KAWASAKI MED. J. VOL. 16 : NO. 1, 1-8 (1990)

Message from Gokei

Susumu SHIBATA

Curator, Educational Museum of Modern Medicine, Kawasaki Medical School, Kurashiki 701-01, Japan

Accepted for publication on October 1, 1990

ABSTRACT This is the document of an assigned speech delivered in the Katsurahama Conference of Clinical Pathology (in Kochi, 1989) which was presided by Prof. Masahide Sasaki of Kochi Medical School. The speaker emphasizes the importance of arrangement of laboratory tests to be carried out in sets and facilitation of clinical diagnosis by use of a computer which enables the diagnostic interpretation of test results (CALD: computer-assisted laboratory diagnosis). The laboratory will be able to make a service by CALD to the extent that possible disease groups relevant to each patient are mentioned on a report sheet.

Key words : clinical chemistry — CALD: computer-assisted laboratory diagnosis

Since I retired from the position of Dean of Kawasaki Medical School last March, I have been spending a dreamy life in a house which commands a beautiful view of the hills and valleys of a rural area of Okayama Prefecture called Gokei.

Dr. Sasaki's recent call to me from Kochi, however, suddenly awakened me up and has brought me across the Inland Sea to learn the present progress in laboratory automation systems in Korea, Taiwan, Switzerland, the United States of America and Japan from many distinguished clinical pathologists and clinical chemists including Dr. Lee, Dr. Shen, Dr. Ruegg, Dr. Straumfjord and other ladies and gentlemen who assembled in this hall at the Second Katsurahama Conference.

Modern medicine is characterized by the utilization of laboratory examinations for clinical diagnosis.[1] During the last century, during the period of the first generation of modern medicine, physicians employed tools such as the stethoscope. In this century, on the other hand, physicians of the second generation of modern medicine rely a great deal on the laboratory test results[1] supplied by instruments created for the purpose of clinical diagnosis (Table 1).

However, present day physicians must earnestly ask specialists in engineering to invent and prepare such instruments, since such tasks are beyond their ability. In response to our requests, the engineers have done a good job, providing physicians with highly efficient instruments. Furthermore, they have successfully invented a considerable number of instruments which make automatic laboratory management feasible, thus leading to the saving of money spent for personnel expenditures (Table 2).

Needless to say, Professor Sasaki is an exceptional representative of physicians,

柴田 進

TABLE 1. Medical Care

- *Ancient and Medieval Medicine* ..... ~ 1800
  inspection with *Empty Hands*
- *Modern Medicine*
  - *First Generation* ..... 1819 ~ 1900
    examination with *Tools* (*Stethoscope*)
  - *Second Generation* ..... 1900 ~
    examination by use of *Instruments* (*Machinery*)

TABLE 2. Modern Medicine

- *First Generation* ..... 1819 ~ 1900
  Physicians invented tools by themselves
- *Second Generation* ..... 1900 ~
  Physicians unable to make instruments, and ask engineers for help.
  Engineers manufacture a lot of excellent
  Instruments → *Automatic Machineries.*

who has been actively engaging in making laboratory instruments with his own hands. He invented the minipette ultramicroanalytic system[2,3] and the belt-conveyer system,[4–7] which promoted the advances in the automatic management of laboratory examinations.

In the late fifties and early sixties we used labotatory tests in order to detect those clinical signs of patients that could not be obtained through the conventional techniques of physical diagnosis, such as observation, percussion, auscultation and palpation. Shortly thereafter, however, we proceeded in a new direction, attempting to make clinical diagnoses mainly based on laboratory examinations which, in the past, had been used in a supplementary manner. Through our experience, we thought it was possible to appraise the general condition of a patient and the impaired functional status of his major metabolical organs, such as the liver and the kidneys, and to interpret test results on the whole for a clinical diagnosis based mainly on laboratory examinations, provided that the tests were chosen and arranged in accordance with the diagnostic purposes. This idea led to the BLOOD SPECTRUM diagnostic system.[8,9]

Prior to the years in which Professor Sasaki's minipett system[2] was employed the volume of the laboratory test results obtained in our laboratory was in good balance with the capacity of clinical pathologists to make clinical interpretation. Therefore, the clinical pathologists did their job, with the satisfaction that they were making their diagnosing in cooperation with the physicians directly in charge of the patient's care.

As soon as the minipett system was introduced, however, the test results increased rapidly due to its high efficiency, and the test results obtained surpassed the capacity for clinical interpretation by clinical pathologists. It was keenly realized that the advancement in the techniques of chemical analysis necessitated the advances in the level of clinical interpretation of relevant test results, probably through the use of a quote "thinking machine" unquote if such a device were obtainable.

Fortunately, at that time computer made its appearance in the field of scientific research. Dr. Miyaji and Dr. Ueda. with the assistance of a mathe-

matician, were able to put the thinking processes of clinical pathologists into computer soft-ware. This was achieved around 1970, and was given the name CALD, that is computer-assisted laboratory diagnosis.[10] At present Dr. Matsuda is exploring this area in Dr. Ueda's laboratory as a mathematician with the career of a clinical pathologist.

Today, in this conference, we have listened to the enlightening speeches delivered by the four authorities on laboratory automation systems and have been impressed by the rapid progress that has been made. Thanks to laboratory automation we, the clinical pathologists, may now do en masse analysis of various kinds of tests within a relatively short time and can obtain accurate test results to deliver to the clinicians working on the wards or in the outpatient's clinics. We are indeed happy. However, an undersirable profile is arising in present-day laboratory examinations.

(1) Laboratory examinations are being requested and performed easily and rapidly without earnest contemplation of the clinical diagnosis.
(2) There is a tendency towards unnecessary performance of laboratory tests.
(3) Some hospital administrators have predicted that the installation of automatic analytic machines in the hospital laboratory will lead to savings on laboratory personnel expenses, and recommendations will be made for laboratory tests to be done in commercially managed laboratory centers outside of hospitals.
(4) Clinicians on the ward and in outpatient clinics are being confronted with indigestion from too many unsatisfactorily interpreted report sheets of test results which cannot be adequately utilized for clinical diagnosis.
(5) Patients and the Ministry of Welfare, are complaining about the rise in the medical care costs.

Nevertheless, we hope that every patient may obtain his share in the benefits of laboratory examinations served by automation systems. The essential fault of present day laboratory examinations lies in the defective way in which information from test results are issued without accompanying clinical interpretation. Laboratory test results are handed over to the clinicians in raw form without cooking.

As a result, complete laboratory testing which should include the performance of tests as the first step, is rarely carried out together with the clinical interpretation of the results as the second step. In the majority of cases laboratory testing ends with the first step and the second step is curtailed.

Tissue pathologists are esteemed in the hospitals and are trusted by clinicians as their advisors.

(1) They prepare the stained tissue section specimens necessary for pathological microscopy, which corresponds to the first step of turning out the test results, and
(2) then they examine them under the microscope to provide a clinical interpretation together with tissue diagnosis on the report sheet, which corresponds to the second step.
(3) The tissue pathologists hand over the stained tissue section specimens plus the report sheet to the clinicians who have requested their help.

In the same way

(1) Laboratory testing is made complete when procedures are carried out by automation and manual systems and then

(2) their results are interpreted from the viewpoint of clinical diagnosis by use of CALD, followed by clinical pathologist's checking.

Based on our experience, several pre-requisites should be satisfied for the performance of complete testing.

(1) Clinicians should be requested or persuaded to ask us for tests which will enable us to carry out clinical interpretations, which include appraisal of general condition and assessment of functional disorder of major organs, instead of ordering only special isolated tests.
(2) Clinical pathologists should evaluate and select the diagnosis-effective as well as cost-effective tests which are served routinely, through his own experience in clinical interpretation works and consultation with clinicians.
(3) Clinical pathologists should refrain from reporting the test results in raw form as much as possible.
(4) Efforts should be made to improve CALD in order to facilitate the clinical interpretation of test results.

However, I suspect that you may be afraid of the reaction of the clinicians, if these recommendations are carried out in your laboratory, because clinicians believe that it is presumptuous and impossible for clinical pathologists working in the realm of laboratory without any direct contact with patients to make a clinical interpretation or clinical diagnosis. Courage and perseverance are demanded to remove this obstacle from the path of reporting clinical interpretations. We have to improve our clinical interpretation of test results until a time when we can evaluate them on a level equaling that of tissue pathologists comes.

Incidentally, I would like to thank the medical technologists who are working with clinical pathologists and making great contributions to the performance of laboratory tests. Please, be attentive to unexpected test results which you may get in the course of routine work. Don't discard them until you have determined the reason for such results. If you do so, you may, by chance, be praised as a man or woman who discovered a new aspect of medical biology.

Last autumn we held the 36th General Meeting of Japan Society of Clinical Pathologists in Kyoto. The meeting was successful, and a considerable number of participants gathered in a hall to learn and discuss Igaku-handan-gaku that is the art of medical decision making. They were earnest. I am glad and happy to know through this meeting that the clinical pathologists in this country are now aware of complete laboratory testing, in which clinical interpretation, that is the second step is as important as the test results, that is the first step.

To close message from Gokei, allow me to speak about our recent experience in the clincal interpretation of laboratory tests, particularly by use of CALD. Clinical interpretation was not and still is not an easy task, indeed.

(1) Dr. Matsuda created the 110 blood chemistry diagnostic codes for CALD so that a computer might print out 51 types of possible diseases relevant to the codes. He applied his CALD to 55 autopsied patients who were previously discussed in clinico-pathological conferences, and obtained correct clinical diagnosis in 90% of cases.

One examples is presented in these Figures (Figs. 1,2). This concerns with test result report sheet. His CALD interpretation began with the appraisal of the patient's general condition, followed by a list of possible diseases mentioned in the order of degree of possibility from top to bottom.

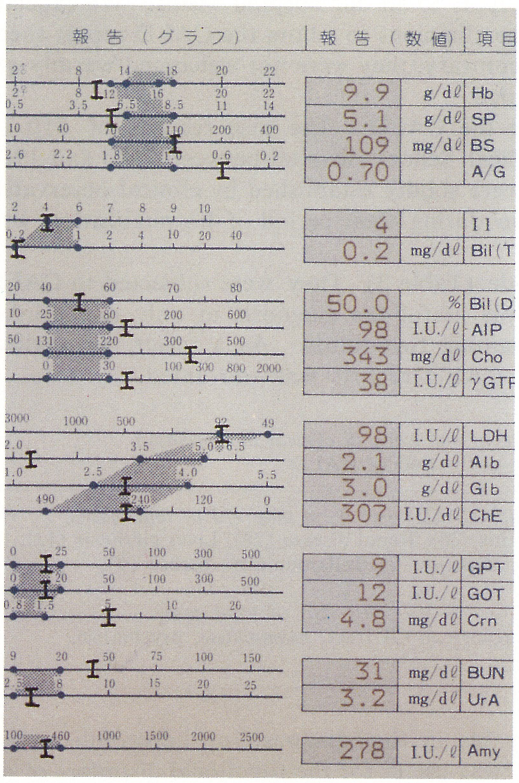

Fig. 1.
Blood spectrum diagnostic system. Shaded areas refer to normal ranges of relevant blood chemical ingredients.

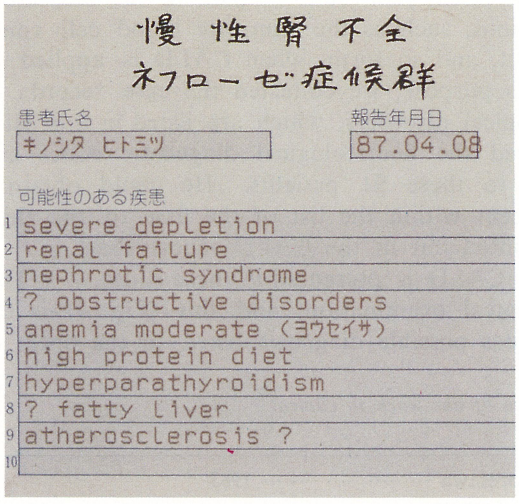

Fig. 2.
CALD of blood spectrum (Fig. 1), reporting the patient's general condition and possible diagnoses listed in the order of magnitude of possibility.
(chronic renal failure, nephrotic syndrome)

(2) We expanded the use of CALD to all our hospital wards. We expected a warm reception from the clinicians to whom the CALD report sheets were delivered. On the contrary, they were not welcomed warmly and were occasionally disregarded.
(3) This led us to re-evaluate the CALD. The case records of 510 in-patients of Kawasaki Medical School Hospital between 1985 and 1987, whose clinical diagnoses were solidly established by clinical observation and laboratory examination during their period of hospitalization were checked.

They are presented in this slide (Table 3). They were subjected to CALD. The results revealed that CALD was useful for diagnosis in only one third of the cases and useless for the remaining two-thirds. As a result, we realized that clinician's disregarding of the CALD reports was warranted.

TABLE 3. *Recent experience of our work iu clinical interpretation*
Result of self-re-evaluation of CALD

○ *Successful hit of possible diagnosis (CALD)* ····· *in only 1/3 of total cases,*
Diabetes mellitus (43), Hepatitis (36), Renal disease (28), Liver cirrhosis (12), Neoplasm (24), Biliary Tract Disease (2), Inflammatory disease (5), Pancreatic disease (4)
○ *Failed to hit the correct dianosis* ····· 2/3 of total cases.
Circulatory, respiratory, neurological, GI tract, *hematologic*, psychiatric, ·····, and surgical diseases.

However, the CALD was valuable in the diagnosis of hepatobiliary and renal diseases. In other words, it was useful for the functional disorders of the major organs of metabolism. In contrast, CALD was seldom useful in the diagnosis of hematological disorders, in which populations of blood cells are affected more profoundly than the blood chemical ingredients.

It was, therefore, thought that attention should be paid to the laboratory examination of blood cell populations, such as the complete blood cell count and the leukocyte differential count, and so forth, when CALD is applied to hematological disoroders. For this purpose, we collected the case records of 91 patients with various hematological disorders, which are listed in this slide (Table 4). Dr. Koresawa prepared the hematological diagnostic codes and applied his hematological CALD to these 91 patients. He could obtain a correct diagnosis in 70 to 80 percent within the list of the first to the third possible diagnoses, which were printed out in the CALD report sheet.

An example of hematological CALD is presented in these slides. — This (Fig. 3) is the report of hematological examination, and this (Fig. 4) is the clinical interpretation, which includes possible diagnosis listed in the order of

TABLE 4. *Recent experience of our work in clinical interpretation*

Hematological CALD by Dr. S. Koresawa ····· 1983
91 patients with various hematologic diseases
aplastic anemia (18), IDA (5), polycythemia (8), thrombocytopenic purpura (14), agranulocytosis (7), CML (12), CLL (2), ALL (4), AGL (9), APL (9), AMOL (3), MDS (12)
Successful hit of possible diagnosis in 70-80%.

167	RBC×10⁴/μl (M410-550 F360-480)	MORPHOLOGY			
6.5	Hb g/dl (M13.5-17.5 F11.5-14.5)	ANISOCYTOSIS	MODER.		
19.0	Ht % (M39-52 F34-44)	SIZE	正球性		%
114.0	MCV fl (M87-103 F87-99)		小球性		%
38.9	MCH pg (M29-35 F28-34)		大球性	*	%
34.2	MCHC % (33-36)	COLOR	正色素性	*	%
	網状赤血球% (0.5-1.5)		低色素性		%
NORMO	多染性赤血球		多色素性		%
	PLATELET	POIKILOCYTOSIS	SLIGHT		
4.4	直接法×10⁴/μl (15-35)	1 Pointed cell		*	
8400	WBC/μl (6000±2500)	2 Basophilic stippling			
WBC DIFFERENTIAL COUNT (%)		3 Howell Jolly body			
36	Blast (or pathol.cell)	4 Rouleaux formation			
2	Progranulo (or pathol. cell e.granules)	5 Target cell			
2	N. Myelocyte	6 Ovalocyte		*	
(+)	N. Metamyelocyte	7 Bizarre cell			
2	N. Band (2-10)	8 Red cell fragment			
25	N. Segmented (50-70)	9 Microspherocyte			
0	Eosinophil (1-5)	11 Dohle body			
0	Basophil (0-1)	12 Toxic granules			
1	Monocyte (1-6)	13 Vacuoles			
32	Lymphocyte (20-40)	14 Hyperseg・N			
0	Atypical Lympho	15 Crenated cell			
(+)	赤芽球 /100WBC	16 Burr cell			
	巨赤芽球 /100WBC	17 Leptocyte			
	巨核球 /100WBC	18 Elliptocyte			
(+)	アウエル小体 /100Blastoid	血球粒度分布	WSCC (/μl)		
	血小板 Fonio ×10⁴/μl		WSCR (%)		
*	血小板 Forming clumps		RDW (fl)		
		PDW (fl)		PLCR (%)	
Specific findings		MPV (fl)		PCT (%)	

Fig. 3.
Hematological pattern of peripheral blood examination. Normal values of relevant blood cells are presented in parentheses.

AML

技師コード 閲

ﾋｮｳﾄﾞｳ ﾁｻｺ 88.09.07

1.Acute leukemia
blastoid cell-38 Auer rod-0
? high WBC-8400 hiatus(+)
neutroph.-27 low plt-4.4
2.Leukocytosis
? high WBC-8400
3.? thrombocytopenia/follow up
low plt-4.4
4.Macrocytic anemia
anemia-marked low Hb-6.5
high MCV-114
NOTE : Check BM smear.
Borderline leukocytosis. Follow up. Check BM/folate/VB-12. R/O malignancies.
Refer to hematologist

Fig. 4.
CALD of the hematological pattern (Fig. 3), reporting diagnoses, abnormalities and recommendation of further tests.

possibility and note of recommendation for further examination.

There are no almighty sets of laboratory tests which are applicable to and useful for the diagnosis of diseases of various sorts. Selection of sets of laboratory tests with the aim of clinical diagnosis in mind is mandatory for the success of CALD.

From our bitter experiences in clinical interpretation and CALD we have come to the following conclusion.

(1) Laboratory tests should be chosen and arranged in sets with diagnostic purposes in mind.

(2) We should refrain from pointing out the names of special diseases as much as possible in the CALD report sheet, and mention only the terms related to disease groups, instead.

(3) CALD can often be useful for the detection of complications or concealed diseases. CALD can be used for sequential following up of the clinical course.

REFERENCES

1) Race, J.R.: Laboratory Medicine, vol. 1~4 Revised. Philadelphia, Harper V Row. 1985
2) Sasaki, M.: Minipette system, a convenient ultramicro performance of routine clinical chemistry by means of a semi-automatic pipet (minipette) and a drain-system colorimeter of new design. Bull. Yamaguchi Med. School **13** : 19–33, 1966
3) Sasaki, M. and Shibata, S.: Minipette system®: A simple and convenient ultramicro technique for routine clinical chemistry (Part I and Part II). Bull. Yamaguchi Med. School **16** : 111–130, 131–162, 1969
4) Sasaki, M.: How to make and manage clinical laboratory system using robotic facilities. *In* Proc. I UPAC 3rd International Congress. (Kobe) : Automation and New Technology in clinical laboratory (ed. by Okuda, K.). London, Blackwell Scientific Publication. 1988, pp. 97–101
5) Sasaki, M.: An innovative conveyor belt system for a clinical laboratory. *In* Proc. 4th Asian-Pacific Congress. Biochem. (Hongkong), ed. by Lin, H.S. and Swaminatham, R. Hongkong, Gardiner Cold Well Communication Ltd. 1988, pp. 301–306
6) Sasaki, M. and Ougra, K. : A fully robotic assay for human hormone analysis. Clin. Chem. **36** : 1–5, 1990
7) Sasaki, M. : The automated laboratory. Japanese hospital builds its own robot analysers. Asian Hospital ISSN 1011-596X : 18–20, 1990
8) Shibata, S. : Blood spectrum, a system of graphical representation of twelve chemical constituents of blood for the purpose of clinical diagnosis. Bull. Yamaguchi Med. School **3** : 27–49, 1955
9) Shibata, S. and Ohba, Y. : Routine hepatic test. Bull. Yamaguchi Med. School **13** : 223–231, 1966
10) Shibata, S., Ueda, S. and Matsuda, N. : Computer-assisted laboratory diagnosis and its clinical usefulness. Kawasaki Med. J. **11** : 191–213, 1985