

fluenced by heat and are practically destroyed at about 100° C. The difference probably depends upon coagulation of the protein and consequent failure of absorption.

Dried sensitive guinea-pig blood serum, containing anaphylactin, withstands at least 100° C. for ten minutes.

44 (382)

A skin reaction in carcinoma from the subcutaneous injection of human red blood cells.

By **CHARLES A. ELSBERG.**

[From the Mount Sinai Hospital.]

Numerous investigators have shown that if the blood serum of a patient suffering from carcinoma be mixed with normal human red blood cells hemolysis occurs. The reaction takes place in from 50 per cent. to 80 per cent. of patients with malignant disease. It occurs with considerable frequency in tuberculosis, and more rarely in other diseases.

It occurred to the writer, that, by the injection of red blood cells under the skin of the carcinoma patient, it might be possible to produce a local reaction at the site of the injection. Logically, a local hemolysis should take place. Theoretically, such a reaction might prove to be a delicate one ; it might give more positive and definite results than the test-tube method. In the technique which is used for the test-tube method the presence and degree of hemolysis is indicated by the amount of laking of the red cells — that is, by the amount of hemoglobin which has been set free. The tube reaction gives no evidence of other substances than the hemoglobin which have been liberated. A small amount of hemolysin in the serum which is being tested might not be capable of detection. If normal human blood cells are injected under the skin of a patient whose serum is hemolytic, fresh quantities of hemolysin would be continually carried to the cells, and therefore even a small amount of hemolysin might cause hemolysis of the cells. Every organic substance which was set free would enter the tissues and might there have its effect.

Accordingly, after some experimentation, normal blood was in-

jected under the skin of patients suffering from carcinoma or other disease. In patients with malignant disease, a decided local reaction was observed. The technique employed was a very simple one. Under aseptic precautions, blood was aspirated from the median basilic vein of a normal individual (preferably a child), every possible precaution being taken that the individual was healthy and free from hereditary or acquired disease. The blood was defibrinated, and the cells washed four times in normal saline solution, care being taken that the washings and centrifuging was thoroughly done. A 20 per cent. emulsion of the red cells in normal saline solution was made and kept in the ice-box for 24-48 hours before it was used. Five minims of this 24-48 hour old suspension of washed red blood cells were subcutaneously injected into the anterior surface of the forearm of the patient. In the patients in whom a "reaction" was obtained, the following changes were noted in the skin at the site of the injection. Six to eighteen hours after the injection, the affected area was slightly raised and slightly tender, it had a more or less well defined margin, it measured from two to four centimeters and it was of a somewhat dusky red color. The changes in the skin reached their maximum within one or two hours, and the red area then began to fade, rapidly or slowly. Eight to twenty four hours after the injection, the skin lesion had either entirely disappeared, or more often, a brownish, bluish or lemon-yellow discoloration remained, which persisted for a number of days.

In the patients who did not show this reaction, there was either nothing to be seen at the site of the injection excepting the needle puncture, or a brownish discoloration of the skin, or a bluish discoloration, as is often seen after a hypodermic injection.

My investigations of this cutaneous lesion are very incomplete. I have given thirty four injections to twenty patients with known carcinoma, and every one of the cases had a positive reaction. In most of the patients several injections were given of different blood cells. With succeeding injections, the reaction was either less marked or failed to appear. Of four patients with known sarcoma, three gave a positive reaction. Injections were given to over one hundred normal individuals or to those suffering from diseases other than sarcoma or carcinoma. These included a

variety of diseases, such as nephritis, tuberculosis of lungs, bladder, kidneys (7 cases), leukemia, syphilis (2 cases), benign tumors, acute and chronic inflammatory affections, etc. In all but three cases, the reaction was negative. One patient with a septic endocarditis gave a suspicious, but not a positive reaction. Two other injections made in this patient were negative. This case was among the earliest of our series, and therefore must be accepted with caution. A patient who had been operated on for a large rapidly growing lymphangioma of the suprapubic region and had several large angiomas of the thigh with a large post-operative hematoma of the scrotum, gave a marked positive reaction. A patient with gastric symptoms, absence of hydrochloric acid and presence of lactic acid, with a loss of thirty pounds in weight, gave a positive reaction. The operation failed to show any carcinoma. I obtained no reaction in several patients in whom malignant disease was suspected but in whom no malignant disease was found at operation or at autopsy, and have obtained positive reactions in several patients in whom carcinoma was not suspected, but in whom carcinomatous disease was found at operation. Jaundice seemed to have no influence upon the appearance of the reaction.

In order to gain a more definite idea of the causation of the skin changes, normal defibrinated blood was laked with distilled water, and, after the tubes had been centrifuged, the supernatant fluid was injected into a number of patients. For purposes of control, hypodermic injections of sterile distilled water were given. All of the patients, whether suffering from malignant disease or not, who received hypodermic injections of laked blood, presented a skin lesion similar to that which was observed in carcinoma patients after the injection of washed red blood cells. This seemed to show that in the patients with carcinoma the reaction from the blood cell injection was due to a local hemolysis. In the normal individual or one suffering from some other disease, on the other hand, there was no hemolysis and therefore no reaction. When, however, the hemolyzable substances extracted from the red cells by laking were injected, the characteristic local lesion was observed. I have not yet been able to obtain pure human hemoglobin for injection purposes.

A fuller account of the technique employed and a more exact description of the cutaneous lesions observed, of the possible value of red blood cell mixtures, *i. e.*, of suspensions of the mixed red blood cells of several individuals, of the possible value of some animal red blood cells for injection purposes, of the significance of the persistence or disappearance of the reaction after an operation, and many other aspects of the subject will be discussed in a future communication. The number of injections thus far given is far too small to allow of positive conclusions as to the reliability of this method for diagnostic purposes. The results obtained thus far have been striking. The purpose of this preliminary report is to call attention to the fact that it is possible to cause a local hemolysis in the living body by the subcutaneous injection of washed normal human red blood cells, and that in patients with malignant disease, especially carcinoma, a characteristic and easily recognizable local skin lesion is caused by this injection.