

REPORT ON THE APPLICATION OF POLAROGRAPHIC EFFECT OF PROTEINS IN CANCER DIAGNOSIS

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WITH the aid of a grant assigned by the Cancer Research Society of Montreal, a study was carried out at the University of Montreal, with the following objectives.

1) To test Bredickas's claim that is possible to differentiate between carcinomatic and non carcinomatic *blood sera* by means of the dropping mercury *electrode* (polarography).

2) To test the possibility of differentiating between *normal and cancer tissue* by means of polarized electrodes.

This study was begun in the fall of 1946, at which time the Cancer Research Society of Montreal put at our disposal a bursary which permitted us to buy the necessary equipment to carry out the first step in our research project.

In 1930, a polarographic effect of proteins was described which consisted of a characteristic wave at the voltage of 1.6 on the current voltage curve of a solution of ammonium chloride containing traces of proteins, this effect has been shown to be due to the electrolytic evolution of hydrogen catalysed by the presence of the protein at the cathode interphase.

Since the protein effect has been investigated in the physico-chemical Institute of the Charles University by Dr. R. Bredicka, who introduced a more specific polarographic reaction for the proteins by adding to the IN. solution of ammonium chloride and ammonia a solution of a cobaltous or cobaltic salt,

he has shown that proteins containing sulphur cause in such solutions a *new* wave at a smaller voltage (1.4) and ascribed this effect to the sulphhydryl & di-sulphydic groups of the proteins.

In 1936, Purr & Russel found that carcinomatic blood shows in certain biological reaction less activity than normal blood.

Waldsmidt & Leitz and his collaborators attempted to use this reaction for cancer diagnosis and expressed the opinion that the lack of activity of the carcinomatic serum is due to decreased activity of the sulphhydryl groups in the proteins of blood serum.

In our clinical application we have combined somewhat the Bredicka & Waldsmidt-Leitz methods and have found them both satisfactory in arriving to a diagnosis of blood serum associated with cellular proliferation.

The pathological state indicated by the abnormal height of Bredicka's protein wave has been ascertained to be due to carcinoma or sarcoma, *if acute cases* of inflammation or fever are eliminated. The serum in the latter pathological state gives with either reaction an abnormal that is a "positive" effect. Investigations are now being directed towards distinguishing whether the decomposition products of the serum proteins due to cancer are different from those due to other diseases (inflammation, fever,) so as to make the polarographic reaction in this respect more specific.

At the outset it may be stated that we have been unable to confirm the fool proof diagnostic claims made by Bredicka and Heyrovsky. We feel however that the present study has been valuable in an exploratory sense, as it seems to open a promising field for further systematic research.

The first systematic research using the polarographic diagnosis of cancer was carried out by Bredicka in collaboration with F. N. Novak, director of radio therapeutic Institute Prague: from 187 cases the polarographic diagnosis agreed in 102 out of 107 histologically ascertained carcinomatous cases, 11 of the 13 sarcoma cases, whilst one the 38 normal sera showed a positive polarographic reaction; of the 29 non carcinomatous diseases, 14 were polarographically positive and 15 negative.

A similar agreement was found in the Finson Institute and Radium Station (Copenhagen) where amongst the positive reactions, some cases of hepatic disorder were ascertained.

SINCE 1948, THE POLAROGRAPHIC CANCER DIAGNOSIS IS BEING APPLIED FOR FURTHER CLINICAL investigation & research at the Cancer Institute of Montreal, and where the director, Dr. Simard, a member of the Cancer Research Society, Medical Advisory Board, has given his whole hearted cooperation to the research project.

We are herewith including in this report our results of the polarographic cancer diagnosis as applied to cancerous patients at the Cancer Institute of Montreal. From 1948, to March 1949, blood serum obtained from 560 patients were submitted to polarographic investigation. The patients were classified into two distinct groups :

I — Patients attending the Tumor Clinic, having received surgical, Radium and X Ray therapy following a positive

diagnosis of cancer. This group was made up of 165 patients.

II — 395 patients attending the outdoor clinics, or were sent to the hospital for routine laboratory investigation or occupied the hospital wards for various ailments.

In the first group, made up exclusively of patients suffering with cancer, the polarographic cancer diagnosis was positive, as to the height of the cystine catalytic wave, and as to the results of the split product waves (Waldsmit Leitz) in 163 cases of cancer. Two negative results in one cancer of breast and one cancer of cervix receiving deep X Ray therapy.

In the second group of 395 taken at random in the outdoor or in the hospital wards, there were 13 false positive polarographic cancer results, in noncancerous patients. But there has been no false negative polarographic cancer diagnosis in those cases which subsequently have been proved to be carcinomatous sera.

The 13 false positive were made up of the following: 3 patients with inguinal hernias, 1 patient with diabetes, 3 with cholecystitis stone, 2 with pulmonary tuberculosis, 1 renal calculus, 1 osteoarthritis of knee, 1 subacute appendicitis, 1 Ludvig's angina.

The acute or subacute inflammations, as well as patients receiving high doses of penicillin show a positive polarographic serum reaction. No explanation can be presently advanced as why this should take place. This will be later investigated.

A point which requires further research is to find out if the polarographic serum reaction of cancer patients which have undergone radical surgical, Radium and deep X Ray therapy, show a change in the polarographic effect of the proteins, and which may indicate further presence or complete irradiation.

cation of the cancer. This part of the research project is now under investigation and the object is to compare the polarographic cancer diagnosis before and after treatment has been considered efficacious.

Conclusion and Remarks.

In this report to your society we have not presented our experimental data. We are reserving this more technical aspect for a publication in the near future, and in which due credit is given to the financial support and encouragement, that the Cancer Research Society of Montreal, has given to this research project.

By means of the dropping mercury electrode and by the pepsin, alcohol and sulphosalysilic acid, deproteinisation methods, we have determined the cystine content in various carcinomatic and non carcinomatic samples of blood serum.

The maximum high of cystine wave for normal patient serum was 25 mm. and for carcinomatous serum from 35 to 46 mm.

The present study, altho only exploring in nature has yielded results of

such promise that it is our opinion, the inauguration of a research program on a larger scale is now in order. *Polarography may become a new blood test in cancer diagnosis.*

In concluding we wish to call attention to a few of the most important conclusions derivable from the present study.

1) Using Bredicka's procedures and Walchmitz-Leitz procedure, we have been able to substantiate partly the claims of Bredicka and other workers, that the polarograph can be used for the serological diagnosis of cancer. At the present time, the clinical value of this technique is promising, but has to be proven further.

The manipulation of a polarograph still requires a well trained and well specialized personal.

However, results of both scientific and clinical importance may be obtained after further research.

Indications have been obtained that a systematic study of the content of sulphur containing proteins (cystine) in *blood* cells may yield new information which is not only of physiological, but also of clinical importance.