

of the twins described comparable to the other emphasize the variability of the abnormality.

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REFERENCES

- Beck, F., and Lloyd, J. B. (1966). In *Advances in Teratology*, edited by D. H. M. Woollam, vol. 1, p. 131. London.
 Boyd, J. D. (1960). *Med. Press*, 243, 157.
 Carey, E. J. (1919). *Anat. Rec.*, 16, 45.

- Curtis, A. H., and Helmholtz, H. F. (1911). *Trans. Chic. path. Soc.*, 8, 127.
 Hendricks, A. G., Axelrod, L. R., and Clayborn, L. D. (1966). *Nature (Lond.)*, 210, 958.
 Lenz, W., and Knapp, K. (1962). *Arch. environm. Hlth*, 5, 100.
 Milaire, J. (1965). In *Organogenesis*, edited by R. L. DeHaan and H. Ursprung, p. 283. New York.
 Oertel, O. (1962). *Mtschr. Kinderheilk.*, 110, 481.
 Saunders, J. W., jun., Cairns, J. M., and Gasseling, M. T. (1957). *J. Morph.*, 101, 57.
 Smithells, R. W. (1966). In *Advances in Teratology*, edited by D. H. M. Woollam, vol. 1, p. 251. London.
 Stockard, C. R. (1931). *Physical Basis of Personality*. New York.
 Zwilling, E. (1956). *Cold Spr. Harb. Symp. quant. Biol.*, 21, 349.

ABO Blood Groups and Polyps of the Colon*

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Though it appears that a significant proportion of villous adenomas or papillomas of the large bowel develop malignant properties, the debate still continues on the importance of adenomatous polyps as the sources of large-bowel cancer. Evans (1966) feels that the associations between multiple cancers of the colon and adenomatous polyps, and multiple polyps and cancer of the bowel, do not necessarily indicate an orthogenetically determined polyp-carcinoma sequence. He favours the view that they represent varying degrees of genetically determined large-bowel proneness to both cancer and adenoma.

With the exception of polyposis coli, no genetic locus has been associated with cancer of the large bowel or polyp-formation, though Veale (1965) has postulated an unfavourable allelic modifier of the polyposis gene which in double dose produces a few adenomas of the rectum or colon. The ABO locus which is implicated in the causation of cancer of the stomach (Aird *et al.*, 1953), multiple primary cancers (Fadhli and Dominguez, 1963; Tsudaka *et al.*, 1964), and possibly chronic lymphatic leukaemia or lymphoma and carcinoma of the colon (Hyman *et al.*, 1963), does not appear to be a factor in carcinoma of the colon.

This paper reports the ABO blood group distributions in 373 patients with polyps of the colon or rectum and an association between group O and papillary adenoma of the colon.

Materials and Methods

Case records of all patients seen at Columbia-Presbyterian Medical Center between 1948 and 1960; at Montefiore Hospital, Bronx, N.Y., between 1952 and 1959; and at the Bronx Veterans Hospital, Bronx, N.Y., between 1952 and 1959 who had the diagnosis of polyps of the colon or rectum were

checked. Only Caucasian patients whose blood types were known and whose polyps were removed and examined histologically were selected, and any family history of polyps or of carcinoma was carefully noted. For all cases from this centre the ABO blood groups were determined in the Presbyterian Hospital Blood Bank and were done on admission before transfusion. The cases totalled 317 from Columbia-Presbyterian Medical Center, 22 from Montefiore Hospital, and 34 from the Veterans Hospital. Follow-up was not complete, but 90% (335) of the patients were examined by barium meal, proctoscopy, or both to determine whether carcinoma or additional polyps had developed. During a five-year follow-up 58% (217) of the patients were seen several times. Patients were assigned to groups depending on pathological diagnosis, the number of polyps, and the family history.

For the purposes of this study adenomatous polyps are defined as being composed of a rounded, lobulated compact mass of branching glandular tubules, lined by columnar epithelium and supported by branching connective tissue. They are usually pedunculated, with the pedicle covered by normal mucosa (Grinnell and Lane, 1958). Papillary adenomas are defined as sessile growths, composed of innumerable branching villi clothed in stratified or pseudostratified columnar epithelium and usually covered by a coating of mucus (Grinnell and Lane, 1958).

Case records of all patients seen at Columbia-Presbyterian Medical Center between 1930 and 1966 with the diagnosis of polyposis of the colon, defined as 10 or more polyps, were checked. Of the 18 cases found 12 were examples of intestinal polyposis and seven had a positive family history. All patients with polyposis coli had their colon removed surgically and were found to have large numbers (from hundreds to thousands) of adenomatous polyps. The six patients with as few as 10 polyps have been included in the multiple polyposis group because it is thought by some (Veale, 1965; McConnell, 1966) that these patients may have inherited a weakly expressed polyposis gene.

As most of the patients were treated at the Columbia-Presbyterian Medical Centre the control group was chosen from this hospital's blood bank records. Non-profit Caucasian donors at the Presbyterian Hospital Blood Bank for the year 1960 were decided to be the most appropriate control, since the few Negroes with polyps were excluded from the study. In spite of careful selection there was a higher incidence of group B and a lower incidence of group A in the Presbyterian Hospital series than in other control groups (see Table I). This

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finding may be the expression of bias inherent in a non-profit donor group which is composed of friends and relations replacing blood used in the treatment of one of their family as well as public-spirited blood donors. Nevertheless, when this control group is compared, O to Not-O, with the pooled control groups from other regions in the U.S.A. the heterogeneity test gives $\chi^2=0.114$; $0.80>P>0.70$, and so the smaller control group has been used for the comparisons.

TABLE I.—ABO Blood Groups in Control Caucasian Populations

Group	A	B	O	AB	Total
Caucasian non-profit donors at Presbyterian Hospital in 1960 (group chosen as overall control)	928 36.8%	344 13.6%	1,122 44.4%	131 5.2%	2,525
Caucasians, Columbus, Ohio*	2,535 43.19%	539 9.19%	2,585 44.04%	210 3.58%	5,896
Caucasians, Detroit*	2,359 41.0%	683 11.9%	2,396 41.8%	299 5.2%	5,728
Caucasians, Massachusetts*	9,263 39.7%	2,465 10.6%	10,810 46.3%	794 3.4%	23,332
Caucasians, Rochester, N.Y.*	9,937 41.8%	2,394 10.1%	10,562 44.4%	894 3.8%	23,787
Caucasians, region unspecified*	8,200 41%	2,000 10%	9,000 45%	800 4%	20,000
Ranges of control populations	36.8- 43.2%	9.2- 13.6%	41.8- 46.3%	3.4- 5.2%	
Average	41.3%	10.3%	44.5%	3.8%	

* Fadhli and Dominguez (1963).

Results

The results (Table II) and the statistical analysis (Table III) are summarized below.

TABLE II.—ABO Blood Groups of Patients with Polyps

	A		B		AB		O		Total
	No.	%	No.	%	No.	%	No.	%	
A. All polyps	137	37	48	13	17	5	171	46	373
(1) Adenomatous polyps only	128	39	43	13	16	5	139	43	326
B. (2) One adenomatous polyp	76	38	25	13	9	5	87	44	197
(3) Two or more adenomatous polyps	52	40	18	14	7	5	52	40	129
C. Papillary adenomas only	2	10	3	14	0	0	16	76	21
D. Both adenomatous and papillary polyps in same patient	7	29	2	8	1	4	16	62	26
E. All patients with papillary adenoma (C+D)	9	19	5	11	1	2	32	68	47
F. Polyposis coli	6	33	1	6	0	0	11	61	18

TABLE III.—Statistical Analysis

Comparison O/Not-O	χ^2	Degree of Freedom	Significance
A. All polyps/control	0.261	1	0.70 > P > 0.60
B. Adenomatous/control polyps	0.378	1	0.60 > P > 0.50
C. Papillary adenomatous/control	8.496	1	0.005 > P > 0.001
D. Papillary/control adenomatous polyps	3.046	1	0.10 > P > 0.05
E. Groups C and D/control	10.432	1	0.005 > P > 0.001
F. Polyposis coli/control	2.012	1	0.20 > P > 0.10

A. Three hundred and seventy-three patients had one or more polyps, and there was no statistical difference in the distribution of blood groups between these and the controls.

B. Three hundred and twenty-six patients had one or more adenomatous polyps, and there was no statistical difference in the distribution of blood groups between these and the controls.

C. Twenty-one patients had one or more papillary adenomas, and 16 (76%) of these were blood group O. This increase was statistically significant ($P>0.001$) when compared with the control group.

D. Twenty-six patients had both papillary adenomas and adenomatous polyps, and 16 (62%) of these were type O. This finding was not statistically significant.

D

E. Groups C and D can be combined (heterogeneity test C+D gives $\chi^2=0.57$, $0.50>P>0.40$) to make a group of 47 patients, all of whom had at least one papillary adenoma. Thirty-two (68%) of these patients were group O, and this finding was significant ($P<0.005$). If the combined control group from other regions in the U.S.A. is used for comparison $\chi^2=10.958$, $P<0.001$.

F. Eighteen patients had multiple polyposis, and 11 (61%) of these were type O, but this increase was not statistically significant.

G. Only 16 of 373 patients with polyps had a family history of colonic carcinoma or polyps of the colon. Two of these had multiple polyposis and 13 had one or more adenomatous polyps.

Discussion

Analysis of the data indicates that the ABO blood group distributions in patients with polyps of the colon are not significantly different from control populations except in the subdivision of papillary adenomas.

The data suggest that papillary adenomas can be distinguished from adenomatous polyps, familial and non-familial, since the ABO locus is involved in the papillary adenoma group. Furthermore, this finding indicates that papillary adenomas have a different cause from adenomatous polyps in that the ABO locus is one of the polygenic factors conditioning the susceptibility to the disease.

The limitation of a study of this type is well recognized, particularly in view of the small number of patients and difficulty in selecting a proper control group because of the racial differences in blood type in the heterogeneous population of New York City. We hope that this study will stimulate further investigations of the ABO blood groups in patients with papillary adenomas and adenomatous polyps of the colon in other populations.

Summary

The ABO blood groups have been determined in 373 patients with polyps of the colon, divided into adenomatous polyps and familial and non-familial and papillary adenomas. In the two subdivisions of the adenomatous polyps the blood group distributions did not differ from the control group, but a significant excess of blood group O was found in the patients with papillary adenomas. This finding indicates that papillary adenomas have a different cause from adenomatous polyps and supports the separation, on histological and clinical grounds, of the two kinds of growths.

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REFERENCES

- Aird, I., Bentall, H. H., and Roberts, J. A. F. (1953). *Brit. med. J.*, **1**, 799.
 Evans, R. W. (1966). *Histological Appearances of Tumours*, 2nd ed. Edinburgh.
 Fadhli, H. A., and Dominguez, R. (1963). *J. Amer. med. Ass.*, **185**, 757.
 Grinnell, R. S., and Lane, N. (1958). *Int. Abstr. Surg.*, **106**, 519.
 Hyman, G. A., Ultmann, J. E., and Slanetz, C. A. (1963). *J. Amer. med. Ass.*, **186**, 1053.
 McConnell, R. B. (1966). *The Genetics of Gastro-Intestinal Disorders*, pp. 147-169. London.
 Tsukada, Y., Moore, R. H., Bross, I. D. J., Pickren, J. W., and Cohen, E. (1964). *Cancer (Philad.)*, **17**, 1229.
 Veale, A. M. O. (1965). *Intestinal Polyposis. Eugenics Laboratory Memoirs*, **XL**. London.