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An Evaluation of the Bolen Test as a Screening Test for Malignancy*

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Bolen (2) in 1942 reported the blood droplet pattern as distinctive in cancer and proposed it as a valuable aid in the diagnosis of the disease. He found the test to be accurate in 91.4 per cent of all cancer patients studied. Giron (5) in 1943, using the method of Bolen, obtained similar results.

In our study the test was performed on 857 individuals. First, a preliminary study was performed on 195 healthy subjects and on 157 patients with histologically proved cancer, to familiarize us with features of the normal or negative and positive blood patterns.

Grossly, the normal pattern (Fig. 1) is a uniform, compact design with the central portion showing a dense, dark spot or nucleus. The pattern associated with cancer is different in most cases (Fig. 2). There is a breaking-down of the compact design near the mid-central part of the drop, and the central nucleus or spot becomes less distinct or completely absent. In advanced cancer, the appearance is that of a "dotted curtain" (Fig. 3).

Microscopically, the normal pattern (Fig. 4) reveals a well defined weblike fibrin meshwork extending over the entire drop. There are occasional leukocytes and normal appearing, tightly packed red cells with rouleau formation.

In cancer (Figs. 5 and 6), the fibrin meshwork is absent, and only small fibrin threads are seen. There are many small plasma lakes throughout the drop. The plasma lakes are clear, vary in size, and are devoid of erythrocytes. The red cells appear in clumps, are irregular in outline and shape, and rouleau formation is absent.

A normal or negative blood pattern was found in all 195 healthy individuals, and a positive pattern was found in 87 per cent of the 157 patients with a histologically proved cancer. No attempt was made to select the cancer patients as to site or extent of the disease (Table 1).

These findings are comparable to the results found in the literature (Table 2), except for a small

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series (25 patients) reported by us with Finnegan (4), in which a positive pattern was found in only 13 patients.

We then studied 505 successive new patients who entered the diagnostic and cancer-detection clinic at Firmin Desloge Hospital of St. Louis University from July, 1949, to October, 1949. This group included patients with a variety of diagnoses, and the test was performed and interpreted

TABLE 1
BLOOD PATTERN IN NORMAL AND CANCER PATIENTS

SUBJECTS	BLOOD PATTERN		TOTAL	PER CENT POSITIVE
	Positive	Negative		
Normal	0	195	195	0
Cancer (histologically proved)	140	17	157	87

TABLE 2
RESULTS REPORTED IN THE LITERATURE OF THE BLOOD PATTERN IN MALIGNANCY

Year	Author	No. cancer patients	Per cent positive pattern
1942	Bolen (2)	140	91
1943	Giron (5)	150	90
1943	Coltman (3)	35	97
1950	Inkley <i>et al.</i> (6)	100	88
1950	Finnegan <i>et al.</i> (4)	25	53
1950	Black and Speer (1)	100	80
1950	Present paper	157	87

on each patient without any knowledge of the clinical history or findings. The test was applied to this particular group as a screening test.

METHOD¹

The patient's fingertip is cleansed with ether or alcohol, allowed to dry, pricked with a lancet, and a free flow of blood obtained. Six or seven drops, varying in size and thickness, are collected on a slide by lightly touching the drop present on the fingertip, being careful not to touch the finger with the slide. This may interfere with the formation of the pattern. The slide is placed on a flat surface and allowed to stand until the drops are dry. The pattern formed in each drop is examined both

¹ As described by Bolen, in 1942, with a few minor variations.

macroscopically and microscopically at the examiner's convenience.

RESULTS

Analysis of the 505 clinic patients, studied without reference to the clinical findings, revealed 439 patients with a negative or normal blood pattern and 66 with a positive blood pattern (Table 3).

TABLE 3

RESULTS OF THE BOLEN TEST ON 505 SUCCESSIVE NEW PATIENTS FROM THE DIAGNOSTIC CLINIC*

Diagnoses (grouped)	Positive	Negative	Total patients
Pregnancy	36	46	82
Neoplasms			
Benign	0	9	9
Malignant	12	2	14
Heart disease	2	27	29
Ear, eye, nose, throat diseases	2	71	73
Gastro-intestinal disease (benign)	2	40	42
Dermatitis	2	12	14
Tuberculosis, pulmonary	1	6	7
Pelvic inflammatory disease	2	58	60
Arthritis (degenerative)	2	11	13
Syphilis	1	19	20
Genito-urinary disease	1	20	21
Neuro-psychiatric disease	1	22	23
Menopausal syndrome	1	9	10
Pulmonary disease (not tuberculosis or tumor)	1	19	20
Essential hypertension	0	10	10
Thyroid disease	0	12	12
Dietary deficiency	0	5	5
Arteriosclerosis (general)	0	28	28
Diabetes mellitus	0	3	3
No disease found	0	5	5
Skeletal diseases (fractures)	0	2	2
Peripheral vascular diseases	0	3	3
Totals	66	439	505

* Children 14 years of age and younger excluded from this study.

There were 14 malignant neoplasms found in these 505 patients. Twelve of the 14 patients showed a positive pattern, while the remaining 2 patients showed a negative pattern. One of the negative patterns was found in a case of far advanced adenocarcinoma of the breast and the other in a patient with bronchogenic carcinoma with metastases. The droplet pattern in subsequent examinations was constantly negative in these two cases. The remaining 54 patients with a positive blood pattern did not have cancer, and all except those pregnant were re-examined at regular intervals for 1 year after treatment. The blood pattern returned to normal in all but 1 patient (Table 4).

There were 2 false negative and 54 false positive tests found in this group of 505 patients.

DISCUSSION

The fourteen neoplasms found in the screening group are divided into two groups: those in patients having an obvious cancer and in those having a "hidden" cancer—that is, one which is not

readily identified by the common clinical examinations (Table 5).

In ten of the fourteen cases the clear-cut diagnosis of cancer was made without difficulty by the conventional clinical examination. The blood pattern was found to be positive in eight of these patients, who were shown to have the following lesions: squamous-cell carcinoma of the tongue with cervical metastases, adenocarcinoma of the stomach, squamous-cell carcinoma of the skin (4), squamous-cell carcinoma of the tongue, and adenocarcinoma of the rectum. The blood pattern was negative in two of these ten patients—one having an adenocarcinoma of the breast, with axillary and pulmonary metastases, and the other a far advanced bronchogenic carcinoma with cervical metastases.

A positive blood pattern was found in all four of the patients with neoplasms which were not readily detectable by the usual clinical diagnostic procedures. Thus, a persistently positive blood pat-

TABLE 4

RESULTS OF RE-EXAMINATION OF PATIENTS SHOWING FALSE POSITIVE BOLEN TEST, BEFORE AND AFTER TREATMENT

Diagnosis	First examination	Positive pattern after 4 months or more
Pregnancy	36	(Not followed)
Rheumatic heart disease	2	0
Pelvic inflammatory disease	2	0*
Acute appendicitis	1	0
Common duct obstruction	1	0
Dermatitis	2	0
Acute epididymitis	1	0
Pulmonary tuberculosis	2	0*
Neuro-psychiatry	2	0
Acute pan-sinusitis	2	0
Syphilis, tertiary	1	1
Arthritis (degenerative)	2	0
Totals	54	1

* Only one case re-examined.

TABLE 5

VALUE OF THE BOLEN TEST IN CANCER

NEOPLASM	No.	BOLEN TEST	
		Positive	Negative
Obvious cancer	10	8	2
"Hidden" cancer	4	4	0

There were 14 histologically proved cancers found in the 505 patients examined in the medical diagnostic and cancer detection clinics.

tern provoked further scrutiny in these cases to establish a diagnosis of cancer as will be shown in the following case presentations.

CASE 1

Carcinoma of the prostate gland.—J. R., a 68-year-old white man, entered the clinic August 23, 1949; the Bolen test was positive. He complained

of pain in his left eye. He was diagnosed and treated for a corneal ulcer. The repeat Bolen test was positive on September 10, 1949. Further examination revealed a large, nodular prostate gland, not thought malignant. August 18, 1950, he re-entered the hospital, complaining of nausea, vomiting, and epigastric pain. Physical examination revealed tenderness in the epigastrium and a hard nodular prostate. The pathological diagnosis of the prostate gland was adenocarcinoma. The gastric lesion is thought to be a benign ulcer and is still under observation. (#49-8093, F.D.H.)

Comment.—Because the Bolen test remained positive for a year, the diagnosis of carcinoma was suggested in this patient. He originally reported with a corneal ulcer and a nodular prostate which the urologist thought benign. After a year prostatectomy revealed carcinoma present in the prostate.

CASE 2

Bronchogenic carcinoma.—R. B., a 63-year-old white man, entered the clinic July 15, 1949; the Bolen test was positive. He complained of chest pain, cough, 10 pounds' weight loss, and gave a history of tuberculosis. Physical and roentgenologic examinations resulted in a diagnosis of tuberculosis. On August 23, 1949, the Bolen test was positive. He was admitted to a sanatorium for treatment. A diagnosis of tuberculosis was not confirmed, and after exhaustive diagnostic studies, an exploratory thoracotomy was suggested. The Bolen test remained positive upon repeated examinations.

On November 12, 1949, a right pneumonectomy was performed, with an operative diagnosis of chronic abscess of right lung. The pathological report was bronchiectasis, chronic bronchitis, peribronchitis, lung abscess, and organized pneumonia. No carcinoma was seen. The post-operative course was complicated by a broncho-pleural fistula, which closed spontaneously, and the patient was discharged from the hospital January 21, 1950, greatly improved.

He was re-admitted to the hospital August 7, 1950, extremely ill with nodules in the pneumonectomy scar. Biopsy showed these to be metastatic carcinoma. He died September 26, 1950. At autopsy, bronchogenic carcinoma was found, involving the right bronchial stump, with widespread metastasis. (#49-5175, F.D.H.) Unfortunately, the surgical specimen was misplaced during the interim. Therefore, one cannot be sure whether this lesion was present in the specimen and overlooked or left behind in the right bronchial stump.

Comment.—Again, a Bolen test, positive for a

year, pointed correctly to the diagnosis of carcinoma, despite clinical evidence to the contrary. Admitted as a tuberculosis suspect, the right lung of the patient was removed after 3 months for abscess, and no carcinoma found histologically—only abscess and bronchiectasis. However, after 9 months carcinoma became clinically apparent because of nodules beneath the scar of pneumonectomy, and the diagnosis was ultimately confirmed by necropsy.

CASE 3

Bronchogenic carcinoma.—E. T., a 68-year-old white woman, entered the clinic October 3, 1949; the Bolen test was positive. She complained of constant coughing, pain in the right chest, and gave a history of having been treated for pneumonia 6 weeks previously. A diagnosis of inflammatory disease of the right lung with right pleural effusion was made, and the patient was admitted to the hospital. A repeat Bolen test was positive October 10, 1949. Examination of the pleural fluid revealed malignant cells, and a bronchial biopsy confirmed the diagnosis of bronchogenic carcinoma. The Bolen test was positive on last follow-up, December 17, 1949. (#49-9702, F.D.H.)

Comment.—Here, in another patient with lung cancer, the Bolen test was positive upon admission, and the clinical diagnosis was lung abscess or unresolved pneumonia. Thoracentesis yielded fluid with cells, histologically malignant upon centrifugation.

CASE 4

Carcinoma of the left breast (male).—C. S., a 59-year-old white man, entered the clinic July 21, 1949; the Bolen test was positive. He complained of headache and a small mass just beneath the skin in the left temporal region. Roentgenologic and physical examination revealed no positive diagnosis. The Bolen test was positive again August 20, 1949. He was admitted to the hospital, and the mass was removed from the head. A diagnosis of metastatic carcinoma was made. Exhaustive tests and examinations failed to reveal the primary lesion. He died September 26, 1949, and at autopsy a very small, deep-seated, primary lesion was found in the left breast, and a diagnosis of adenocarcinoma of the breast with metastasis was made. (#49-6319, F.D.H.)

Comment.—A suspicion that the subcutaneous mass in the temporal region might be carcinoma was aroused, in this patient, by a positive Bolen test, and clinical study during the ensuing month yielded no positive data. Upon removal, the mass was then proved to be carcinoma. The primary site remained undiscovered until necropsy, when a

hidden carcinoma, primary in the (male) breast, was found.

All but 2 of the 14 patients were treated either surgically or with radium. The blood pattern returned to normal the fourth month post-operatively in a surgically treated adenocarcinoma of the rectum and has been negative upon subsequent examinations. The remainder of the treated cases continued to show a positive blood pattern.

The 54 patients showing a false positive blood pattern were re-examined and grouped as those obviously not having cancer and those suspected of having cancer (see Table 6). Thirty-six patients, all those pregnant, were not followed. Thus, of the remaining 18 patients with a false positive test, only one failed to show a normal pattern after treatment had been instituted. This was a 43-year-old white male (E. G., #49-9693, F.D.H.) complaining of pain and swelling in the right knee. There was a history of syphilis. Physical examination revealed swelling of the right knee and bloody effusion. The Bolen test was positive upon admission and at all the subsequent examinations for the past year. Exhaustive examinations including a biopsy of the right knee joint capsule failed to reveal any evidence of malignancy. To date, this case remains a false positive, and a diagnosis of tertiary syphilis with Charcot's disease stands.

The occurrence of the positive blood pattern is interpreted as a "clue" and should encourage the physician to perform exhaustive studies to exclude or prove the presence of cancer. A normal blood pattern does not exclude the possibility of cancer and should be ignored especially when there are clinical manifestations suggestive of malignancy.

SUMMARY

We have screened 505 patients for malignancy by the Bolen test. There were 66 positive tests, of which 12 were substantiated by histologic evidence of malignant neoplasm, while 54 appear to be false positives. With one exception, all the false positive tests subsequently reverted to negative.

There were 14 histologically proved cancers in the entire group of 505 patients. Two of these tumors gave repeated negative reactions to the Bolen test.

We may conclude that a negative Bolen test does not exclude the diagnosis of cancer. Nor does a positive test necessarily indicate the presence of cancer. However, a positive test should be followed by intense diagnostic effort before the diagnosis of malignant neoplasm is abandoned.

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TABLE 6

"FALSE POSITIVE" BOLEN TESTS AFTER TREATMENT AND ONE-YEAR FOLLOW-UP

NEOPLASM	No.	BOLEN TEST	
		Positive	Negative
Obviously not cancer	36 pregnancy	(Not followed)	
	17 inflammatory disease	0	15*
Suspected cancer	1	1	0

* Two lost to follow-up.

There were 54 false positive tests in 491 noncancer patients upon admission to the clinic.

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FIG. 1.—Normal blood pattern. Mag. $\times 5$.

FIG. 2.—Blood pattern in early cancer. Mag. $\times 5$.

FIG. 3.—Blood pattern in advanced cancer. Mag. $\times 5$.

FIG. 4.—Microscopic view of the normal pattern taken from the central area of the drop. Mag. $\times 100$.

FIGS. 5 and 6.—Microscopic appearance of the blood pattern in cancer as found in the central area of the drop. Mag. $\times 100$.

