

# *Acta Medica Okayama*

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*Volume 31, Issue 4*

1977

*Article 5*

AUGUST 1977

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# Preoperative blastformation rate in gastrointestinal cancer patients\*

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## Abstract

The rate of blastformation of peripheral blood lymphocytes in response to stimulation by phytohemagglutinin (PHA) was assessed preoperatively in 393 patients with gastrointestinal cancer. The series consisted of 291 cases of gastric cancer and 102 cases of colon cancer, all patients being under 70 years of age. The blastformation rate was related to the stage of cancer ground at operation. Preoperative blastformation rates for both colon cancer and gastric cancer decreased as the cancer progressed. With Stage I gastric cancer 81.4% of those that underwent curative resection had preoperative blastformation rates greater than 40%. However, the number of those with blastformation rates over 40% decreased markedly in the curative cases of gastric cancer Stage II to stage IV. Eighty three percent of cases that underwent curative resection with colon cancer, including advanced cancer, had preoperative blastformation rates of over 40%. These results indicated that the correlation of the preoperative blastformation rate with success of curative resection better for colon cancer than for gastric cancer.

Acta Med. Okayama **31**, 257—262 (1977)

## PREOPERATIVE BLASTFORMATION RATE IN GASTROINTESTINAL CANCER PATIENTS

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*Received April 23, 1977*

*Abstract.* The rate of blastformation of peripheral blood lymphocytes in response to stimulation by phytohemagglutinin (PHA) was assessed preoperatively in 393 patients with gastrointestinal cancer. The series consisted of 291 cases of gastric cancer and 102 cases of colon cancer, all patients being under 70 years of age. The blastformation rate was related to the stage of cancer ground at operation. Preoperative blastformation rates for both colon cancer and gastric cancer decreased as the cancer progressed. With Stage I gastric cancer, 81.4% of those that underwent curative resection had preoperative blastformation rates greater than 40%. However, the number of those with blastformation rates over 40% decreased markedly in the curative cases of gastric cancer Stage II to stage IV. Eighty three percent of cases that underwent curative resection with colon cancer, including advanced cancer, had preoperative blastformation rates of over 40%. These results indicated that the correlation of the preoperative blastformation rate with success of curative resection better for colon cancer than for gastric cancer.

Many attempts have been made to analyse cancer patients clinically at an immunological level. It is now possible to predict the progress of cancer from the cell-mediated immunity of the cancer-bearing host (1-3). For the past ten years, we have been studying cell-mediated immunity in cancer-bearing patients, concentrating on the use of nonspecific immune reactions as a parameter for assessing the development of cancer and the possibility of curative resection.

So far, the blastformation rate of peripheral blood lymphocytes against PHA (as abbreviated to the blastformation rate) has proved the most effective nonspecific immune reaction in the case of gastric cancer (4, 5). The present paper is an extension of this study to include cases of colon cancer as well as many cases of gastric cancer. It does, therefore, provide a general picture of gastrointestinal cancer and confirms the usefulness of the preoperative blastformation rate in determining surgical treatment for gastrointestinal cancer patients.

### MATERIALS AND METHODS

*Subjects.* The rate of blastformation of peripheral blood lymphocytes was assessed preoperatively in 393 patients with gastrointestinal cancer who had

been admitted to our surgical department. The series consisted of 291 cases of gastric cancer and 102 cases of colon cancer, all patients being under 70 years of age, and was divided into three groups after operation: curative resection, noncurative resection, and nonresectable. Recurrent cases (6), and those of over 70 years old (7) whose cell-mediated immunity was markedly low were excluded from the series.

*Methods.* Fairly pure, small lymphocytes were isolated from a 5 ml preoperative specimen of heparinized peripheral blood by the Ficoll-Conray method. These lymphocytes were suspended in 2 ml of TC-199 solution containing 20% calf serum at a concentration of  $10^6$  cells/ml, then 1% (v/v) PHA-M (Difco) added. The lymphocytes were cultured in TD-15 for 72 hr, centrifuged, and the sediment smeared on a slide glass and stained with May-Giemsa stain. The number of lymphocytes over  $(8\mu\text{m})^2$  in size in  $10^3$  lymphocytes was used to estimate the blastformation rate as in the following formula (4-6):

$$\text{blastformation rate (\%)} = \frac{\text{number of lymphocytes over } (8\mu\text{m})^2 \text{ in size}}{10^3 \text{ lymphocytes}} \times 100$$

#### RESULTS

In gastrointestinal cancer patients under 70 years of age who received curative resection, the mean  $\pm$  SD for the blastformation rate was  $50 \pm 15\%$  and the incidence of those having blastformation rates over 40% was more than 70%. In similar patients over 70 years of age, the blastformation rate was  $38.5 \pm 16.9\%$  and 43.8% of them were over 40%. The blastformation rate was sometimes low in cases over 70 years old. It was not considered appropriate, therefore, to analyse blastformation rates without respect to age, so all of following results are for those under 70 years of age.

The preoperative blastformation rate in gastrointestinal cancer patients was, as already reported previously (4), markedly low about 1/2 that of normal individuals or patients with diseases other than cancer.

The relationship between the preoperative blastformation rate and the stage classification at the time of operation in 291 cases of gastric cancer was as follows: the blastformation rate at Stages I, II, III, and IV was  $51.1 \pm 15.5$ ,  $45.9 \pm 17.3$ ,  $41.3 \pm 15.0$  and  $27.8 \pm 14.4\%$  respectively, indicating that the blastformation rate decreased as gastric cancer advanced (Fig. 1). The blastformation rate in 80 cases of Stage I and II, all of whom received curative resection, was  $49.3 \pm 16.9\%$ , while 38 of 57 cases of Stage III and 9 of 84 cases of Stage IV all of whom underwent curative resection had preoperative blastformation rates of  $46.6 \pm 16.5\%$ . When the cases of Stage IV were divided resectable and non-resectable groups, the blastformation rate was  $36.5 \pm 16.3\%$  in the former and  $27.8 \pm 14.4\%$  in the latter. Cases of gastric cancer undergoing curative resection with preoperative blastformation rates over 40% decreased in number with cancer advance. An unexpected finding was that, in the cases Stage II gastric cancer in which

curative resection had been almost always possible, number with a blastformation rate of greater than 40% was extremely low (Table 1).

With colon cancer, the preoperative blastformation rate in 47 cases of curative resection was  $48.6 \pm 14.3\%$ ,  $35.7 \pm 13.3\%$  in 23 cases of noncurative resection, and  $25.4 \pm 11.4\%$  in 32 cases of the nonresectable group. These results show a more clear-cut trend than that seen in the gastric cancer patients (Fig. 2). In cases of colon cancer (including advanced cases) which underwent curative resection, the numbers with preoperative blastformation rates over 40% were higher than in gastric cancer cases (Table 1).

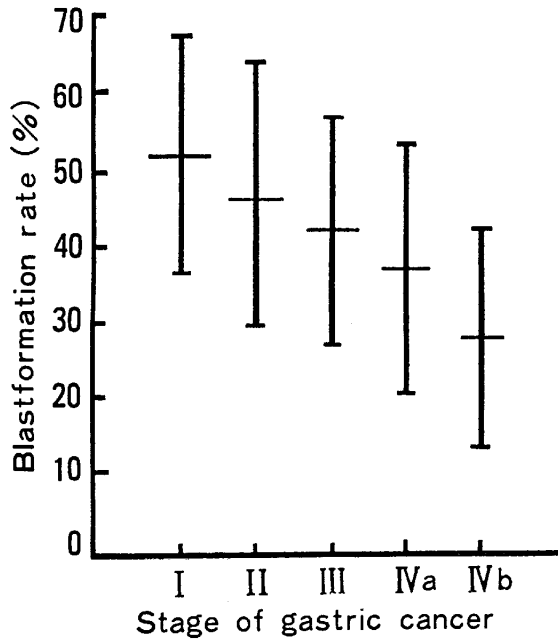


Fig. 1. Advance of gastric cancer and blastformation rate. Numbers of cases of the stage I, II, III, IVa and IVb are 43, 37, 57, 84 and 70, respectively. Data indicate mean  $\pm$  S.D. IVa, resectable; IVb, nonresectable.

TABLE 1. FREQUENCY OF CASES WITH THE BLASTFORMATION RATE OF OVER 40% IN THOSE UNDERGOING CURATIVE RESECTION OF GASTROINTESTINAL CANCER

Diseases	No. of cases	%	
Gastric cancer (Stage)	I	35/43	81.4
	II	25/37	67.6
	III	25/38	65.8
	IV	5/9	55.6
Colon cancer	39/47	83.0	

} 70.9  
 } 74.1

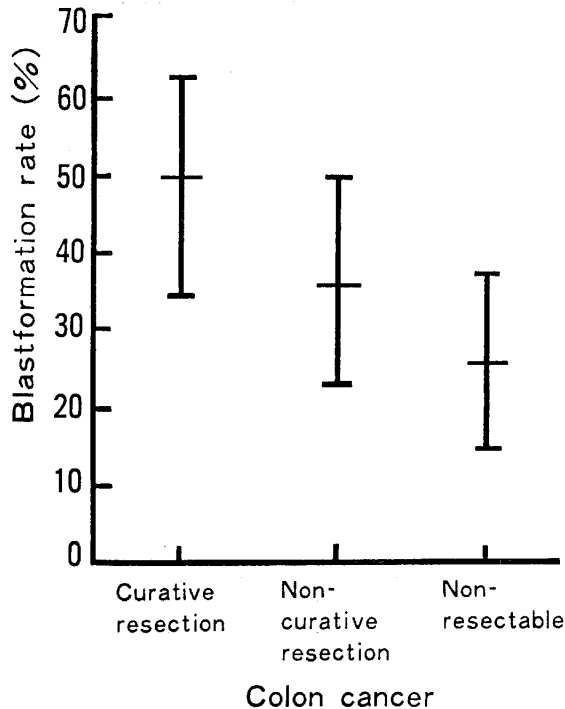


Fig. 2. Advance of colon cancer and blastformation rate. Numbers of cases are 47 for curative resection, 23 for noncurative resection and 32 for nonresectable cases. Data indicate mean  $\pm$  S.D.

The overall results for preoperative blastformation rates in this series of gastrointestinal cancers were: curative resection,  $47.2 \pm 15.7\%$  and nonresectable operation,  $27.1 \pm 13.5\%$ .

#### DISCUSSION

An immunological approach to the clinical assessment of cancer is being developed and, at present, is based on cell-mediated immunity. Specific immune tests for estimating this cell-mediated immunity include macrophage migration inhibition test (8) and the mixed lymphocyte tumor cell reaction. Nonspecific tests include *in vitro* estimation of the blastformation rate of peripheral blood lymphocytes against PHA, pokeweed mitogen, or concanavalin A, the incidence of T-cells and B-cells (9), and carcinoembryonic antigen. *In vivo* tests include skin tests to mumps antigen and tetanus toxoid as well as DNCB and PPD (1-3).

The specific immune tests are based on the response of lymphocytes of the cancer-bearing patient to antigenic material from cancer of the same patient and are a good indication of the clinical condition of that cancer patient. Since the

antigenic material used is cancer tissue, however, it is not possible to assess the cancer progress by this test prior to operation.

The nonspecific immune tests reflect the response only from the cancer-bearing patient and dose not need cancer tissue. It has been reported, however, that the nonspecific immune tests using DNCB and PPD indicated fairly accurately the cancer progress and prognosis in lung and breast cancer patients (1, 10). There are, as yet, few reports of the use of immune tests with gastrointestinal cancer (3, 5, 11).

In our previous report (5), we examined 188 cases of surgery for gastric cancer, and found that when gastric cancer progressed, the blastformation rate decreased. We postulated that the preoperative blastformation rate might reflect the extent of gastric cancer such that, if the preoperative blastformation rate was over 40%, curative resection might be considered, whereas if it was less than 30%, palliative surgery should be the treatment.

In the present paper, we report that not only in gastric cancer, but also in colon cancer and in gastrointestinal cancer as a whole, the preoperative blastformation rate enabled us to determine before operation whether or not curative resection was possible. That is if the preoperative blastformation rate is over 40%, curative resection might be considered, whereas if it is less than 40% non-curative resection or nonresection should be the treatment in gastrointestinal cancer.

The blastformation rate is also useful for assessing the prognosis of gastrointestinal cancer patients. We previously reported that the blastformation rate in gastrointestinal cancer patients suddenly fell 2 months before recurrence after curative resection. So the blastformation rate should be a significant improvement in predicting recurrence of cancer if routinely monitored postoperatively (6). When the clinical course is good and cancer recurrence is avoided, the blastformation rate is maintained at over 40% in gastrointestinal cancer patients after curative resection. We intend to report in detail on this point in the near future.

*Acknowledgment.* The authors wish to express their profound thanks to Professor Sanae Tanaka for his painstaking proof reading and kind guidance throughout this work.

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