DIAGNOSTIC VALUE OF THE BLOOD PATTERN IN CANCER

H. LEONARD BOLEN, M.D.
Fall River, Massachusetts

IN the hope of bringing about improvement in the results of therapy in cases of carcinoma through earlier diagnosis of the lesion the blood pattern test explained in detail hereafter and previously reported in 1942[1] and 1944[2] has been employed at the Tumor Clinic of the Union Hospital since July 3, 1947.

The test is simple and requires very little time and equipment. The pulp of the middle finger is punctured with a Hagedorn or other type of sharp needle. A needle which makes a round wound should not be used because of too rapid sealing, yet the wound should be deep enough to permit the blood to flow freely. A clean glass slide is then touched lightly to the finger tip; too much pressure will dilute the blood with tissue fluid. Three drops of blood are collected at intervals on the slide which is righted and set aside to dry, care being taken not to smear the drops. Upon drying a pattern becomes visible if the blood is not too thick; this pattern can be examined macroscopically and microscopically. It is wise to prepare two slides at each examination.

The macroscopic appearance of the normal blood pattern is seen in Figure 1. It should be noted that the first drop taken is usually too thick and the pattern less discernible. The pattern formed on drying in the second and third drops is a more reliable indicator of the presence or absence of malignancy. If all the drops are too thick, the test must be repeated with less pressure applied to the finger tip.

After the drops on the slide have been allowed to dry thoroughly undisturbed, they may be examined macroscopically and under high dry power magnification. The blood of non-cancerous individuals differs markedly from that taken from patients with cancer. As the normal drop dries, a dark mass appears centrally. Under the microscope the fibrin content of the

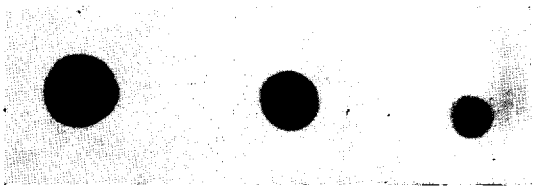

FIG. 1. Normal, macroscopic.

blood is seen in the well formed strands of varying size and thickness which interlace to form a web enmeshing the corpuscles. Leukocytes are few and the red cells tightly packed. Rouleau formation is present, with no variation in the size or shape of the red blood corpuscles. (Fig. 2.)

The fibrin is one of the valuable constituents of normal blood. It is a fine, invisible network circulating in the blood continually. Upon exposure to the air the fibrin oxidizes and contracts and becomes visible under the microscope in the negative blood pattern.

In the drop of cancerous blood no mass can be made out in the center. The blood breaks down into "dots." Microscopically no rouleau formation can be made out. The red cells are grouped in disorderly heaps and some appear shrunken and of indistinct outline. Many of the cells have hemolyzed, the time of hemolysis varying, and this abnormal change is more pronounced in cases with metastases. The appearance is one of agglutinated cells in lakes of plasma. Granules, spicules or rays are numerous, occurring either singly or in clumps. The fibrin content is greatly reduced, almost nil. (Fig. 3.)

After preparing thousands of slides on cancerous subjects it has become possible to discern different degrees of malignancy

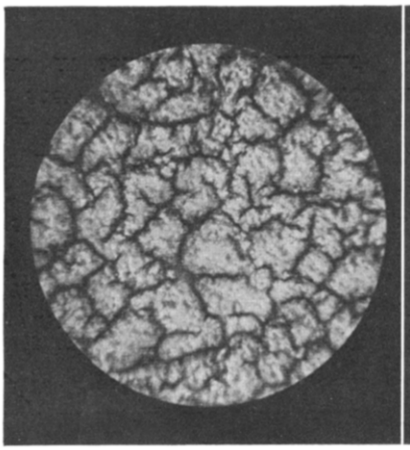

FIG. 2. Normal pattern, microscopic.

FIG. 3. Positive pattern, microscopic.

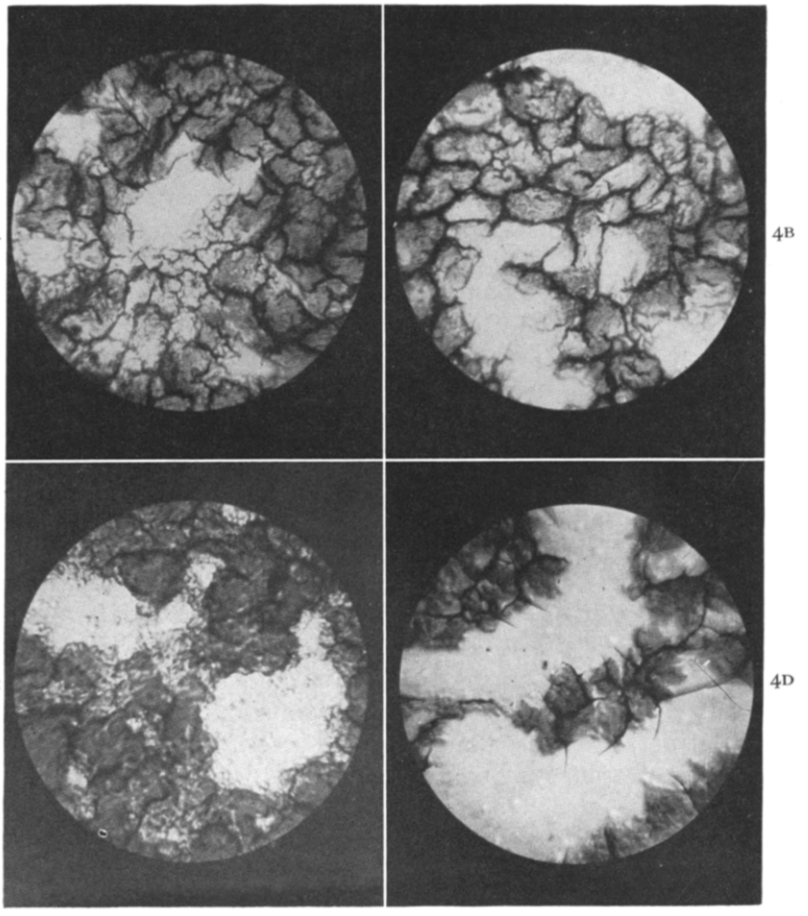

FIG. 4. A to D, transition from early lesion to full bloom cancer.

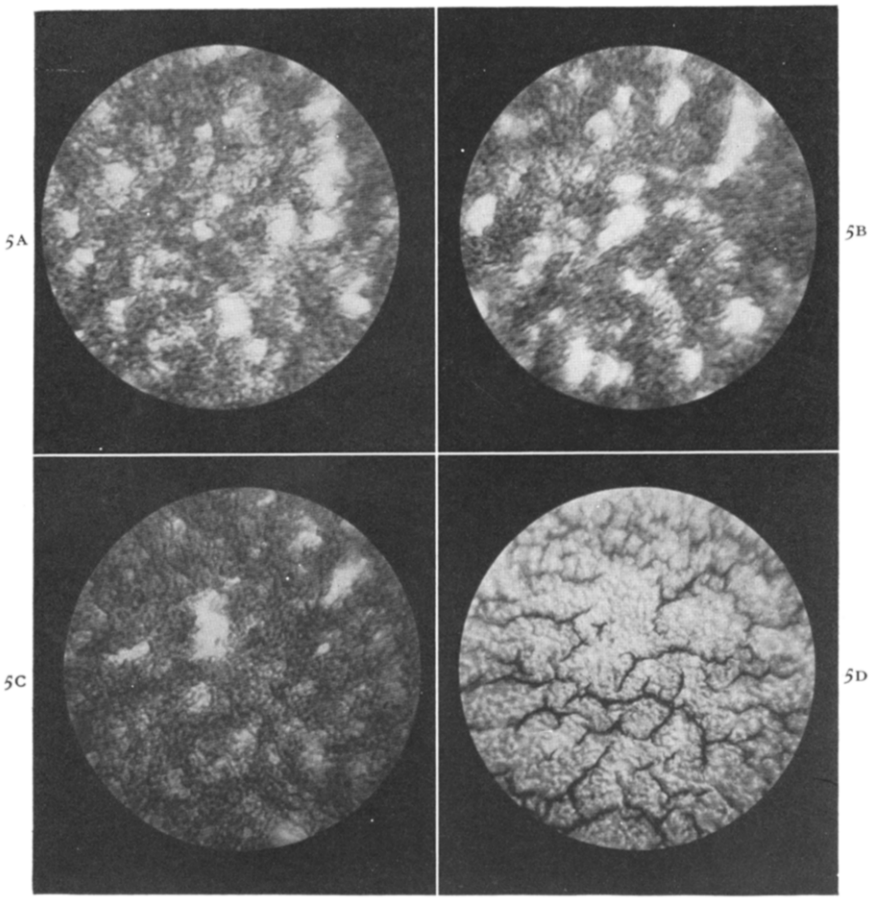

FIG. 5. A to D, transition of negative fluid drop; high power magnification.

from the early to the full bloom pattern. There is a progressive change in the fibrin formation and an increase in the size and number of the plasma lakes, with a decrease in the number of red blood cells. The cells become more and more distorted, agglutinate and form thick islands with many three-cornered, tri-asteroid spicules scattered throughout, as in Figure 4. Thus, any given specimen can be compared with one of these four positive patterns and the stage of malignancy approximately determined.

In an endeavor to discover what took place in the drop of blood during the drying process, photomicrographs were made at intervals of three minutes under high power dry magnification. (Fig. 5.) Eight transitional images of the fluid drop of negative blood were photographed; then the same procedure was carried out with the fluid drop of positive blood and the two series of photomicrographs compared. (Fig. 6.)

It was noted that in the negative drop the circulating cells did not agglutinate. Small lakes formed at first but the red cells remained uniform, began to pack together to form rouleaux. Fibrin emerged from the periphery, formed strands, became heavier and seemed to force the cells closer together until the strands filled the whole field. The final image showed the reticular network with cells enmeshed—the pattern of normal or non-cancerous blood.

By contrast, in the positive drop the blood cells became disarranged early and small, numerous lakes appear. Rouleau formation did not take place. There was clumping of the red blood cells with some

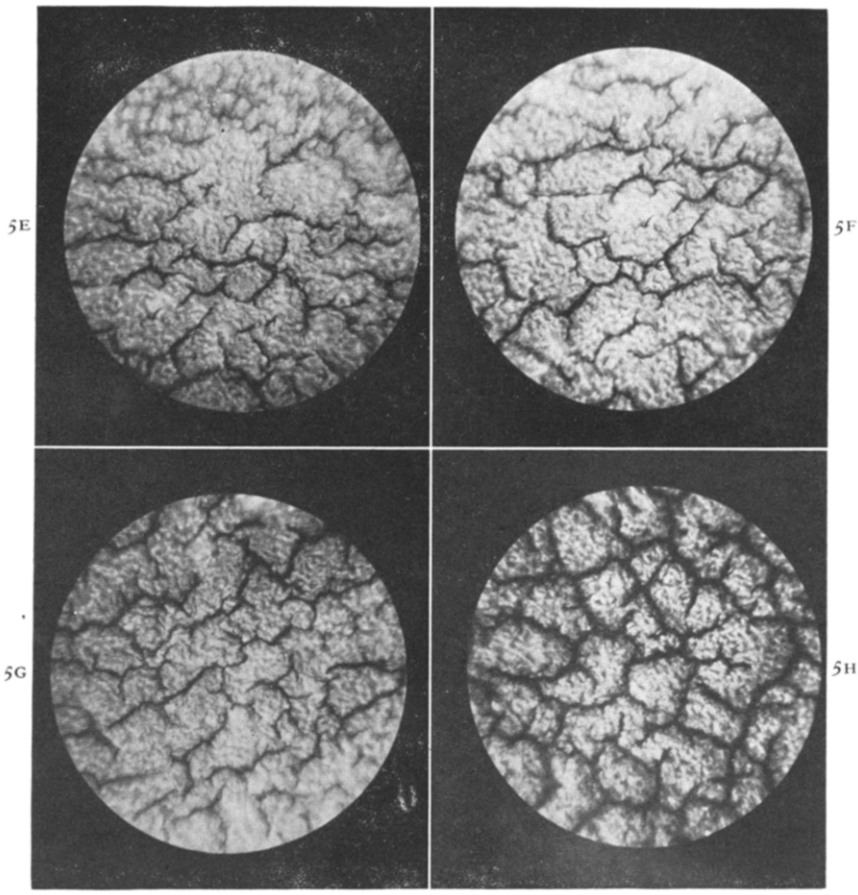

FIG. 5. E to H, transition of negative fluid drop; high power magnification.

becoming superimposed on others; as the breaking-down process continued, granules appeared in the lakes and an adhesive, protein-like substance caused the circulating cells to agglutinate. The final photomicrograph was that which we have come to know so well as the characteristic cancer pattern.

The criteria for diagnosis may be summed up as follows:

Negative Pattern	Positive Pattern
Appearance of fibrin in a reticular network	Absence of fibrin
Rouleau formation	Lack of rouleau formation
Rapid blood spread	Viscid blood
Stability of the red cells	Agglutination of the red cells
Close, even, mosaic pattern or meshwork	Formation of lakes and islands interspersed with granules and spicules

In order to determine the reliability of this simple cancer test it was decided to chart the results in 800 individuals who are classified in four different groups according to their reaction to the test.

Group one comprised 137 subjects, 15 male and 122 female, among the hospital personnel, all apparently in excellent health. In two of the women the test brought to light the presence of early malignancy, cancer of the cervix in one and cancer of the breast in the other.

The second group of subjects examined comprised those patients with a variety of conditions which were known to be benign. Slides were not made on pregnant women or patients receiving transfusions, factors which give a positive reaction; in this group of 337 patients the blood pattern was negative in every instance, as seen in Table 1.

The third group consisted of 198 cases

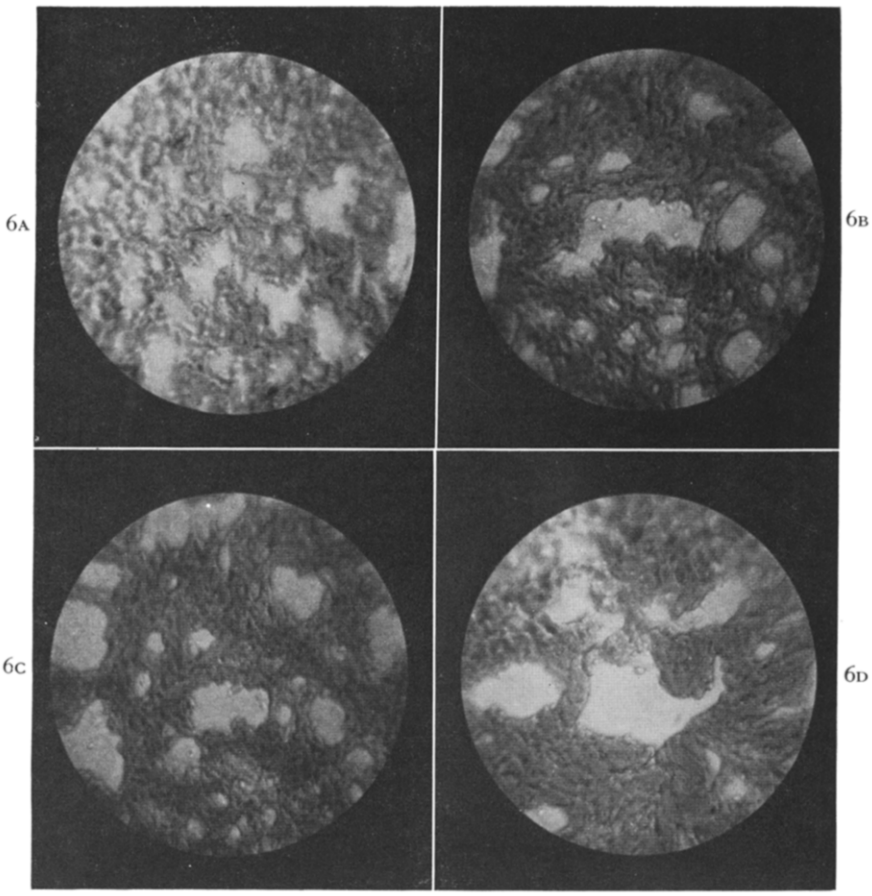

FIG. 6. A to D, transition of positive fluid drop; high power magnification.

of proved cancer. All of these individuals were admitted to the Tumor Clinic of the Union Hospital since July, 1947. They were given the usual routine diagnostic tests including the collection of drops of blood on the slides.

Table II lists the site of the lesion, type of neoplasm, result of the test and the total number of cases. In 191 of the 198 cases the blood drop showed the positive pattern of malignancy; thus, the results were correct in 96.5 per cent of the cases. The test was evaluated along with clinical and laboratory findings but in some cases it was the sole clue to the presence of malignancy somewhere in the body. The test proved to be more accurate in this group than in the group of 140 patients reported in 1942, in which results were correct in 128 cases, or 91.4 per cent.

The false negative slides, seven in number, were reviewed in an effort to discover a reason. In the four cases of basal cell carcinoma of the skin the drops on the slide appeared rather thick; this may have accounted for the incorrect reading. Also, in the case of carcinoma of the pancreas operation and biopsy proved the slide incorrect. When the test was repeated at intervals during follow-up study of the patient, the pattern was always positive, indicating that operation did not bring cure. The patients with cancer of the lung and cancer of the cervix had both been given blood transfusions; this may have been the factor which changed the composition of the blood at the time the sample was taken.

The last group includes the results of the test made on patients treated with surgery, irradiation or radium implantation for

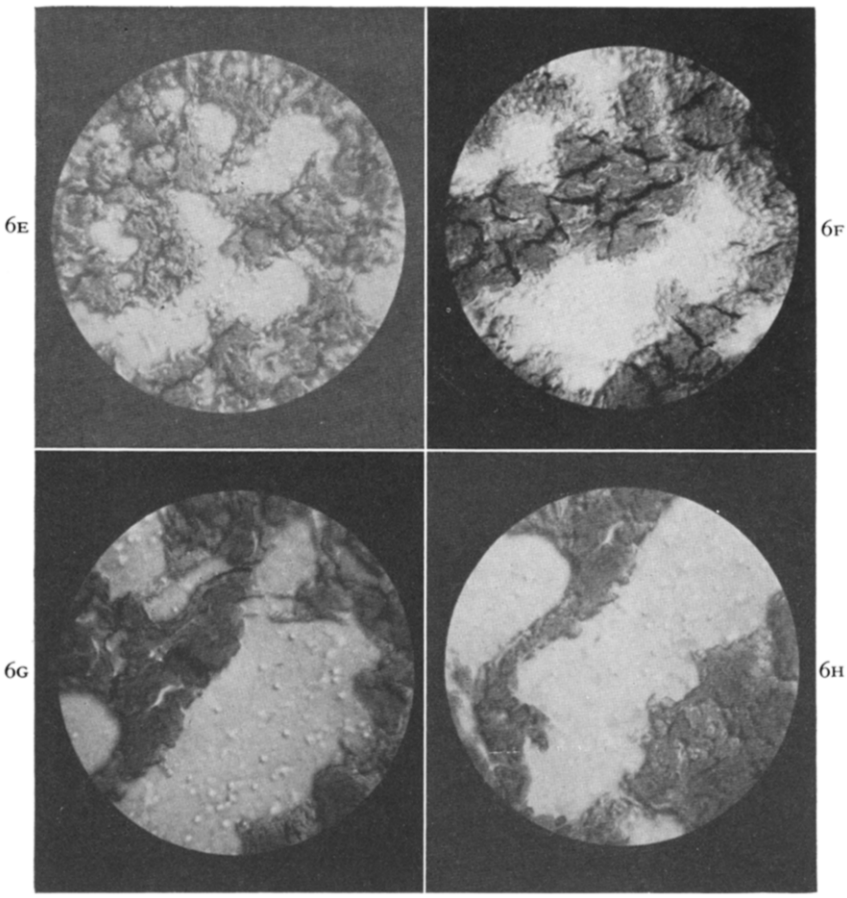

FIG. 6. E to H, transition of positive fluid drop; high power magnification.

malignancies of various kinds who returned to the Clinic for a check-up at frequent intervals. Seventy-seven of the 128 patients treated showed the same positive pattern after therapy. However, in some instances the change in the pattern from positive to negative was dramatic after therapy and, as a rule, the blood pattern paralleled the clinical course.

The following four case reports illustrate the unfortunate end result when the blood pattern was ignored or when the search for the site of the neoplasm was not thorough enough:

CASE REPORTS

CASE 1. V. F., a female aged thirty-eight, was first seen at the office in February, 1941, with a swelling in the right forearm of two months' duration. The blood pattern was found positive for cancer. She was referred to Pondville Cancer Hospital for study. X-ray examination revealed an irregular area of new bone formation in the region of the upper third of the shaft of the right ulna. No definite destructive changes were found in the bone. Two Hinton blood examinations were positive. An exploration was carried out and a tumor mass which involved the periosteum of the shaft of the right ulna was excised. The histopathologic diagnosis was luetic osteitis. Antiluetic treatment was given by her local physician.

The following May x-ray examination revealed only a very slight trace of periosteal thickening in the region of the previous lesion. The blood pattern, however, remained positive. The Hinton blood examination was negative and remained so.

In January, 1944, an osseous growth was excised from the right forearm at the Truesdale Hospital. The pathologic diagnosis was myositis ossificans of the right forearm. The blood pattern was still positive. She was readmitted to

the Truesdale Hospital in January, 1945, for excision of the recurrent growth. The pathologic report was again myositis ossificans of the right forearm; there were no signs of malignancy. The blood pattern was positive.

In January, 1946, she was admitted to the Fall River General Hospital for excision of a recurrent growth at the same site. The report was again myositis ossificans. Excision was necessary again in August, 1946, and for the first time the pathologic report was (?) osteogenic sarcoma.

In October, 1946, tissue removed for biopsy showed osteogenic sarcoma, sclerosing type, and an amputation of the right arm was performed.

This woman returned to the Tumor Clinic June 3, 1948, complaining of hoarseness, difficulty in swallowing and cough, and stated that she had had one hemorrhage from the throat or lungs. The blood pattern was now more definitely positive (3). X-ray examination of the chest revealed markedly increased markings involving both lung fields together with many small, dense bodies. These markings were old and consistent with pulmonary tuberculosis. At the right base was an area of increased density which appeared new and active; this was interpreted as pneumonitis.

She continued to complain of dyspnea and bloody sputum and was referred to Massachusetts General Hospital where after bronchoscopy and x-ray examination a diagnosis was made of multiple pulmonary metastases. The

TABLE I

GROUP OF 337 PATIENTS WITH A VARIETY OF BENIGN CONDITIONS

BLOOD PATTERN NEGATIVE IN EACH CASE	
Anemia, macrocytic	10
Aneurism, aortic	2
Appendicitis	4
Arthritis	7
Benign hypertrophy, prostate gland	5
Benign tumors	54
Bronchitis	8
Cardiospasm	5
Cervical and endometrial polyps	5
Cholecystitis	10
Cirrhosis of liver	2
Cystocele and rectocele	4
Diverticulosis	8
Duodenal ulcer	7
Eczema	20
Endocervicitis	23
Gastritis	6
Goiter	8
Hernia	6
Herpes zoster	2
Hypertension	15
Hypothyroidism	4
Keratosis	38
Lymphadenitis	6
Mastitis, chronic cystic	29
Metrorrhagia	5
Menopause	10
Osteitis deformans	4
Parotitis	4
Syphilis	1
Urethral calculi	2
Uterine fibroids	9
Uterine prolapse	4
Varicose ulcers	2
Visceroptosis	8
	337

TABLE II

DISCOVERED CASES OF CANCER

Site	Type	Positive Pattern	Negative Pattern	Total No. Cases
Femur	Osteogenic sarcoma	1	..	1
Humerus	Osteogenic sarcoma	1	..	1
Radius	Ewing's sarcoma	1	..	1
Mandible	Epidermoid carcinoma	1	..	1
Mandible	Osteogenic sarcoma	1	..	1
Ribs	Reticulum cell sarcoma	1	..	1
Breast	Adenocarcinoma.. 18 Medullary..... 8 Scirrhous... 10 Comedo..... 1 Intraductal..... 1	38	..	38
Ear	Basal cell carcinoma	1	..	1
Eye	Melanosarcoma	2	..	2
Face	Basal cell carcinoma	1	..	1
Lip	Squamous cell carcinoma	4	..	4
Tongue	Epidermoid carcinoma	2	..	2
Tongue	Adenocarcinoma	2	..	2
Skin	Epithelioma	10	..	10
Skin	Basal cell carcinoma	28	4	32
Skin	Squamous cell carcinoma	16	..	16
Skin	Melanoma	1	..	1
Cervical lymph node	Adenocarcinoma	1	..	1
Salivary gland	Adenocarcinoma	1	..	1
Parotid gland	Medullary carcinoma	2	..	2
Stomach	Adenocarcinoma	5	..	5
Cecum	Adenocarcinoma	1	..	1
Transverse colon	Adenocarcinoma	1	..	1
Sigmoid	Adenocarcinoma	1	..	1
Rectum	Adenocarcinoma	9	..	9
Liver	Adenocarcinoma	2	..	2
Pancreas	Adenocarcinoma	2	1	3
Kidney	Adenocarcinoma	2	..	2
Bladder	Papillary carcinoma	3	..	3
Prostate gland	Adenocarcinoma	6	..	6
Lung	Epidermoid carcinoma	2	1	3
Larynx	Epidermoid carcinoma	5	..	5
Cervix	Epidermoid carcinoma	21	1	22
Uterus	Adenocarcinoma	8	..	8
Ovary	Thecoma 1	...	..	...
	Dysgerminoma 1	2	..	2
Vagina	Mesodermal carcinoma	1	..	1
Vulva	Epidermoid carcinoma	1	..	1
Leukemia	.....	2	..	2
Hodgkin's disease	.....	1	..	1
Lymphoblastoma	.....	1	..	1
		191	7	198

patient failed steadily. The last blood pattern was taken February 12, 1949, and was a positive 4. She entered the Fall River General Hospital in March, 1949, and died May 20, 1949.

CASE II. E. M., a sixty-eight year old male, was seen at the Union Hospital Tumor Clinic June 19, 1947, complaining of vomiting, weakness and loss of weight. For several months he had had a considerable amount of gas and belching and vomited occasionally; he found that he got along better if he ate soft foods. There was no pain. His past history included a prostatectomy at the Truesdale Hospital in 1943 for benign hypertrophy of the prostate. In 1944 he was readmitted for hematuria. Cystoscopy revealed only cystitis. During 1944 he was given three blood transfusions and seemed to improve for a time. He was treated for cystitis but seemed to lose ground gradually and in the next three years his weight loss was from 190 to 152 pounds. When seen in July, 1947, he looked decidedly ill and his skin was flabby and dry. The blood pattern was a positive 4 and a diagnosis of cancer of the stomach was made. X-rays of the gastrointestinal tract and gallbladder were made. The stomach was normal in size and position with no evidence of deformity. Over a period of sixty-eight hours sluggishness of the barium flow was noted; otherwise the examination was negative. The gallbladder showed poor function but there was no evidence of stones.

The blood pattern repeated July 16, 1947, was strongly positive, but the examiners were unable to find any site of malignancy. Blood patterns taken August 7th, September 11th and September 15th did not change. When admitted to the hospital on this last date the patient was considered too weak to withstand an exploratory laparotomy. He died October 5th. Postmortem examination revealed carcinoma of the left kidney with pulmonary metastases.

CASE III. M. P., a sixty-four year old female, was first seen at the Tumor Clinic July 8, 1948. She stated that dilation and curettage with radium implantation was done June 12, 1947, for vaginal bleeding of five weeks' duration. The pathologic report was carcinoma of the cervix, grade III. She also had deep x-ray therapy, a total of 860 r. When examined August 14, 1947, the blood pattern was positive (3), although the cervix had completely healed and there was no vaginal bleeding, and clinically it seemed to be an excellent end result. Blood patterns on September 11th, October 9th and 25th and January 8, 1948, and April 8th were all positive. At the last examination the patient said that she had noted rectal bleeding for about two weeks. A barium enema on April 23rd showed no evidence of deformity. On June 15, 1948, the intestines were explored and a number of scybala were found along with a considerable number of adhesions, but no malignant lesion. In the face of the persisting positive blood pattern, operation was performed July 8, 1948, and a new growth was discovered on the anterior wall of the rectum high in the ampulla, which had eluded the sigmoidoscope. The pathologic diagnosis was adenocarcinoma of the rectum. The blood pattern remained positive until the death of the patient on December 31, 1948.

CASE IV. J. L., a seventy-eight year old male, was first seen at the Union Hospital Tumor Clinic September 1, 1948, having been referred because of an enlarged prostate gland. He stated that his gallbladder was removed in 1918 and he had since remained well until June, 1948, when he began to have episodes of vomiting and diarrhea and some rectal pain. Rectal examination on September 1st revealed a very large, soft prostate gland with no evidence of malignancy. The blood pattern was a positive 1. The patient was referred to the Genitourinary Clinic but discharged because all findings were otherwise negative.

Nothing further was done for this man until he again visited the Tumor Clinic April 14, 1949 for persistent diarrhea and pain in the right lower quadrant of the abdomen. The blood pattern by now was a positive 4. Physical examination disclosed a large mass in the right lower quadrant which proved to be carcinoma of the cecum. The tumor mass was removed with wide excision of the bowel. The pathologic report was adenocarcinoma of the cecum. This patient remained in the hospital until his death on May 23, 1949.

These cases eloquently illustrate the tragic consequences of failure to heed the warning of the positive blood pattern. The site of the lesion was not always where the past history would suggest and for this reason one must be very vigilant and weigh all the evidence at hand. Whitney[3] pre-

sents an excellent list of diagnostic aids to be thoroughly and systematically carried out and emphasizes the need of interpreting the cancer pattern along with the results of many other diagnostic aids such as laboratory tests, a thorough history, clinical findings and roentgenograms.

Girón[4] in 1943 reported that his results were 90.4 per cent correct in 150 cases. He noted that sex, menstruation, age, exercise, food and hour of taking the test had no effect on the blood pattern. Pregnancy was the one physiologic state which changed the pattern and offered confusion in the interpretation of the blood pattern, but these cases were easy to differentiate. After delivery the blood pattern reverts to negative.

Norman and Slicher[5] state that the early diagnosis of cancer in any of its stages is the most important factor in the fight against it, and that the need for a simple, inexpensive, universally applicable test is a desideratum. They report their experience with a test meeting these specifications which should be an integral part of routine examinations performed in offices of physicians and dentists, in hospitals, clinics and public health surveys.

Tests were made routinely on all patients during the past two years. During that time more than 350 patients were tested, and in each case from eight to ten drops of blood examined, giving a total of about 4,000 drops. Their results obtained from the Bolen slide technic with the available clinical data showed an average accuracy of 97 per cent. This result corroborated the findings of Bolen, Gruner and Girón.

CONCLUSION

1. Early diagnosis remains a crucial factor in the discovery and control of cancer.

2. In contrast with the complicated technic required by the majority of tests now proposed for the detection of cancer, the bedside or office test outlined herein is simple, inexpensive and extremely accurate. Very little training is necessary to take the sample of blood and evaluate the different patterns on the slides which can be filed away and will keep indefinitely.

3. If the sample of blood is properly taken and accurately read and weighed with clinical evidence and laboratory and x-ray reports, every doctor's office might well become a detection center for cancer.

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