AN INVESTIGATION OF THE EFFECTS OF URINE EXTRACTS FROM CANCER PATIENTS ON RAT GONADS AND SPLEEN

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CHAPTER I

DEFINITION AND PROBLEMS INVOLVED IN THE INVESTIGATION OF CANCER TESTS

Any laboratory procedure carried out on a person to determine the presence or absence of a malignant tumour can be called a cancer test. These procedures vary greatly in technique, from the simple skin reactions and dye tests, to the more complex bioassays and polarographic analysis. Most are carried out on the serum and urine, a few on the skin. The most commonly used method is the conventional biopsy. As the value of early diagnosis of cancer became more apparent, tests to supplement or replace biopsy have been sought from many different approaches. For malignant tumours in inaccessible regions, a reaction for cancer comparable to the Wassermann test for syphilis, or the Aschheim-Zondek test for pregnancy would be highly desirable. To be of general use such a test should have an accuracy approaching that obtained in biopsy examination and should be capable of duplication in different centres.

It soon becomes evident on reviewing published reports on cancer tests that an accurate assessment of the relative value of the different procedures is difficult. With any given procedure the reported degree of accuracy varies from fifty to one hundred per cent, so that one cannot accept the figures directly; obviously one of the investigators is reporting incorrect results. If one were to set down rigid criteria to be followed in the investigation of a cancer test,

and exclude all reports that do not meet these criteria, there would be few reports with which to deal. Since the figures derived from these reports are of limited value, they have not been included individually in the review of the literature here. The chief value of the review is to form a background for a better understanding of "new" cancer tests that appear in the literature yearly; most have a very familiar ring.

There are certain fundamental criteria to be used in the investigation of cancer tests. If these requirements have not been fulfilled by the investigation, the value of the report is questionable. Many reports give the positive results obtained with a particular test in patients "with cancer." It is often not stated how the diagnosis of cancer was established, and one must conclude that it is by clinical examination only. Clinicians engaged in the diagnosis of malignant tumours have a fairly wide margin of error, and a very strong suspicion of cancer in a patient may be wrong. On the other hand the embarrassment of a clinically unsuspected malignant tumour appearing at autopsy happens only too frequently.

Few reports give any indication of the general clinical status of the patient. There is no doubt that changes in the urine and serum occur in terminal cachectic stages of malignant neoplasms, but it is no tribute to any reaction which will give one hundred per cent positive results in the final stages of the disease only. Furthermore these changes are well established and better followed by standard quantitative biochemical procedures, i.e., fractionation of serum

proteins.

Many tests are designated by the originator's name, and the procedure should not be modified if it is to be a critical evaluation of that test. One can however, compare the results obtained with a certain test and the results obtained with a modification of that test. It is probable that most reports are actually on modifications of the original test. This, together with errors in technique may explain some of the varied results obtained.

Over enthusiasm must play some part in the good results reported. An example of this is the isolation of fungi from sputum as proof of cancer. Excellent results were reported on a small series of patients with this test initially; the results may very well be true but the incidence of fungi in sputum in the terminal states of any disease must also be assessed. Results such as these promote a very critical approach to any other reactions claiming a high per centage of accuracy unless the basic criteria are fulfilled.

Essential technical data must be given if one is to judge the validity of an author's claims.

Criteria to be used in the investigation include first a definite diagnosis. This must be based on microscopic examination of tissue removed by biopsy. Most tests will be done on patients with well established disease, and a few with early localized lesions. In this manner evaluation of the test for early cancer will also be revealed.

The clinical status of the patient must be considered and the

control series be comparable to the series of cancer patients. The selection of the control series poses a problem as great as the selection of cancer patients. One is dealing usually with an age group in which cancer is prevalent and despite the exclusion of cancer by the best means possible, it is probable that some are harbouring an "occult" neoplasm. Follow up on these cases is important, and a post mortem carried out on those that die. The control cases should of course be the same sex as the cancer patients.

For special types of procedures special precautions are necessary. Most difficult are probably the bioassays as they are subject to so many variables and these must be reduced to a minimum. A relatively large number of test animals with controls in each test and a relatively large series of tests should be used. The control series must be carefully selected and placed under similar conditions of stress particularly when one is using body and organ weights[91]. Thus each special type of procedure is subject to inherent errors and unless one knows the procedure used to control these errors it is difficult to assess the results.

CHAPTER II

REVIEW OF THE LITERATURE

It is impractical to include here a summary of all reports that are to be found in the literature dealing with cancer tests. By far the greatest amount of work has been done in countries other than the United States of America and Canada; much work has been done in Germany, France, Italy and Argentina. These reports have been summarized in the American literature and this has served as the main source of material for this review. Since 1940, however, tests of this nature are to be found not infrequently in the American literature and by American and Canadian investigators. These have been for the most part dye tests and tests dependent on the postulated presence of a substance in the serum or urine of patients with cancer that is specific for that disease.

Cancer tests are of many different types and will be classified for the purpose of this review into five groups:

1. Biochemical
2. Bacteriological
3. Endocrinological
4. Physical
5. Miscellaneous

It is difficult to classify some tests into any one group as the underlying mechanism of the test is not clear. Such tests are placed in the miscellaneous group. Needless to say there is some

overlapping, as some procedures could be placed in either of two groups. This applies particularly to the antigen-antibody and the precipitation and flocculation reactions.

I. BIOCHEMICAL PROCEDURES

The group of tests classed as biochemical include:

1. Analysis of serum and urine for variations in organic and inorganic constituents.
2. Semi-empiric dye tests, some depending on oxidation-reduction reactions.
3. Precipitation and coagulation procedures, most depending on alterations in plasma proteins.
4. Tests dependent on enzyme action.

Analysis of the blood of patients with cancer has revealed:

1. Alterations in the absorption spectrum[18, 29].
2. Elevated iodine number on ether extracts[55].
3. Acceleration of rates of glycolysis by addition of carotin[98, 110, 111].
4. Decrease in cholesterol content[15, 21, 38, 96, 103].
5. Elevated fibrinogen levels[65].
6. Increase in amid nitrogen content of plasma proteins[6, 70, 71].
7. Increase in d-peptidase activity[1, 11, 52, 68].
8. Increase in protease nitrogen[112].
9. Increase in erythrocyte glutathione[88].
10. Decrease in magnesium[8, 64], phosphorus[67], and calcium[30].

11. Increase in potassium content of erythrocytes[23, 27].

12. Variations in potassium-calcium ratio[83].

13. Hypoproteinemia and alterations in protein fractions[6, 17, 77, 90].

14. A state of alkalosis[46, 89].

15. Absence of bile salts in the serum of cancer patients[2].

Urine analysis has revealed an elevation in cholesterol content[96] and imidazole bodies in cancer patients[94].

There is no doubt that these alterations and probably many others may occur at some stage in the malignant disease. These changes are now considered to be the result of the disease process and are non-specific, occurring in the terminal stages of many chronic diseases. They are probably best interpreted in the light of the most commonly observed variation, that of plasma proteins. Frequently there is a marked decrease in the total protein in the late stages of cancer due most likely to nutritional deficiencies. Usually the fractions are depressed uniformly, but with metastatic lesions in the liver the albumin may be decreased considerably more than the globulin with an alteration in the ratio. Some malignant diseases, such as multiple myeloma, are associated with an increase in total protein due to marked increase in the globulin. Proteins are affected in so many diseases other than cancer, particularly in abnormal nutritional states and renal disease, that their estimation as an aid in the diagnosis of cancer is of no value.

Dye tests utilizing methylene blue[99], brilliant cresyl blue, and cresyl violet[14] are based on changes in the reducing power of

plasma. The reducing groups are in the protein fractions, probably albumin. Roffo's neutral red reaction depends on an increase in the serum lipoids of patients with cancer and has been used more extensively than any of the other dye tests[72, 23, 16]. To point out the simplicity of this type of reaction the technique is as follows: blood collected from the patient is stored under oil at 20° C for twenty-four hours, to 1 ml. of this serum is added 0.26 ml. of an 0.001 per cent solution of neutral red; the development of a red colour is a positive reaction which is claimed to indicate that the patient harbours a malignant neoplasm.

Flocculation, precipitation, and coagulation reactions vary greatly in technique, but are all, probably, dependent on alterations in protein, or on the presence of an abnormal protein. Examples of this type of reaction include Botelho's[56, 42], the Kahn albumen A[92, 93], Bendien's[36, 85, 66], Lederer's[115], Weiss coagulo-flocculation[60], Kopaczewski's[61, 41, 47], Weltmann's[107, 24], and innumerable modifications of each of these. Some are fairly complex; others, such as Kopaczewski's, are quite simple and have been used extensively. In this procedure 2 ml. of serum are mixed with 2 ml. of lactic acid and the time is observed for coagulation to occur. Coagulation in less than eight hours is taken to indicate carcinoma. Weltmann's serum coagulation reaction is a well known test and is used in Europe much the same as the sedimentation rate is used on this continent. A shift to the left in the reactions suggests cancer, but this effect occurs also in such conditions as lobar pneumonia and

nephrosis.

Procedures dependent on enzyme action include Fuch's[113, 58, 84], Abderhalden's[109], and Robertson's[81]. Of all the older cancer tests encountered, Fuch's reaction has been subject to the least amount of adverse criticism. However, some contradictory results have been obtained, that of Panton being the most convincing[76]. This reaction depends on the proteolization of blood fibrin of normal people by serum from cancer patients. Normal serum does not digest fibrin from normal patients. There have been numerous modifications of the test, none adding anything to its accuracy.

Abderhalden's and the test used by Robertson are carried out with urine or blood, and depend also on the presence of a proteolytic enzyme.

II. BACTERIOLOGICAL PROCEDURES

This group of tests include those procedures utilizing bacteria and antigen-antibody reactions. Some of these depend on complement fixing antibodies; in others the demonstration of antibodies is carried out as a skin test.

Some of the initial cancer tests were bacteriological in nature and many now seem entirely unrelated to a neoplastic process. The recovery of fungi from the saliva was at one time considered to be specific for cancer[22]. Other procedures claiming to reveal the presence of cancer include:

1. The agglutination of Bacillus proteus OX K by cancer patient's serum[75].
2. A skin reaction following the injection of a suspension of killed organisms recovered from papillomas of cattle[3].
3. Decreased bactericidal power of cancer patient's serum against coliform bacilli and staphylococci[100].
4. The isolation of an abnormal strain of E coli from feces. (indication of cancer predisposition[63])

Such a group of tests stimulate a skepticism which influences one's views on all cancer tests, because results are reported from these as good as any of our best diagnostic procedures.

Many tests are based on the principle that a malignant tumour stimulates the development of antibodies in the host. Usually an alcoholic extract of tumour tissue is used as antigen; cholesterol is added to increase the sensitivity. There are as many ways of mixing this with the serum as there are procedures for doing serological tests for syphilitic antibodies. The most commonly used test of this type is the Lehmann-Fascius reaction[109, 80, 26]. A positive result is denoted by the formation of a fine precipitate.

Some authors believe that complement fixing antibodies develop earlier than agglutinins and precipitins, and have devised procedures to test for these complement fixing antibodies[4]. Most methods employ an hemolytic system as indicator, and resemble the procedure for a Wassermann test. Hirszfeld's reaction is the most commonly used complement fixation test for cancer[74, 50].

The Klein test depends upon the destruction of tumour cells by normal serum and not by serum from patients with cancer[31, 39, 95, 49, 44]. In normal serum this lytic action is presumed to be the result of an antibody-like substance, which has been neutralized in patients with a malignant disease.

Skin tests have been popular because of their simplicity compared with the in vitro demonstration of antibodies. Different methods of making up the antigen constitute the basis for the different reactions. The Freund-Kaminer skin test is the most commonly used of the group[25, 62, 78]. The antigen in this case is made up from the gastric juice of cancer patients, the supposition being that it contains a specific fatty acid found only in persons harbouring cancer. The gastric juice is prepared as an emulsion in sodium bicarbonate and 0.1 ml. is injected intradermally for the test. In cancer patients a nodule is anticipated at the injection site after forty-eight hours and remains for two to three weeks.

III. ENDOCRINOLOGICAL PROCEDURES

Endocrinological procedures have been used extensively and are rather complicated, using animals for the assay of endocrine and related substances. The Aschheim-Zondek test for testicular neoplasms has proven its value beyond all doubt[104]. Attempts to extend its usefulness into the field of general cancer have for the most part been unsuccessful[35]. The Aschheim-Zondek test for testicular neoplasms is based upon the production of gonadotropic

hormone by the cells of the neoplasm. These cells are potentially totipotent, and are capable of producing a substance normally produced only by placental tissue.

Cancer tests developed from this are based either on alterated excretion of a hormone already present in the body, or appearance of some new related substance, usually of steroid composition. Rabbits and rats have most commonly been used for the assay. Urinary extracts from cancer patients have been reported to contain:

1. Excess prolan B[48].
2. Abortifacient substances[102, 32].
3. A necrosin of adrenals[13, 86].
4. A substance causing follicular dilatation of ovaries of immature rabbits.
5. A substance producing a melanocyte reaction in frogs[105].
6. Anti-gonadotropic substances[106].
7. A substance designated as steroid E, found only in the urine of cancer patients has been reported by Roffo[82]. Shortly after this Beard independently reported the presence of a substance which he designated as steroid X in the urine of cancer patients[9]. These two substances are demonstrated in the urine by means of bioassays. The published results to date on these two procedures have been favourable. Roffo reported 1000 cases of cancer with positive results in all and Beard 40 cases of cancer with 39 positive results. An investigation of the procedure described by Beard constitutes the subject of this thesis.

IV. PHYSICAL PROCEDURES

Tests using physical methods are, in some cases at least, based on chemical or endocrine alterations, and these changes are detected by physical means. Examples include:

1. Low blood pressure with an increase following the successful removal of the neoplasm[33, 34].
2. Elevated B.M.R. with a decrease following the successful removal of the neoplasm[57].
3. The polarization microscope used by Boch to determine the distribution of "points of light" in blood smears[43]. A particular distribution indicated not only the presence of a malignant tumour, but the organ involved.
4. Use of the darkfield microscope[37]. In the darkfield examination of serum from normal people yellow glistening points with Brownian movement are seen, measuring up to 1 micron in diameter. In serum from cancer patients these points measure up to 4 microns in diameter.
5. Polarographic examination of serum[19, 20, 12]. In this procedure sulphydryl groups of serum proteins are acted upon by iodoacetate in alkaline solution and the denatured product subjected to polarographic examination. The protein effect consists of an abnormal wave in the current voltage curve and is less prominent in serum from cancer patients than in normal serum. Here again we have a test dependent to some extent on alterations in serum

proteins. Whether by this more involved procedure something is added to render the change sufficiently specific and sensitive is doubtful.

V. MISCELLANEOUS PROCEDURES

This group includes a number of procedures having no relation to one another and no relation to any of the previous groups. The Moppett test is a relatively recent one, and is entirely different from any of the procedures described above[101]. Normal blood is placed on one side of a diffusion vessel and blood from a person to be tested for cancer is placed on the other side. Chick embryo cells placed in the centre of the chamber diffuse toward the normal blood and away from the blood to be tested if that blood is from a patient having a malignant neoplasm. The Citelli-Piazza reaction depends on the production of anaphylactic shock and leukopenia in patients with cancer when injected subcutaneously with a fresh emulsion of tumour tissue[27, 40]. Other procedures that may be mentioned here include the Widal hemoclastic index[73], the triad of Ascoli[10], the Velez hematological index[87] and the Reid-Hunt reaction[97].

The erythrocyte sedimentation rate has been used extensively as a cancer test, with varied views as to its value; modifications have added nothing to its accuracy[5, 69, 59, 114]. Its widespread use in medicine has aided in a better understanding of the test and in the interpretation of results than is found with any other procedure. The reaction depends on an alteration in the alpha

globulin fraction of serum proteins.

It is well known that elevated sedimentation rates occur in many conditions other than cancer. It is also well known that many cancer patients die without ever having had an elevated sedimentation rate[53]. In some patients with cancer the elevation of the sedimentation rate occurs late in the disease[51]. These are all important factors that reduce the value of the test.

A sufficient number of people with cancer show an elevated sedimentation rate for the test to be regarded as an aid in the differential diagnosis of cancer. Although subject to error it is also regarded as of some value in prognosis following the removal of malignant tumours when an elevation due to other factors can be reasonably excluded. Persons with a negative history and physical examination but a persistently elevated erythrocyte sedimentation rate should be investigated further. This is possibly the chief value of the procedure as an aid in cancer diagnosis.

VI. OBSERVATIONS ON THIS REVIEW

It is impossible to make a completely satisfactory concise statement regarding the value of cancer tests. One can say definitely that none of the above procedures are as specific for cancer as is the conventional biopsy; however, very few laboratory procedures are as accurate as this although there are circumstances such as internal tumours where others may be useful. In any test with a high degree of sensitivity one usually finds some lack of

specificity and with a high degree of specificity one finds lack of sensitivity.

One person may demand a cancer test as sensitive and as specific for cancer as the Wassermann test for secondary syphilis. Another person may consider this accuracy desirable but not mandatory and deems a procedure that aids even slightly in the diagnosis of cancer as worthy of further use.

Different workers using the same tests report accuracies ranging from fifty to one hundred per cent. Although these figures are of little value in assessing the various procedures, one can probably conclude that the procedures are reproducible only with difficulty in different laboratories. This is significant when one realizes the many useful laboratory procedures that have been initiated in one laboratory and are readily reproducible in many others.

Laboratory procedures of undoubted aid in the diagnosis of cancer are the biopsy and the Aschheim-Zondek test. The disadvantages of the biopsy are its lack of sensitivity and even its specificity is not one hundred per cent in all cases. The Aschheim-Zondek has a very limited use, being confined to neoplasms of the testicle.

Tests that may be of use as screening procedures include the sedimentation rate, the methylene blue reduction test and electrophoretic analysis of serum[90]. One of the main attributes of the erythrocyte sedimentation rate is that results are usually properly

interpreted and its limitations are well known. It is of some value as a screen test. It seems doubtful if the results with the methylene blue test and electrophoretic analysis warrant their use in place of the sedimentation rate[77].

Investigations of cancer tests of this nature should be encouraged, but their use in practice must be controlled until their value and interpretation are well established. Two recent publications serve to emphasize this. Huggins observed the deficient coagulative ability of cancer serum as measured by iodoacetate and found it useful as a diagnostic instrument but not specific for cancer[54]. Commercial laboratories however, are advertising standardized reagents for carrying out the iodoacetate acid index as a diagnostic test for cancer. There is no doubt that the wide use of this test would result in many errors in diagnosis.

The second publication is in the Journal of the American Medical Association, in the report of the Council on Pharmacy and Chemistry[28]. This deals primarily with therapeutic agents, but the Beard test for cancer is also described in the reproduction of an advertisement. This reproduction is as follows:

CANCER

Is CANCER in any part of your body?
BREAST, LUNG, STOMACH, KIDNEY, LIVER, CHEST,
NECK, THROAT, HEAD, LIMBS, or
INTERNAL ORGANS?

A Labatory URINE TEST will show.

Labatory Analysis is done by the following Doctors

Howard H. Beard, Ph.D.
Albert B. Katz, Ph.D.
C. N. Wylie, Ph.D.

This new method is less painfull than a Surgeon's Knife.

CANCER in the early stage can be cured
with CHYMOTRYPSIN
and shall be administrated by your PHYSICIAN.

Urine-tests are by appointment only.
Hours 2-3 p.m. Except Saturday and Sunday.
CANCER - - DIVISION
OF

MASSACHUSETTS SPEECH CLINIC
16 CENTRAL AVENUE
SUITE 419
Lynn, MASS.

Information received by the Council by way of inquiries indicated that the test is publicized on a commercial basis for a fee of two hundred dollars per person. Much more serious than the financial loss to the individual is the delay in diagnosis of malignant tumours.

CHAPTER III

MATERIALS AND METHODS

The materials and methods used were based on a cancer test published in 1947 by Beard[9] depending on the enlargement of spleen and/or gonads of rats following intra-peritoneal injection of extracts from urine of cancer patients. A similar test was reported in 1944 by Roffo[82] on a larger series with equally good results.

At the beginning of the project various modifications, particularly in the extraction, concentration and routes of administration were tried with no significant differences being noted between the organs of the control and the test animals. Following this it was decided to adhere to the method as described by the original author except that the control series of animals be injected with extracts of urine from non-cancer patients.

Twenty-four tests were carried out, each test including a cancer patient and a non-cancer patient as control. All cancer patients had the diagnosis confirmed by biopsy and histological examination; the malignant tumours were of varying types, but were all extragenital. The patients serving as controls were selected as close to the age of the cancer patients as possible and in a similar general physical condition. The possibility of an occult cancer in a few of these cannot be completely excluded, although this possibility was considered in the selection of each case.

Bottles of the Winchester type containing 50 ml. of 95% ethyl

alcohol (Canadian Industrial Alcohol Ltd.), marked at the 850 ml. level, with attached written instructions for the urine collection, were left in the patient's room. The bottles were returned to the laboratory when the specified level was reached. Paired samples (one from a cancer patient and one from a control) were placed in identical all glass extractors of the Koch type (No. 6840 - Ace Glass Co., Vineland, N. J., U. S. A.). Ether (Merck) was added to each sample in the main flask of the apparatus until the level of the side arm was reached. One hundred and fifty ml. each of ether and alcohol were placed in the side flask, which was connected to the side arm and heated at a temperature just sufficient to yield a slow steady drip from the condenser. The ether-alcohol mixture in the side flask was removed at the end of the second day, fresh ether and alcohol placed in the flask and the extraction continued for another two days. This ether-alcohol mixture was added to that previously removed and then concentrated.

The concentration was carried out under reduced pressure in a constant temperature bath just below 50° C., the volume being reduced to 2 ml. The concentrate showed no bacteria on direct films or culture. It was then diluted with normal saline so that 1 ml. was the equivalent of 50 ml. of the original urine. Six selected rats were each injected intraperitoneally with 2 ml. of the neutralized extract from the cancer patient and six comparable animals were injected with the extract from the non-cancer patient.

Two strains of albino rats were used; the strain developed in

the Department of Biochemistry, University of Manitoba, and animals obtained from the Carworth Farms Inc., New City, Rockland County, N. Y., U. S. A. The two strains of rats showed comparable results in separate series. Male rats weighing from 90 to 100 gm. were used for eighteen of the series; females of the same weight for six. The early experiments showed a variation of 10 to 15 gm. in the weight of the gastro-intestinal contents. Therefore the animals were starved for sixteen hours and the initial body weight was taken just prior to the injection.

Illuminating gas was used to kill the animals in the first twelve tests, pentothal sodium for the last twelve. All animals were killed forty-eight hours after injection, the liver, spleen and gonads were removed immediately and weighed on an analytical balance. The condition of the uterus and oviducts was observed in the female animals. In the last twelve tests the epididymis was removed with the testicle and weighed separately. These organs were then incised, immersed in ten per cent formalin and microsections made for histological examination.

A synopsis of cases used is presented in Table I and includes experiment number, patient's initials, hospital number, age, and diagnosis. The number preceding the diagnosis refers to the Winnipeg General Hospital Surgical Pathology report number. The last two digits indicate the year; most are for 1948. In a few cases the patient died some time after the cancer test was done and in these the autopsy number is given with the diagnosis.

TABLE I

PRESENTATION OF CASES

Ca - Cancer
Co - Control

Exp. No.	Name	Hosp. No.	Age	Diagnosis
57 Co	Mr.J.F.	A1540	61	Hypertensive cardiovascular disease.
57 Ca	Mr.P.S.	A1238	62	Chronic lymphatic leukemia, Hematology - W.G.H.
58 Co	Mr.A.C.	A797	72	Surg.Path. No. 404/48 - Fistula between two segments of colon.
58 Ca	Mr.W.G.	A2422	71	Autopsy No. 6734 - Infiltrating epidermoid carcinoma of esophagus grade 3.
59 Co	Mr.C.A.	A2119	72	Surg.Path. No. 966/48 - Benign prostatic hypertrophy.
59 Ca	Mr.J.F.	A1840	82	Surg.Path. No. 343/48 - Infiltrating adenocarcinoma of rectum grade 2.
61 Co	Mrs.M.S.	A1462	35	Surg.Path. No. 588/48 - Caseating renal tuberculosis.
61 Ca	Mrs.S.F.	A2215	35	Surg.Path. No. 3434/40 - Malignant melanoma, skin of cheek. 1948 - metastatic to liver.
62 Co	Mr.W.A.	A1734	52	Rheumatic heart disease. Mitral stenosis and calcification.
62 Ca	Mr.W.W.	A2682	57	Surg.Path. No. 4723/47 - Infiltrating adenoid cystic carcinoma of bronchus.
66 Co	Mr.D.P.	A2434	56	Electrical burns of both feet.

TABLE I

PRESENTATION OF CASES

Ca - Cancer
Co - Control

Exp. No.	Name	Hosp. No.	Age	Diagnosis
66 Ca	Mr.J.Y.	A4057	51	Surg.Path. No. 1107/48 - Biopsy of pelvic peritoneum - metastatic adenocarcinoma, primary stomach.
67 Co	Mr.M.P.	A3031	70	Surg.Path. No. 2041/48 - Benign prostatic hypertrophy.
67 Ca	Mr.T.N.	A2127	68	Surg.Path. No. 714/48 - Infiltrating epidermoid carcinoma of bladder.
68 Co	Mr.C.S.	A2635	79	Bronchial asthma, emphysema.
68 Ca	Mr.W.C.S.	A2896	73	Surg.Path. No. 1248/48 - Adenocarcinoma of rectum.
69 Co	Mr.A.C.	A797	72	Surg.Path. No. 404/48 - Fistula between two segments of colon.
69 Ca	Mr.O.K.	A5012	72	March 20/48 - Gastric secretions - adenocarcinoma. April 9/48 - operation - metastatic to liver.
70 Co	Mr.C.B.	A3455	77	Duodenal ulcer, general arterio-sclerosis.
70 Ca	Mr.W.B.	A3679	71	Surg.Path. No. 1416/48 - Infiltrating adenocarcinoma grade 2 of rectum.
71 Co	Mrs.R.K.	A2840	69	Surg.Path. No. 527/48 - Varicose ulcer of leg.
71 Ca	Mrs.C.J.	A3012	76	Autopsy No. 6988 - Infiltrating adenocarcinoma of colon grade 3.

TABLE I

PRESENTATION OF CASES

Ca - Cancer
Co - Control

Exp. No.	Name	Hosp. No.	Age	Diagnosis
72 Co	Mr.J.H.	A3078	69	Surg.Path. No. 1290/48 - Chronic cholecystitis, with cholelithiasis.
72 Ca	Mr.J.F.	A3607	69	Surg.Path. No. 1425/48 - Metastatic adenocarcinoma grade 2, consistent with stomach origin.
73 Co	Mr.D.P.	A2434	56	Electrical burns of both feet.
73 Ca	Mr.O.W.	A3880	55	Surg.Path. No. 5281/47 - Liposarcoma of buttock.
80 Co	Mr.A.L.	A6092	56	Congestive heart failure. Left bundle branch block and left hemiplegia.
80 Ca	Mr.E.Z.	A5689	57	Surg.Path. No. 1894/48 - Infiltrating epidermoid carcinoma of bronchus grade 2.
81 Co	Mr.D.P.	A2434	56	Electrical burns of both feet.
81 Ca	Mr.H.A.	A6014	53	Surg.Path. No. 2330/48 - Infiltrating epidermoid carcinoma of urinary bladder grade 3.
82 Co	Mr.W.C.	A4851	64	Autopsy No. 6760 - Coronary occlusion, myocardial infarction.
82 Ca	Mr.R.M.	A5874	60	Multiple myeloma, Hematology - W.G.H.
83 Co	Mrs.H.McM.	A6481	80	Arteriosclerotic ulcer of left foot.
83 Ca	Mrs.E.R.	A5947	81	Surg.Path. No. 2270/48 - Infiltrating adenocarcinoma of rectum grade 2.

TABLE I

PRESENTATION OF CASES

Ca - Cancer
Co - Control

Exp. No.	Name	Hosp. No.	Age	Diagnosis
84 Co	Mr.E.M.	A6813	46	Fracture of left fibula.
84 Ca	Mr.F.W.	A6613	47	Surg.Path. No. 2745/48 - Spindle cell epidermoid carcinoma of face.
85 Co	Mr.J.V.	A7036	71	Bilateral inguinal hernial repair.
85 Ca	Mr.J.C.	A6878	67	Surg.Path. No. 2759/48 - Omental biopsy - metastatic carcinoma.
86 Co	Mrs.E.D.	A6871	50	Chronic bronchial asthma.
86 Ca	Mrs.A.R.	A7244	50	Surg.Path. No. 751/44 - Infiltrating duct carcinoma grade 3, metastatic to axillary nodes. 1948 - X-ray: metastatic to lungs and vertebrae.
87 Co	Mr.J.C.	A7009	57	Lobar pneumonia.
87 Ca	Mr.E.Z.	A5689	57	Surg.Path. No. 1804/48 - Infiltrating epidermoid carcinoma of bronchus grade 2.
91 Co	Mr.R.B.	A5979	61	Left ventricular failure, secondary to coronary occlusion.
91 Ca	Mr.M.S.	A7338	57	June 18/48 - Bronchial washings - Squamous cell carcinoma. June 24/48 - Sputum - tumour cells.
92 Co	Mr.J.M.	A8237	70	Fracture of neck of left femur.
92 Ca	Mr.I.L.	A8489	73	Surg.Path. No. 3763/49 - Infiltrating adenocarcinoma of rectum grade 2.

TABLE I

PRESENTATION OF CASES

Ca - Cancer
Co - Control

Exp. No.	Name	Hosp. No.	Age	Diagnosis
96 Co	Mr.J.A.	A10214	80	Congestive heart failure, coronary occlusion.
96 Ca	Mr.P.J.	A9991	76	Autopsy No. 7010 - Lymphosarcoma.

A follow up has been carried out on the twenty-four control cases. One case developed a cancer of the lip and another died of arteriosclerotic heart disease.

Mr. R. B., A5979, age 62, died April 23/49 of arteriosclerotic heart disease. No post mortem was done.

Mr. C. B., A3455, age 78, developed an ulcer on his lower lip in June, 1949, which was excised 25 August, 1949. The Surgical Pathology report is as follows:

Superficial epidermoid carcinoma, gr. 1.

Margins and base clear of tumour, measure 4 mm.

CHAPTER IV

RESULTS

The results of microscopic examination of the gonads, spleen, and liver in the twenty-four cases showed no significant differences between the series of rats injected with the urine extract from cancer patients and the control series. Some variations were seen in the female genital organs and the spleen in both series. Variations in the ovaries and uterus were correlated with changes in the cellular pattern of vaginal smears. In the early stages of the cycle there is follicle enlargement with general enlargement of the ovary. The uterus is congested and distended up to 4-5 mm. in diameter with fluid. The vaginal smear at this time shows predominantly cornified epithelial cells with only a few non-cornified. Later in the cycle the corpora lutea are formed with regression of some follicles and the ovary is generally smaller. The uterus at this stage is small and pale, measuring 2-3 mm. in diameter. The vaginal smear shows leucocytes and epithelial cells. These cyclical changes in the ovary, uterus and vaginal smears of normal and control rats were similar to those seen in rats injected with extracts of urine from cancer patients. In the spleen, much blood in the red pulp makes the margin of the white pulp stand out sharply. If the red pulp contains but little blood, the margin of the white pulp fades into it. This range of changes was similar in normals, controls, and rats injected with urine extracts from cancer

patients.

The weights of liver, spleen, and gonads of rats in the control and test series are shown in Table II. The results obtained have been used to compute the "percentage decrease," which is a ratio worked out by the originator of the test. For each experiment the calculations are as follows:

"Percentage decrease" is:-

$$\frac{X - y}{X} \times 100$$

X is:-

$$\frac{\text{Average body weight (control group)}}{\text{Average organ weight (control group)}}$$

Y is:-

$$\frac{\text{Average body weight (cancer group)}}{\text{Average organ weight (cancer group)}}$$

For a result to be considered positive the "percentage decrease" must be 20 or more for the spleen and/or gonads. In the twenty-four cases presented in Table II, there are six positives and eighteen negative results, whereas twenty-four positive results should have been obtained.

TABLE II

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
57 Co	93	0.225	0.300	6.52							
57 Co	94	0.560	0.365	7.90							
57 Co	95	0.827	0.345	6.45							
57 Co	101	0.803	0.335	7.81							
57 Co	104	0.575	0.350	7.61							
57 Co	105	0.747	0.390	8.20							
Av.	99	0.623	0.348	7.42	Male	159	284	133			
57 Ca	92	0.395	0.590	5.88							
57 Ca	93	0.660	0.530	8.03							
57 Ca	95	0.557	0.300	5.24							
57 Ca	96	0.585	0.800	7.77							
57 Ca	100	0.447	0.325	7.87							
57 Ca	110	0.547	0.325	7.61							
Av.	98	0.532	0.478	7.07	Male	184	205	139	-16	28	-4
58 Co	79	0.222	0.340	6.60							
58 Co	80	0.316	0.355	5.95							
58 Co	81	0.460	0.365	5.70							
58 Co	85	0.395	0.400	6.34							
58 Co	89	0.500	0.395	7.39							
58 Co	90	0.600	0.415	6.32							
Av.	84	0.416	0.378	6.38	Male	202	222	132			
58 Ca	77	0.490	0.320	6.77							
58 Ca	78	0.292	0.350	5.93							
58 Ca	78	0.570	0.325	7.63							
58 Ca	83	0.610	0.375	6.84							
58 Ca	86	0.572	0.315	5.93							
58 Ca	90	0.555	0.355	6.19							
Av.	82	0.515	0.340	6.55	Male	159	241	125	22	-9	5

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
59 Co	81	0.464	0.539	6.94							
59 Co	79	0.555	0.495	7.41							
59 Co	80	0.405	0.520	7.22							
59 Co	80	0.560	0.595	6.37							
59 Co	82	0.375	0.555	6.52							
59 Co	84	0.425	0.530	7.16							
Av.	81	0.464	0.539	6.94	Male	175	150	117			
59 Ca	81	0.395	0.335	6.07							
59 Ca	83	0.510	0.340	6.13							
59 Ca	83	0.385	0.375	6.21							
59 Ca	85	0.372	0.390	5.70							
59 Ca	92	0.457	0.365	6.42							
59 Ca	94	0.647	0.380	7.22							
Av.	86	0.461	0.364	6.29	Male	187	236	137	-7	-57	-17
61 Co	83	0.715	0.375	6.06							
61 Co	86	0.710	0.405	6.10							
61 Co	97	0.720	0.435	6.92							
61 Co	99	0.777	0.480	7.31							
61 Co	100	0.570	0.420	6.50							
61 Co	102	0.650	0.440	5.37							
Av.	95	0.690	0.426	6.38	Male	138	223	149			
61 Ca	81	0.317	0.280	4.66							
61 Ca	83	0.657	0.330	6.87							
61 Ca	92	0.470	0.350	5.82							
61 Ca	93	0.705	0.330	6.49							
61 Ca	101	0.520	0.410	7.95							
61 Ca	100	0.542	0.330	7.54							
Av.	92	0.535	0.338	6.56	Male	172	272	140	-25	-15	5

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
62 Co	87	0.502	0.360	6.75							
62 Co	87	0.562	0.355	7.13							
62 Co	89	0.542	0.320	6.18							
62 Co	91	0.632	0.330	4.68							
62 Co	90	0.300	0.310	4.42							
62 Co	95	0.560	0.395	6.70							
Av.	90	0.516	0.345	5.98	Male	174	261	151			
62 Ca	81	0.315	0.315	6.07							
62 Ca	84	0.580	0.300	7.70							
62 Ca	93	0.510	0.370	7.56							
62 Ca	99	0.762	0.360	8.26							
62 Ca	82	0.447	0.270	7.37							
62 Ca	90	0.650	0.335	6.33							
Av.	88	0.544	0.325	7.22	Male	162	271	122	7	-4	19
66 Co	79	0.272	0.320	6.52							
66 Co	93	0.535	0.415	7.00							
66 Co	96	0.590	0.350	6.61							
Av.	89	0.466	0.362	6.71	Male	191	246	133			
66 Ca	91	0.765	0.350	6.97							
66 Ca	93	0.637	0.355	7.45							
66 Ca	90	0.607	0.335	7.50							
Av.	91	0.670	0.347	7.31	Male	136	262	124	29	-7	7

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease: Rat Wt / Gonad Wt	% Decrease: Rat Wt / Spleen Wt	% Decrease: Rat Wt / Liver Wt
67 Co	86	0.462	0.420	6.90							
67 Co	91	0.657	0.500	7.33							
67 Co	90	0.565	0.435	7.12							
67 Co	101	0.715	0.510	7.42							
67 Co	103	0.237	0.530	7.30							
67 Co	95	0.642	0.520	7.34							
Av.	94	0.546	0.486	7.23	Male	172	193	130			
67 Ca	93	0.770	0.465	8.70							
67 Ca	94	0.735	0.505	7.88							
67 Ca	92	0.552	0.410	7.11							
67 Ca	95	0.712	0.450	7.24							
67 Ca	94	0.735	0.435	7.71							
67 Ca	96	0.740	0.530	8.25							
Av.	94	0.707	0.466	7.82	Male	133	202	120	23	-5	8
68 Co	96	0.027	0.475	7.88							
68 Co	98	0.026	0.325	5.78							
68 Co	93	0.034	0.355	5.33							
68 Co	91	0.018	0.400	6.51							
68 Co	85	0.025	0.375	6.67							
68 Co	92	0.026	0.425	7.40							
Av.	93	0.026	0.393	6.59	Female	358	236	141			
68 Ca	85	0.022	0.350	6.46							
68 Ca	89	0.028	0.425	9.07							
68 Ca	100	0.026	0.480	7.22							
68 Ca	93	0.027	0.370	8.08							
68 Ca	95	0.019	0.480	5.80							
68 Ca	94	0.027	0.435	6.16							
Av.	93	0.025	0.423	7.13	Female	372	220	130	-4	7	8

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
69 Co	94	0.762	0.470	8.37							
69 Co	84	0.672	0.330	6.90							
69 Co	90	0.650	0.315	6.55							
69 Co	89	0.755	0.405	7.12							
69 Co	95	0.785	0.400	6.73							
69 Co	96	0.605	0.405	7.20							
Av.	91	0.705	0.388	7.15	Male	129	235	127			
69 Ca	79	0.570	0.390	6.88							
69 Ca	84	0.570	0.395	8.21							
69 Ca	82	0.642	0.400	8.36							
69 Ca	80	0.635	0.350	6.77							
69 Ca	87	0.775	0.430	8.10							
69 Ca	90	0.675	0.400	7.85							
Av.	84	0.645	0.394	7.70	Male	130	213	105	1	9	17
70 Co	85	0.040	0.340	7.52							
70 Co	92	0.045	0.285	6.15							
70 Co	96	0.040	0.360	7.91							
70 Co	90	0.055	0.375	7.58							
70 Co	86	0.040	0.335	6.17							
70 Co	84	0.050	0.725	7.93							
Av.	89	0.045	0.403	7.21	Female	198	221	123			
70 Ca	95	0.045	0.435	7.28							
70 Ca	98	0.035	0.415	7.75							
70 Ca	96	0.045	0.420	7.01							
70 Ca	90	0.040	0.325	6.10							
70 Ca	89	0.030	0.310	6.28							
70 Ca	91	0.030	0.385	5.65							
Av.	93	0.038	0.382	6.68	Female	245	243	139	-23	-10	-13

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
71 Co	80	0.590	0.760	7.29							
71 Co	85	0.620	0.625	7.68							
71 Co	82	0.505	0.805	7.31							
71 Co	85	0.730	0.860	6.34							
71 Co	87	0.692	1.060	7.15							
71 Co	84	0.747	1.175	7.00							
Av.	84	0.647	0.881	7.13	Male	130	95	118			
71 Ca	79	0.482	0.650	7.00							
71 Ca	96	0.560	0.335	6.72							
71 Ca	89	0.602	0.645	6.00							
71 Ca	80	0.687	0.495	5.80							
71 Ca	82	0.750	0.260	6.13							
71 Ca	95	1.060	0.245	6.35							
Av.	87	0.690	0.438	6.33	Male	126	199	137	3	-104	-15
72 Co	85	0.557	0.350	5.83							
72 Co	78	0.585	0.730	5.89							
72 Co	84	0.747	0.810	5.68							
72 Co	80	0.645	0.670	4.79							
72 Co	87	0.557	0.850	6.97							
72 Co	96	0.677	1.280	7.67							
Av.	85	0.628	0.782	6.14	Male	135	109	138			
72 Ca	80	0.602	0.610	4.48							
72 Ca	85	0.610	0.950	4.94							
72 Ca	76	0.550	0.615	4.62							
72 Ca	84	0.585	0.780	4.45							
72 Ca	80	0.555	0.810	5.50							
72 Ca	93	0.667	0.745	5.15							
Av.	83	0.595	0.752	4.86	Male	139	110	171	-2	-7	-23

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
73 Co	75	0.030	0.745	6.52							
73 Co	98	0.045	1.010	7.44							
73 Co	98	0.050	1.280	9.80							
73 Co	75	0.025	0.990	5.43							
73 Co	76	0.020	1.025	5.32							
73 Co	79	0.025	0.860	6.93							
Av.	84	0.032	0.985	6.91	Female	263	85	122			
73 Ca	74	0.015	0.430	4.06							
73 Ca	79	0.010	0.465	5.35							
73 Ca	72	0.018	0.470	5.05							
73 Ca	79	0.010	0.465	5.03							
73 Ca	75	0.015	0.500	5.73							
73 Ca	87	0.010	0.810	4.45							
Av.	78	0.013	0.523	4.95	Female	600	149	158	-132	-77	-32
80 Co	95	0.040	0.870	5.25							
80 Co	85	0.015	0.840	4.52							
80 Co	92	0.030	0.900	4.93							
80 Co	84	0.020	0.850	4.60							
80 Co	86	0.020	0.700	6.37							
80 Co	105	0.045	0.995	7.34							
Av.	91	0.028	0.859	5.50	Female	325	1059	165			
80 Ca	80	0.035	0.810	4.39							
80 Ca	82	0.025	0.945	6.00							
80 Ca	83	0.020	0.920	5.93							
80 Ca	90	0.015	0.755	5.79							
80 Ca	84	0.030	1.125	6.87							
80 Ca	81	0.020	0.750	8.05							
Av.	83	0.024	0.884	6.17	Female	346	939	135	-14	11	19

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
81 Co	81	0.555	0.650	5.30							
81 Co	89	0.647	0.600	4.95							
81 Co	88	0.680	0.580	6.22							
81 Co	90	0.560	0.670	6.61							
81 Co	81	0.505	0.600	7.00							
81 Co	87	0.595	0.800	7.25							
Av.	86	0.590	0.650	6.22	Male	146	132	138			
81 Ca	87	0.555	0.750	6.89							
81 Ca	90	0.690	0.730	7.51							
81 Ca	96	0.720	0.670	8.55							
81 Ca	90	0.744	0.650	8.66							
81 Ca	87	0.635	0.490	8.35							
81 Ca	110	0.852	1.300	10.32							
Av.	93	0.699	0.765	8.38	Male	133	122	111	9	8	20
82 Co	90	0.655	0.490	5.59							
82 Co	82	0.770	0.710	5.76							
82 Co	88	0.710	0.480	6.77							
82 Co	83	0.692	0.410	6.18							
82 Co	92	0.720	0.430	8.12							
82 Co	84	0.720	0.500	7.85							
Av.	87	0.711	0.503	6.71	Male	122	173	130			
82 Ca	88	0.760	0.370	7.35							
82 Ca	100	0.980	0.550	6.13							
82 Ca	97	0.940	0.390	8.25							
82 Ca	90	0.817	0.380	7.48							
82 Ca	102	0.955	0.570	8.72							
82 Ca	89	0.860	0.590	7.80							
Av.	94	0.885	0.475	7.62	Male	106	198	123	9	-14	5

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
83 Co	88	0.015	0.520	4.40							
83 Co	76	0.020	0.750	4.50							
83 Co	79	0.020	0.630	4.30							
83 Co	80	0.015	0.510	4.20							
83 Co	90	0.020	0.570	4.71							
83 Co	85	0.017	0.670	4.45							
Av.	83	0.018	0.608	4.43	Female	461	137	187			
83 Ca	90	0.015	0.670	5.55							
83 Ca	87	0.015	0.580	6.15							
83 Ca	83	0.015	0.720	4.91							
83 Ca	87	0.015	0.580	4.57							
83 Ca	95	0.020	0.810	6.55							
83 Ca	86	0.015	0.620	5.95							
Av.	88	0.016	0.663	5.61	Female	550	133	157	-8	6	19
84 Co	102	0.890	1.010	5.37							
84 Co	105	1.040	1.290	5.75							
84 Co	100	0.890	1.500	4.82							
84 Co	99	0.915	0.620	4.74							
84 Co	95	0.565	0.740	6.53							
84 Co	101	1.000	0.850	6.62							
Av.	100	0.883	1.000	5.64	Male	113	100	177			
84 Ca	94	0.815	0.690	5.81							
84 Ca	90	0.780	0.480	5.65							
84 Ca	84	0.707	0.720	6.47							
84 Ca	92	0.730	0.480	7.15							
84 Ca	99	0.830	0.730	6.15							
84 Ca	93	0.830	0.410	6.17							
Av.	92	0.782	0.585	6.23	Male	118	157	148	-4	-45	17

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
85 Co	82	0.805	1.130	5.02							
85 Co	105	1.120	0.900	7.04							
85 Co	80	0.760	0.900	7.00							
85 Co	83	0.880	0.620	6.50							
85 Co	84	0.930	0.630	7.42							
85 Co	101	1.090	0.770	6.18							
Av.	89	0.931	0.825	6.53	Male	956	108	136			
85 Ca	90	0.910	0.780	4.72							
85 Ca	102	1.020	1.020	4.93							
85 Ca	104	0.905	1.320	5.47							
85 Ca	91	0.790	0.700	5.45							
85 Ca	100	0.995	0.300	5.15							
85 Ca	89	0.690	0.620	6.87							
Av.	96	0.885	0.790	5.43	Male	108	122	177	-14	-12	-30
86 Co	100	0.870	0.930	5.35							
86 Co	94	0.700	1.100	4.80							
86 Co	95	0.640	0.850	4.70							
86 Co	97	0.815	0.950	4.92							
86 Co	89	0.850	0.560	6.90							
Av.	95	0.775	0.878	5.33	Male	123	108	178			
86 Ca	97	0.765	0.980	5.30							
86 Ca	90	0.555	1.050	5.13							
86 Ca	100	0.865	1.050	5.10							
86 Ca	92	0.795	0.900	5.20							
86 Ca	105	1.030	1.020	8.05							
Av.	97	0.802	1.000	5.76	Male	121	97	168	2	10	7

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease (Rat Wt / Gonad Wt)	% Decrease Rat Wt / Spleen Wt	% Decrease (Rat Wt / Liver Wt)
87 Co	76	0.510	0.570	4.77							
87 Co	75	0.765	0.460	4.80							
87 Co	80	0.750	0.730	5.75							
87 Co	77	0.695	0.520	5.30							
87 Co	74	0.555	0.710	5.30							
87 Co	88	0.805	0.520	5.82							
Av.	78	0.680	0.585	5.29	Male	115	133	147			
87 Ca	78	0.625	0.620	5.35							
87 Ca	85	0.665	0.780	5.25							
87 Ca	85	0.875	1.150	6.25							
87 Ca	94	0.780	0.980	7.35							
87 Ca	75	0.490	0.820	5.75							
87 Ca	77	0.610	0.700	5.35							
Av.	82	0.674	0.842	5.88	Male	122	97	139	-6	27	5
91 Co	70	0.570	1.170	4.70							
91 Co	72	0.625	0.650	5.82							
91 Co	73	0.670	1.020	5.62							
91 Co	75	0.550	0.450	6.80							
91 Co	82	0.685	1.000	7.12							
91 Co	85	0.680	0.770	6.70							
Av.	76	0.630	0.843	6.13	Male	121	90	124			
91 Ca	87	0.635	1.050	5.60							
91 Ca	88	0.575	0.510	7.44							
91 Ca	85	0.800	0.690	5.54							
91 Ca	89	0.710	0.850	5.79							
91 Ca	86	0.610	0.450	6.32							
91 Ca	79	0.520	0.600	6.00							
Av.	86	0.642	0.692	6.12	Male	134	124	141	11	-38	-14

TABLE II (continued)

RESULTS IN 24 CASES (Ca - Cancer. Co - Control)

Case No.	Rat Wt Gm	Gonad Wt Gm	Spleen Wt Gm	Liver Wt Gm	Sex	Rat Wt / Gonad Wt	Rat Wt / Spleen Wt	Rat Wt / Liver Wt	% Decrease Rat Wt / Gonad Wt	% Decrease Rat Wt / Spleen Wt	% Decrease Rat Wt / Liver Wt
92 Co	77	0.025	0.730	5.22							
92 Co	80	0.020	0.820	5.72							
92 Co	82	0.015	0.730	6.80							
92 Co	75	0.020	0.510	6.87							
92 Co	79	0.020	0.850	7.65							
92 Co	75	0.020	0.770	6.82							
Av.	78	0.020	0.735	6.51	Female	390	106	120			
92 Ca	80	0.015	1.220	5.40							
92 Ca	82	0.020	0.720	4.90							
92 Ca	78	0.020	0.770	5.05							
92 Ca	90	0.020	1.200	7.60							
92 Ca	79	0.020	0.980	7.20							
92 Ca	77	0.020	1.130	6.70							
Av.	81	0.019	1.003	6.14	Female	425	81	132	-9	23	-10
96 Co	101	0.725	1.250	5.89							
96 Co	90	0.640	1.550	5.62							
96 Co	78	0.585	0.570	6.03							
96 Co	81	0.385	0.850	5.73							
96 Co	80	0.590	0.950	6.70							
96 Co	92	0.725	1.600	5.52							
Av.	87	0.608	1.128	5.92	Male	143	77	147			
96 Ca	95	0.200	1.010	6.62							
96 Ca	98	0.365	0.850	5.77							
96 Ca	90	0.420	0.820	5.32							
96 Ca	90	0.225	0.850	6.10							
96 Ca	95	0.545	0.550	5.77							
96 Ca	86	0.280	0.720	6.40							
Av.	92	0.339	0.800	6.00	Male	271	115	153	-90	-50	-4

CHAPTER V

SUMMARY AND CONCLUSIONS

I. SUMMARY

A number of cancer tests that have been advocated in the last twenty years have been reviewed and classified into five groups. Some observations have been made on the relative value of these procedures as aids in the diagnosis of cancer.

One of the more recent cancer tests has been investigated. Alcohol-ether urine extracts from twenty-four cancer patients proven by biopsy or autopsy were injected into rats. Patients with genital cancer were not used for these tests. As controls, similar urine extracts from twenty-four patients free of cancer and of approximately the same age and of the same sex were used. The extract from each cancer patient was injected into six young rats. Six young rats also received injections from each non-cancer patient. Forty-eight hours after the injection, liver, spleen, and gonads of the rats were weighed and examined histologically. The results were statistically examined.

II. CONCLUSIONS

1. There is no test highly specific and highly sensitive for cancer.

2. As a screening procedure few if any tests have any advantage over the erythrocyte sedimentation rate.

3. An investigation of a biological test as described by Beard has revealed no significant effect in weight or histological structure in the liver, spleen or gonads of rats following the injection of urine extracts from cancer patients.

4. This procedure has proven to be of no value for the diagnosis of malignant tumours.

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APPENDIX

APPENDIX

STATISTICAL ANALYSIS OF RESULTS

Table III presents a statistical analysis of data shown in Table II, as follows:

Since increases in gonad, spleen, and liver weight are dependent to some extent on original weight, the mean increases for each group of six rats were expressed in terms of the increase for 1000 grams live weight. For example, the means for the first Ca group in Table II for gonad weight are:

rat weight = 98 gr. gonad weight = 0.532.

Then the increase in gonad weight per 1000 grams is:

$$\frac{0.532}{98} \times 1000 = 5.429$$

TABLE III

DATA OF TABLE II EXPRESSED AS MEANS OF 6 RATS AND IN TERMS OF INCREASE IN WEIGHT PER 1000 GRAMS ORIGINAL RAT WEIGHT
Male Rats in First Group of 16 Means,
Female Rats in Second Group of 6 Means

Gonad Wt. per 1000 Gm.

Case No.	Ca*	Co**	Ca-Co
57	5.429	6.293	- .864
58	6.280	4.952	1.328
59	5.360	5.728	- .368
61	5.815	7.263	- 1.448
62	6.182	5.733	.449
67	7.521	5.808	1.713
69	7.678	7.747	- .069
71	7.931	7.702	.229
72	7.169	7.388	- .219
81	7.516	6.860	.656
82	9.415	8.172	1.243
84	8.500	8.830	- .330
85	9.219	10.461	- 1.242
87	8.220	8.718	- .498
91	7.465	8.289	- .824
96	3.685	6.988	- 3.303
	(Ca) 113.385	(Co) 116.932	(Ca-Co) - 3.547
68	.269	.280	- .011
70	.409	.506	- .097
73	.167	.381	- .214
80	.289	.308	- .019
83	.182	.217	- .035
92	.234	.256	- .022
	(Ca) 1.550	(Co) 1.948	(Ca-Co) - .398
(1) 66	7.363	5.236	2.127
(2) 86	8.268	8.158	.110

* Wt. per 1000 grams - rats injected with extracts from cancer patients)
** Wt. per 1000 grams - rats injected with extract from control patients) each figure is a mean

TABLE III (continued)

DATA OF TABLE II EXPRESSED AS MEANS OF 6 RATS AND IN TERMS OF INCREASE IN WEIGHT PER 1000 GRAMS ORIGINAL RAT WEIGHT
Male Rats in First Group of 16 Means,
Female Rats in Second Group of 6 Means

Spleen Wt. per 1000 Gm.

Case No.	Ca*	Co**	Ca-Co
57	4.878	3.515	1.363
58	4.146	4.500	- .354
59	4.232	6.654	- 2.422
61	3.674	4.484	- .810
62	3.693	3.833	- .140
67	4.957	5.170	- .213
69	4.690	4.264	.426
71	5.034	10.488	- 5.454
72	9.060	9.200	- .140
81	8.226	7.558	.668
82	5.053	5.782	- .729
84	6.359	10.000	- 3.641
85	8.229	9.270	- 1.041
87	10.268	7.500	2.768
91	8.046	11.092	- 3.046
96	8.696	12.966	- 4.270
	(Ca) 99.241	(Co) 116.276	(Ca-Co) -17.035
68	4.548	4.226	.322
70	4.108	4.528	- .420
73	6.705	11.726	- 5.021
80	10.651	9.440	1.211
83	7.534	7.325	.209
92	12.383	9.423	2.960
	(Ca) 45.929	(Co) 46.668	(Ca-Co) .739
(1) 66	3.813	4.067	- .254
(2) 86	10.309	9.242	1.067

* Wt. per 1000 grams - rats injected with extract from cancer patients)
** Wt. per 1000 grams - rats injected with extract from control patients) each figure is a mean

TABLE III (continued)

DATA OF TABLE II EXPRESSED AS MEANS OF 6 RATS AND IN TERMS OF INCREASE IN WEIGHT PER 1000 GRAMS ORIGINAL RAT WEIGHT
Male Rats in First Group of 16 Means,
Female Rats in Second Group of 6 Means

Liver Wt. per 1000 Gm.

Case No.	Ca*	Co**	Ca-Co
57	7.214	7.495	- .281
58	7.988	7.595	.393
59	7.314	8.568	- 1.254
61	7.130	6.716	.414
62	8.204	6.644	1.560
67	8.319	7.691	.628
69	9.167	7.857	1.310
71	7.276	8.488	- 1.212
72	5.855	7.224	- 1.369
81	9.011	7.232	1.779
82	8.106	7.713	.393
84	6.772	5.640	1.132
85	5.656	7.337	- 1.681
87	7.171	6.782	.389
91	7.116	8.066	- .950
96	6.522	6.804	- .282
	(Ca) 118.821	(Co) 117.852	(Ca-Co) .969
68	7.667	7.086	.581
70	7.183	8.101	- .918
73	6.346	8.226	- 1.880
80	7.434	6.044	1.390
83	6.375	5.337	1.038
92	7.580	8.346	- .766
	(Ca) 42.585	(Co) 43.140	(Ca-Co) - .555
(1) 66	8.033	7.539	.494
(2) 86	5.938	5.610	.328

* Wt. per 1000 grams - rats injected with extract from cancer patients)
** Wt. per 1000 grams - rats injected with extract from control patients) each figure is a mean

On examining the data it is obvious that since Ca represents results for cancer patients and Co the results for corresponding controls, the value of Ca - Co for any one patient should be positive if the treatment of rats by the urine extract is causing a more rapid increase in the gonad, spleen, or liver weights. The signs of the Ca - Co values are summarized in Table IV.

TABLE IV

SIGNS OF CA - CO VALUES

	Gonad Wt.		Spleen Wt.		Liver Wt.	
	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
Male Rats	6	10	4	12	9	7
Female Rats	0	6	4	2	3	3

This very simple analysis is in itself sufficient to indicate that there is no tendency towards a positive reaction. If the test is to be of any value in a specific instance, all the values in Table IV should be positive. Actually the results with gonad weight and spleen weight indicate a tendency towards a negative reaction--in other words, in the majority of cases the weight increases for the rats treated with urine extract from the cancer patients is less than those treated with urine extract from non-cancer patients.

In order to be certain that any significant indications in the results were not overlooked, the data of Table III were subjected to analyses of variance as given in Table V.

In the analyses of Table V the mean differences indicated by

Ca - Co are not significant at the 5% level. In two cases, that of spleen weight (males) and gonad weight (females), there are indications of significance but as shown by Table IV this is a negative rather than a positive effect. It indicates actually a slower growth due to the extracts from the cancer patients than from the non-cancer patients.

TABLE V

ANALYSES OF VARIANCE ON DATA OF TABLE III

		S S	D F	M S	F	5% Pt.
Gonad Weight (males)	Ca-Co	0.3932	1	.3932	0.52	4.54
	Pairs	54.3142	15	3.6209	4.79	2.41
	Error	11.3303	15	.7554		
Spleen Weight (males)	Ca-Co	9.0685	1	9.0685	3.84	4.54
	Pairs	166.2910	15	11.0861	4.69	2.41
	Error	35.4357	15	2.3624		
Liver Weight (males)	Ca-Co	0.0293	1	.0293	0.05	4.54
	Pairs	14.0646	15	.9376	1.53	2.41
	Error	9.1829	15	.6122		
Gonad Weight (Females)	Ca-Co	0.0132	1	.0132	4.26	6.61
	Pairs	0.0777	5	.0155	5.01	5.05
	Error	0.0155	5	.0031		

TABLE V (continued)

ANALYSES OF VARIANCE ON DATA OF TABLE III

		S S	D F	M S	F	5% Pt.
Spleen Weight (females)	Ca-Co	0.0455	1	.0455		
	Pairs	81.0855	5	16.2171	4.55	5.05
	Error	17.8356	5	3.5671		
Liver Weight (females)	Ca-Co	0.0257	1	.0257		
	Pairs	5.6319	5	1.1264	1.36	5.05
	Error	4.1298	5	.8260		