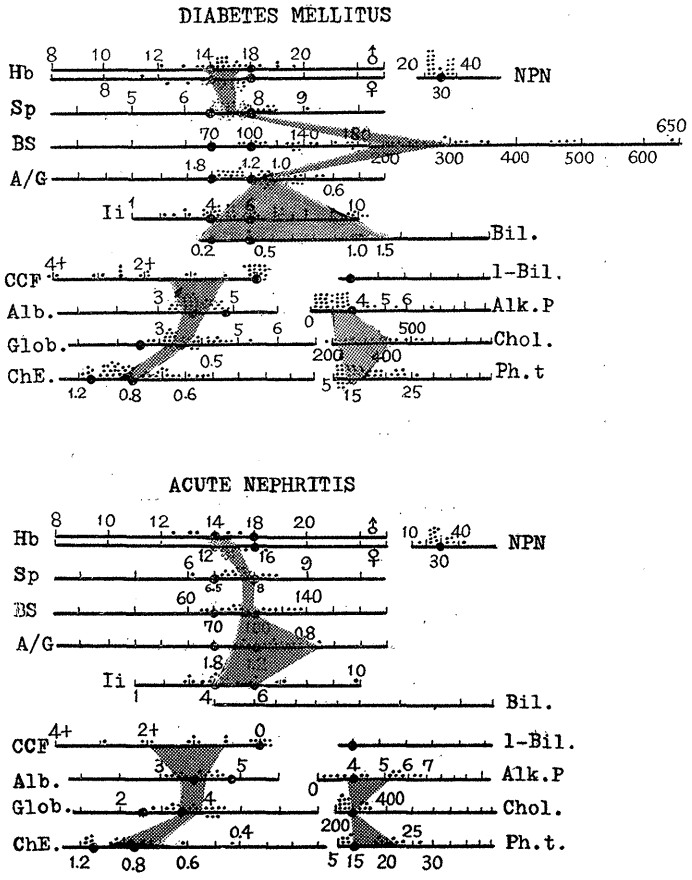


Fig. 13. Blood spectra of diabetes mellitus and acute glomerulonephritis.

Application to the Diagnosis of Various Diseases

The graph was applied with a considerable success for the diagnosis of diseases which were characterized by distorted patten of blood chemistry, as for instance diabetes mellitus. This formed a pronounced rightward protrusion on the connection line (for the appraisal of general condition) in accordance with the position of blood sugar, because hyperglycemia constituted the most salient feature in diabetes (Figure 13). The final diagnosis should, however, await the contemplation of the morbid history and physical examination, and, on occasions, even the glucose tolerance test may be required, because there are a great number of pathological conditions besides diabetes mellitus which cause hyperglycemia (Table VIII), and the diabetes without rise in blood sugar during fasting is not rare.

Table VIII

Pathological conditions which cause hyperglycemia exceeding the level of 120 mg./dl. of fasting blood sugar.

1.	Because of the hepatic disturbances hepatitis, liver cirrhosis, Banti's syndrome, cholelithiasis; dysentery; malignant tumors; skin diseases; eclampsia; circulatory diseses; renal diseases; febrile diseases	87 cases
2.	Because of the hepatic and pancreatic disturbances gastric cancer, gastroduodenal ulcer; diseases of the spinal cord entailing bilateral paralysis of the lower extremities; peritonitis; retroperitoneal tumor	37 cases
3.	Because of the pancreatic disturbances diabetes mellitus, pancreatitis, pancreatic cancer	46 cases
4.	Because of the disturbance of the central nervous system meningitis, encephalitis, poliomylitis, brain tumor, cerebral vascular diseases	13 cases
		183 cases
	out of 1620 casese examined.	

Application of the graph to gastric cancer and gastroduodenal ulcer is summarized in Figure 14 which discloses conspicuous depletion and impaired hepatic function in the former in contrast with the relatively good nutrition and comparatively well-preserved hepatic function in the latter. (Of course a minor part of the cases of gastroduodenal ulcer were indistinguishable from the gastric cancer because of the marked disturbance in nutrition and hepatic function which resulted from the severe homorrhage into the digestive tract)

Anemia has been the greatest thema in which the hematologists cherish special interest, but in the daily practice of medicine profound anemia is

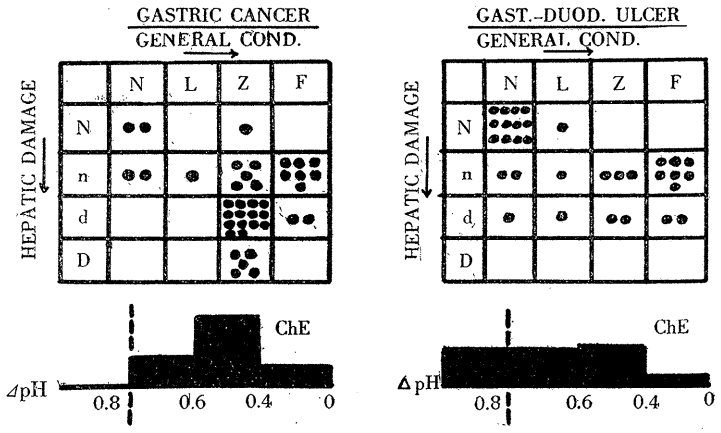


Fig. 14 Application of the blood spectrum to the gastroduodenal diseases N, n, d, and D are the notation of the patterns of connection line for the damage to parenchymatous damage, while N, L, Z, and F are those for the appraisal of general condition. ChE indicates the histogram of serum cholinesterase activity.

common among the diseases of digestive organs and the neoplastic diseases for the diagnosis of which not only the blood hemoglobin concentration but also the appraisal of general condition and organ functions are demanded. Primary blood diseases were not so frequently encountered as the secondary anemia resulting from the diseases of the extra-hematopietic organs (Table IX). The graph was accordingly helpful for the diagnosis of anemia.

TABLE IX

Diseases wich entail profound anemia (blood hemoglobin concentration is below 9 g./dl.)

1.	Digestive diseases ..... 48 gastric cancer, gastroduodenal ulcer, pancreatic cancer etc.	6.	Renal diseases 9
2.	Malignant tumors (excl. gastric cancer) 32	7.	Diseases of the joint 4
3.	Blood diseases 29	8.	Diseases of the respiratory organs ... 4
4.	Hepatobilary diseases 14	9.	Circulatrory diseases 3
5.	Gross lesion of the spinal cord 10	10.	Infections diseases 3
		11.	Parasite diseases 3
		12.	Others 18
			Total 177

cases out of 1620 cases examined.

BLOOD SPECTRUM

The graphic representation of the data of systematic examination of the

various chemical constituents of blood which has been described in the preceding sections has for the past several years been designated by us as BLOOD SPECTRUM, since it provides a convenient measure for the detection of the distorted pattern of blood chemistry in a spectrum-style. It contains twelve selected items at present, but they will in the future be displaced by the new and better, and they will also be either increased or decreased in number with the progress in the technic and knowledge of clinical biochemistry, because they are not the best for the detection of diseases even at the present stage of our study. However, special mention should be made of our experience that a systemic examination of blood chemistry which was applied uniformly to every patient without regard to the kind of diseases was superior in efficiency and fruitfulness of information to the conventional way of arranging various tests for the sole purpose to support or confirm the tentative diagnosis which had been conceived intuitively at the bed side, although at the commencement of our study it was a little feared that systemic examination might entail waste of time and labor. An illustrative case will be given below.

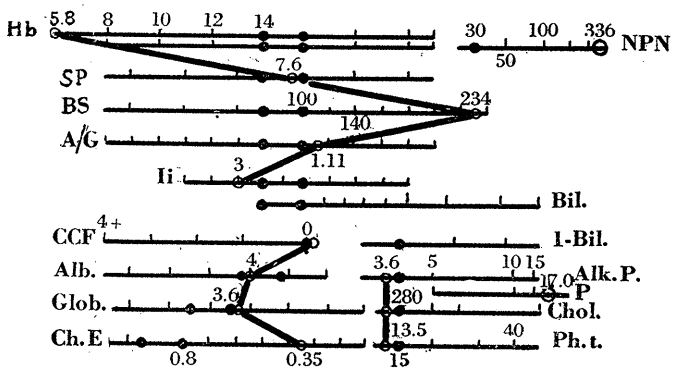


Fig. 15 Blood spectrum of a case of uremia.

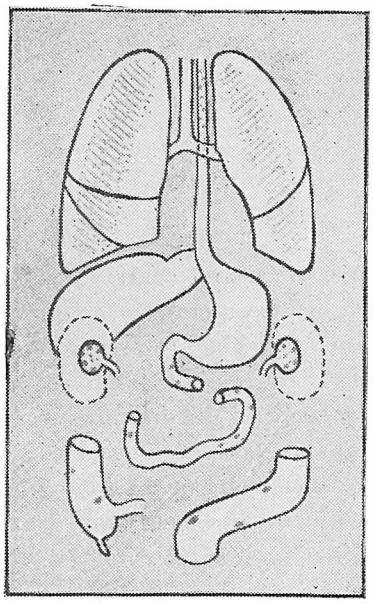
A forty-four-year-old man was admitted to the hospital because of epistaxis and dyspnea.

Six days prior to admission the patient had for the first time epistaxis, odontalgy and swelling of the right cheek. The epistaxis was persistent three days later when he had the onset of dyspnea. On the day of entry he passed tarry stool and became stuporous.

Physical examination revealed an emaciated, stuporous and dyspneic man. The skin of the lower extremities was studded with purpuric petechiae. There were dry sibilant rales all over the chest. The liver edge

was felt 3 cm. below the costal arch. Kidneys and spleen were not palpable. Blood pressure was 100/35 mm. Hg.; pulse rate 60. Urine was negative for protein. Bleeding time was 6.5 minutes. Rumpel-Leede's phenomenon was negative. He expired 18 hours after the admisssion.

A tentative diagnosis of hemorrhagic purpura was instituted, and this would have been quite right as a bed-side diagnosis for this case, because it will be the first which comes to our mind. But had we adhered to the diagnosis, we would have tried in vain to carry out a long series of hematological tests until we would have become aware that we had been misguided and led astray into an enigmatic labyrinth by prejudice, since the blood spectrum which was examined independently clearly demontrated that the patient had an unequivocal uremia, as its data are shown in Figure 15. There was a marked rise in non-protein nitrogen and inorganic phosphorus, hyperglycemia and the diminution of serum cholinesterase activity. The diagnosis was confirmed by autopsy (Anatomical diagnosis : Contracted kidney and hemorrhagic diathesis due to uremia. Figure 16 and 17).



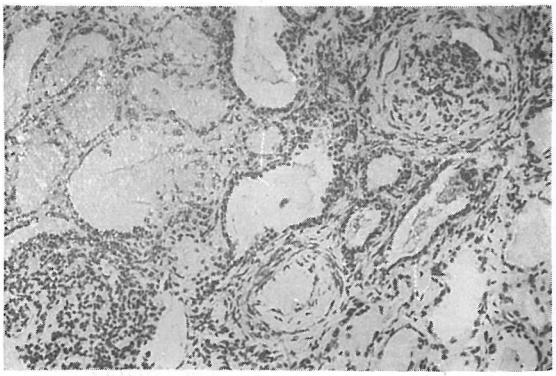


Fig. 17. Photomicrograph of the kidney of the case presented in Figs. 15 and 16. Proliferative and sclerosing glomerulonephritis with atrophy of the tubules which contain protein coagulation. Interstitium is somewhat fibrous and studded with round cells. (Magnification 100×)

Fig. 16. Schematic representation of the autopsy finding of the case whose blood spectrum was presented in figure 15. Hemorrhages in the lungs, esophagus, duodenum, jejunum, coecum, and rectum are indicated by black spots.

Discussion

The case which was presented in the preceding section was not quoted with the intention of exhibiting a unique instance for which systematic examination of blood chemistry was specially efficacious, although it was obviously impressive, because equally impressive examples were not few, and in the daily work of clinical biochemistry the blood spectrum contributed to the clinical diagnosis in various ways. Our experience with 1620 cases which comprise medical as well as surgical patients is summarized in Table X which reveals that the blood spectrum was useful for (1)

Table X

Application of blood spectrum

1.	Clinically Supposed *Diagnosis was confirmed*	58
	Hepatic d. (37), Nephrosis (10)	
	Renal d. (3), Diabetes (5)	
	Rheumatoid arthritis (3)	
2.	Strong *Clue of diagnosis* was obtained	64
	Hepatic d. (52), Nephrosis (3)	
	Renal d. (2), Diabetes (5)	
	Poisoning (1), Hypothyroidism (1)	
3.	*Complication* was revealed	169
	Hepatic d. (142), Azotemia (17)	
	Dehydration (8), Malnutrition (2)	291/1620
	Blood spectrum was *useful in 17.9 %*	

the confirmation of bed-side diagnosis in 3.6 per cent, and contributory to (2) the establishment of clinical diagnosis which had been entirely enigmatic at the bed side on account of the failure to get the clue to diagnosis in 3.9 per cent, while it was helpful for (3) the detection of complications which were covered by the principal diseases (hepatic disturbances, renal disturbances, dehydration, malnutrition etc.) in 10.4 per cent. The blood spectrum served therefore as a useful tool for detection of positive findings of diseases in about 18 per cent of cases which came under our examination, and in a few instances it was also indirectly helpful even for the diagnosis of the remaining 82 per cent, inasmuch as the blood spectrum facilitated the institution of correct diagnosis by affording the negative findings against a particular suspected disease. It will likewise deserve special mention that the detection of complication exceeded the combination of the confirmation of bed-side diagnosis and the institution of clinical diagnosis in frequency. However, a diagnostic measure can not be equally efficient in all kinds of diseases. It is usual that a measure which is so

useful that it is felt mandatory for the diagnosis of one disease is little helpful for that of the next. Blood spectrum is not the exception. It is almost useless for the diseases of nervous system and skin, whereas it serves much for the diagnosis of hepatic, renal and endocrine diseases, because the neurologic and dermatologic maladies hardly entail an appreciable alteration in blood chemistry on which the blood spectrum is established. Here is the limitation of the application of blood spectrum. But this casts no dense shadow upon the clinical significance of blood spectrum, since it gives positive findings for the detection of abnormality in 18 per cent of the cases which are encountered in the daily work of clinical laboratory. As has been stated in the preceding sections, in our experience systematic examination of blood chemistry proved to be superior in efficiency and economy to the repetition of useless tests which were falsely directed and chosen by the prejudice of the erroneous diagnosis which was entertained at the bed-side, although uniform performance of numerous determinations without regard to the kinds of diseases had been feared to entail waste of time, labor and materials.

It is however apparent that the blood spectrum is beyond the capacity of the side-work of internists and surgeons, because there are many determinations contained in it, and this is the very reason why modern clinics require clinical biochemists. But they are unfortunately liable to lose their enthusiasm for their job when they are not well informed of the importance of the examinations which are submitted to them, since routine clinical biochemistry demands labor, patience and meticulous attention for the succession of monotonous and tedious procedures. The blood spectrum was devised partly with the intention of overcoming mental weariness of this kind which might encroach upon the activity of a person engaged in clinical biochemistry. It enables a unique clinical diagnosis which is established on the basis of blood chemistry when morbid history has been given beforehand for the purpose of reference. In our belief clinical biochemists ought to be specialists not only of the biochemical determinations, but also of the efficient application of their data to the clinical diagnosis.

Summary and Conclusion

A system of graphical representation of twelve chemical constituents of blood which were determined routinely was presented as a useful tool for the clinical diagnosis, and this was designated under the name of Blood Spectrum. It contained four graphs: Graph A for the appraisal of general condition—hemoglobin in blood, protein, albumin to globulin ratio

and serum glucose, Graph B for the detection of damage to the hepatic parenchyma—cephalin cholesterol flocculation test, albumin, globulin and cholinesterase in serum, Graph C for the detection of biliary obstruction—icteric index, one-minete bilirubin, alkaline phosphatase, cholesterol and phenol turbidity test of serum, and Graph D for the detection of kidney disturbances—non-protein nitrogen.

Observation in which one thousand six hundred patients were submitted to the blood spectrum revealed that it enabled (1) the appraisal of general condition by means of blood chemistry, (2) the detection of hepatic disturbances and biliary obstruction, (3) the diagnosis of the parenchymatous and the obstructive jaundice, and (4) the differential diagnosis of glomerulonephritis, nephrosis and uremia. The blood spectrum was similarly helpful in the diagnosis of diabetes mellitus, anemia, gastroduodenal ulcer and gastric cancer, and was useful for the diseases of the liver, kidney, pancreas and some endocrine organs in general. It was either positively contributory to the confirmation of bed-side diagnosis, or available for affording strong clues to the diagnosis which had been hard to establish at the bed side in 8 per cent, while it also contributed to the discovery of complications in 10 per cent of the cases. In a few cases the blood spectrum successfully revealed the principal disease which had been entirely enignmatic.

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