TECHNICAL REPORT
RERF TR 7-77
業 績 報 告 書

STOMACH CANCER SCREENING IN THE ADULT HEALTH STUDY POPULATION, HIROSHIMA, 1971-72

成人健康調査対象者の胃癌スクリーニング 広島，1971－72年

MITOSHI AKIYAMA, M.D. 秋山実利
MICHIO YAMAKIDO, M.D. 山木戸道郎
MASANORI OTAKE, Ph.D. 大竹正徳
JOSEPH L. BELSKY, M.D.
JOHN O. PASTORE, M.D.
SADAHISA KAWAMOTO, M.D. 河本定久
TATSUJIRO OKAWA, M.D. 大川辰二郎
DONALD S. DOCK, M.D.

放影研
RERF

RADIATION EFFECTS RESEARCH FOUNDATION
財団法人 放 射 線 影 響 研 究 所

A cooperative Japan - United States Research Organization
日 米 共 同 研 究 機 関

RERF TECHNICAL REPORT SERIES
放影研業績報告書集

The RERF Technical Reports provide the official bilingual statements required to meet the needs of Japanese and American staff members, consultants, and advisory groups. The Technical Report Series is not intended to supplant regular journal publication.

放影研業績報告書は，日米研究職員，顧問，諮問機関の要求に応えるための日英両語による公式報告記録である．業績報告書は通例の誌上発表論文に代わるものではない．

The Radiation Effects Research Foundation (formerly ABCC) was established in April 1975 as a private nonprofit Japanese Foundation, supported equally by the Government of Japan through the Ministry of Health and Welfare, and the Government of the United States through the National Academy of Sciences under contract with the Department of Energy.

放射線影響研究所（元 ABCC）は，昭和50年4月1日に公益法人として発足したもので，その経費は日米両政府の平等分担により，日本は厚生省の補助金，米国はエネルギー省との契約に基づく米国学士院の補助金とをもって運営されている．

放影研 RERF RADIATION EFFECTS RESEARCH FOUNDATION
財団法人 放射線影響研究所

Research Project 研究課題 4-71

STOMACH CANCER SCREENING IN THE ADULT HEALTH STUDY POPULATION HIROSHIMA, 1971-72

成人健康調査対象者の胃癌スクリーニング，広島，1971－72年

MITOSHI AKIYAMA, M.D. (秋山実利)[1]*; MICHIO YAMAKIDO, M.D. (山木戸道郎)[1]*;
MASANORI, OTAKE, Ph.D. (大竹正徳)[2]; JOSEPH L. BELSKY, M.D.[1];
JOHN O. PASTORE, M.D.[1]†; SADAHISA KAWAMOTO, M.D. (河本定久)[1];
TATSUJIRO OKAWA, M.D. (大川辰二郎)[1]**; DONALD S. DOCK, M.D.[1]

Departments of Medicine[1] and Epidemiology & Statistics[2]
臨床部[1] および疫学統計部[2]

SUMMARY

Examinations for parietal cell antibody (PCA) were performed on 1334 subjects of the Adult Health Study (AHS), Hiroshima, during a 1-year period. Findings revealed PCA in 112 subjects (8.4%), but no difference in frequency was noted by sex. The relationship of PCA to age showed the positive rate to be significantly higher in those age 50 or over than in those under 50. No correlation was noted between estimated A-bomb exposure dose and PCA frequency. PCA was found in 58 (11.6%) of the 502 cases presenting achlorhydria on tubeless gastric analysis, and particularly in the age 50 and over group, PCA was demonstrated in 43 (14.2%) of the 302 subjects presenting achlorhydria, which is a significant difference compared with the under 50 age group in which PCA was demonstrated in 15 (7.5%) of 200 such subjects. PCA was detected in 11 (7.2%) of 152 subjects with abnormal, or low, serum pepsinogen levels and in 20 (16.3%) of 123 subjects with high levels. In particular, whereas PCA was found in 11 (13.9%) of 79 subjects presenting a low serum pepsinogen value in the age 50 and over group, there was no positive subject in the under 50

要 約

1年間に検査を受けた広島の成人健康調査対象者のうち，1,334名について胃側壁細胞抗体を検索し，112名(8.4%)に胃側壁細胞抗体を認めたが，性別による頻度の差はなかった．年齢と胃側壁細胞抗体の関係は50歳以上の者はそれ未満の者よりも有意に高い陽性率であった．原爆放射線推定被曝線量と胃側壁細胞抗体頻度の間には相関を認めなかった．無胃管胃液酸度測定で無酸症を示した502名中58名(11.6%)に胃側壁細胞抗体を認め，特に50歳以上で無酸症を示した302名中43名(14.2%)に同抗体を証明し，50歳未満の200名中15名(7.5%)に比べ有意の差が認められた．血清ペプシノーゲン値の異常者，すなわち，低値・高値者では，それぞれ152名中11名(7.2%)，123名中20名(16.3%)に同抗体を認めた．特に50歳以上の者で低血清ペプシノーゲン値を示したものでは同抗体を79名中11名(13.9%)に認めたの

* *Department of Internal Medicine, Hiroshima University School of Medicine* 広島大学医学部内科
** *Chief, Department of Internal Medicine, Saeki Hospital* 佐伯病院内科部長
† *Surgeon, U.S. Public Health Service, Bureau of Radiological Health, Division of Biological Effects, assigned to ABCC.* 米国公衆衛生局放射線保健部生物学的影響研究部門所属医師でABCCへ派遣

Approved 承認 16 June 1977

Printed 印刷 April 1978

age group. The frequency of positive PCA in subjects presenting achlorhydria and abnormal (low or high) serum pepsinogen levels was 19 (19.0%) in 100, which was significantly higher than 7 (6.6%) in 106 in those subjects in whom gastric acidity and serum pepsinogen levels were both normal. The frequency of positive PCA was higher in patients diagnosed on upper gastrointestinal (GI) series as atrophic gastritis than in patients diagnosed as some other gastric disorder.

PCA was negative in both of the two cases in whom a definite diagnosis of stomach cancer was established. However, in light of the finding of abnormal Diagnex Blue (DB) tests and positive PCA at a high frequency in the gastritis group and reports that gastritis provides the groundwork for stomach cancer, it is considered that care should be taken in cases with findings of abnormal DB test, abnormal serum pepsinogen levels, and positive PCA.

INTRODUCTION

A report has been made on the long-term follow-up of AHS subjects who had serum pepsin and tubeless gastric analysis determinations during 1959-62.[1] In that paper it was made evident that the risk for gastric carcinoma was increased in individuals with abnormal results of these two tests, and that a combination of low serum pepsin and an abnormal DB test provided an especially strong risk prediction. Because of the obvious interests in developing an effective screening device for the early detection of this common malignancy, it was decided to establish a prospective investigation of the use of these two tests plus a third, parietal cell antibody, with follow-up confirmation of suspect cases by gastrointestinal X-rays and gastroscopy.

SAMPLE AND TEST METHODS

During May 1971 to May 1972, the AHS subjects, with the exception of those giving a history of previous gastrectomy, were asked to volunteer for DB tests, serum pepsin, and parietal cell antibody determinations. The DB test was performed as described previously.[2] During the months May 1971 through August 1971 a repeat DB test was advised in initially negative cases (by convention an abnormal result, considered suggestive of decreased or absent gastric acid secretion, is termed a "negative" result), and two such abnormal DB tests were an indication for

に対し，50歳未満では陽性者はなかった．無酸症を呈し，血清ペプシノーゲン値が異常（低値または高値）を示したものの胃側壁細胞抗体陽性頻度は100名中19名（19.0%）であり，胃酸度および血清ペプシノーゲン値が共に正常であった106名中7名（6.6%）より有意に高値を示した．上部消化管X線検査で萎縮性胃炎と診断された患者は他の胃疾患と診断されたものより胃側壁細胞抗体検査陽性頻度が高かった．

胃癌と確定診断された2名はいずれも胃側壁細胞抗体検査は陰性であった．しかし，DB検査異常，胃側壁細胞抗体検査陽性が胃炎群に高頻度に認められたことは，胃炎が胃癌の母地になるとも報告されており，DB検査異常，血清ペプシノーゲン異常，胃側壁細胞抗体検査陽性の場合は注意する必要があると考えられた．

緒　言

1959—62年の間に血清ペプシン測定および無胃管胃液酸度（Diagnex Blue — DB）測定検査を受けた成人健康調査対象者について，長期間の追跡調査の結果が報告[1]されている．この報告書では，上記二つの検査結果が異常である者においては胃癌の危険率が増加しており，また，血清ペプシン値が低くDB検査結果が異常である場合には特に高い危険率が予知されることが明らかにされた．頻度の高いこの悪性疾患を早期に発見するためには効果的なスクリーニング方法を開発することに当然関心がよせられ，上記の二つの検査に第三の検査として胃側壁細胞抗体（Parietal Cell Antibody — PCA）検査を加え，計画調査を行うと共に，上部消化管X線検査および胃鏡検査によって疑わしい症例の追跡確認を行うことが決定された．

調査標本および検査方法

1971年5月から1972年5月の間，成人健康調査対象者で胃切除術を受けた者を除いた者に，DB検査，血清ペプシン検査および胃側壁細胞抗体検査を受けるよう求めた．DB検査は前報[2]のように行われた．1971年5月から8月までの間，最初の検査で陰性の結果が出た者（胃酸分泌の減少，または欠如は異常な結果であると考えられているが，慣例的に「陰性」と呼ばれている）にはあらためてDB検査を受けるよう勧めた．そしてDB検査結果が二度異常を示した

advising upper GI series. From September 1971 through May 1972 only one abnormal DB test plus a low pepsinogen value was the agreed indication for GI series. Serum pepsinogen was determined by the method of Wenger and Munro (see Appendix). This method is different from that used to estimate serum pepsin in an earlier ABCC publication[1] and the units used in the present report are for this reason not comparable.[3] A discussion of the normal range of pepsinogen values by the Wenger and Munro method as used here is provided in the Appendix.

Parietal cell antibody was determined by the indirect fluorescent method of Coons and Kaplan[4] as follows:

1) A frozen section of rat stomach was exposed to the test serum for 30 minutes at room temperature and then washed twice for 15 minutes with phosphate-buffered saline (PBS).
2) The specimen was then covered with fluorescent-labelled anti-human gamma-globulin serum for 30 minutes at room temperature and was then again washed twice with PBS.
3) The specimen was then sealed in PBS-glycerine (1:9) and examined under a microscope.

The test was considered positive when an entire population of clearly distinguished parietal cells emitted strong fluorescence. The result was considered negative when the fluorescence was faint or when the individual cells could not be clearly distinguished.

RESULTS

Parietal Cell Antibody. During 20 May 1971 to 31 May 1972, blood samples from 1334 members of the AHS population were analyzed for PCA, and the findings are shown in Table 1. Positive results were found in 8.4% of this group, with no significant difference between the sexes, ($P>0.1$) but a significantly greater ($P<0.001$) prevalence in the group over 50 years of age. Table 2 indicates the relationship between PCA analysis and A-bomb radiation exposure dose, and it is clear that there is no difference in the prevalence of antibody in the different exposure groups ($P>0.1$).

場合は，上部消化管X線検査を受けるよう勧めた．1971年9月から1972年5月の間は，DB検査が一度異常を示し，ペプシノーゲン値が低い場合に上部消化管X線検査を勧めた．血清ペプシノーゲンはWengerおよびMunroの方法(付録参照)によって測定した．この方法は，さきのABCC報告[1]の中での血清ペプシン値推定のために用いた方法とは異なるので，本報告で用いている単位では前者と比較できない．[3] 本書ではWengerおよびMunroの方法によってペプシノーゲン値を測定したが，その正常範囲に関する説明は付録で示した．

胃側壁細胞抗体は下記のようにCoonsおよびKaplan[4]の間接的蛍光法を用いて測定した．

1) 凍結したねずみの胃の切片を室温で30分間被検血清と反応させた後，燐酸緩衝食塩水(PBS)で15分間ずつ二度洗浄した．
2) その後標本を室温で30分間，蛍光色素で標識した抗ヒトガンマーグロブリン血清に浸し，再びPBSで二度洗浄した．
3) PBSグリセリン液(1：9)の中に密閉し，顕微鏡検査を行った．

胃側壁細胞全部が明確に識別でき強い蛍光を放出した場合，検査結果は陽性とみなした．蛍光が弱いか，または個々の細胞が明確に識別できなかった場合は，結果は陰性とみなした．

結　果

胃側壁細胞抗体(PCA)． 1971年5月20日から1972年5月31日の間，1,334人の成人健康調査対象者から採取した血液標本を解析し，胃側壁細胞抗体について調べた．その結果は表1に示す．被検者の8.4％が陽性を示し，男女の間に有意な差はなかった($P>0.1$)が，50歳以上の者の群では頻度が有意に高かった($P<0.001$)．表2は胃側壁細胞抗体検査と原爆放射線被曝の関係を示しており，これによると，被曝線量群別の抗体頻度に差がないことは明らかである ($P>0.1$)．

TABLE 1 PARIETAL CELL ANTIBODY (PCA) FINDINGS BY AGE AT EXAMINATION & SEX

表 1　胃側壁細胞抗体の検査結果；検査時年齢および性別

PCA	Total	Age	
		<50	50+
	Total		
Positive	112	41	71
%	8.4	6.0*	11.0*
Negative	1222	646	576
Total	1334	687	647
	Male		
Positive	39	15	24
%	7.1NS	4.9	10.0
Negative	507	291	216
Total	546	306	240
	Female		
Positive	73	26	47
%	9.3NS	6.8	11.6
Negative	715	355	360
Total	788	381	407

* $P < 0.001$
NS $P > 0.1$

TABLE 2 PARIETAL CELL ANTIBODY (PCA) FINDINGS BY AGE AT EXAMINATION & RADIATION DOSE

表 2　胃側壁細胞抗体の検査結果；検査時年齢および放射線量別

PCA	Total	Not in City	T65 Dose in rad				
			<1	1-49	50-99	100+	Unk
			All Ages				
Positive	112	31	28	30	8	12	3
%	8.4	9.1NS	8.6NS	8.8 NS	7.7NS	6.5NS	7.9NS
Negative	1222	309	297	312	96	173	35
Total	1334	340	325	342	104	185	38
			Age <50				
Positive	41	14	10	11	2	4	0
%	6.0	8.0	6.6	6.4	3.6	3.6	0.0
Negative	646	162	141	160	53	108	22
Total	687	176	151	171	55	112	22
			Age 50+				
Positive	71	17	18	19	6	8	3
%	11.0	10.4	10.3	11.1	12.2	11.0	18.8
Negative	576	147	156	152	43	65	13
Total	647	164	174	171	49	73	16

NS $P > 0.1$

Diagnex Blue Test. Of the 1334 subjects whose serum was analyzed for PCA, 428 refused the DB test or the test was not performed for other reasons.

Of the 906 DB tests performed 502 (55.4%) were negative, 107 (12.0%) were equivocal, and gastric acid production was found to be positive in 297 (33.8%). With separation into the two older and younger age groups there appears to be a greater frequency of negative ("achlorhydria") DB tests among the individuals over 50 years of age ($P<0.01$).

Regarding the interrelationships of these two laboratory tests Table 3 shows that parietal cell antibodies were more frequent among individuals with negative DB tests than in those with slight or normal acid production. This tendency seemed most apparent in the group over 50 years of age although the difference was not statistically significant ($P>0.1$).

Diagnex Blue 検査. 胃側壁細胞抗体についてPCA血清検査を行った1,334人の対象者のうち，428名が拒否またはその他の理由でDB検査を受けなかった．

DB検査を行った906名のうち502名(55.4%)は陰性，107名(12.0%)は不明瞭で，胃酸生産が陽性であったのは297名(33.8%)であったことがわかった．老年群と若年群に分けると，50歳以上の群にはDB検査の陰性(無酸症)頻度が大きいようである($P<0.01$)．

これら二つの検査の相互関係について，表3は，軽度または正常な胃酸生産の人よりもDB検査の結果が陰性だった人の方が胃側壁細胞抗体の頻度が高いことを示している．この傾向は50歳以上の年齢群に最も顕著であるが，その差は統計的に有意ではなかった($P>0.1$)．

TABLE 3 RELATION OF PARIETAL CELL ANTIBODY FINDINGS TO DIAGNEX BLUE (DB) TEST & AGE AT EXAMINATION

表3　胃側壁細胞抗体検査結果とDB検査結果および検査時年齢との関係

DB Test	All Ages			Age <50			Age 50+		
	Total	Positive		Total	Positive		Total	Positive	
		No.	%		No.	%		No.	%
Achlorhydria	502	58	11.6	200	15	7.5**	302	43	14.2**
Hypochlorhydria	107	7	6.5	66	3	4.5	41	4	9.6NS
Normal	297	21	7.1	179	10	5.6	118	11	9.3NS
Test not done	428	26	6.1	242	13	5.4	186	13	7.0
Total	1334	112	8.4	687	41	6.0	647	71	11.0

** $P<0.01$
NS $P>0.1$

Serum Pepsin. Of the 1334 individuals who had PCA analyses, there were 461 subjects for whom serum pepsin results are not available. Data concerning pepsinogen levels in the remaining 873 individuals are given in Table 4. Using the range of normal values discussed in the Appendix, 152 subjects had serum pepsin levels below the normal limit of 880 tyrosine units. Of this number in the low pepsin group all 11 of those with demonstrated parietal cell antibodies were in the over 50 age group ($P<0.01$). The highest percentage of PCA positive subjects were among those in the high serum pepsin category (17.2%).

血清ペプシン. 胃側壁細胞抗体検査を受けた1,334名のうち，461名については血清ペプシン定量は得られなかった．残りの873名のペプシノーゲン値は表4に示した．付録で説明した正常値の範囲を用いて検討した結果，血清ペプシン値が880チロジン単位の正常範囲以下であったのは152名であった．低ペプシン値を示した者のうち，胃側壁細胞抗体を示した11名は全員50歳以上であった($P<0.01$)．胃側壁細胞抗体検査陽性者の割合が最も多く認められたのは，高血清ペプシン群の者であった(17.2%)．

TABLE 4 RELATION OF PARIETAL CELL ANTIBODY FINDINGS TO PEPSINOGEN LEVEL & AGE AT EXAMINATION

表4　胃側壁細胞抗体検査結果とペプシノーゲン値および検査時年齢との関係

Pepsinogen Level	All Ages			Age <50			Age 50+		
	Total	Positive		Total	Positive		Total	Positive	
		No.	%		No.	%		No.	%
Low (<880)	152	11	7.2	73	0	.0**	79	11	13.9**
Normal (880-1969)	598	44	7.4	333	17	5.1***	265	27	10.2***
High (1970+)	123	20	16.3	59	9	15.3NS	64	11	17.2NS
Test not done	461	37	8.0	222	15	6.8	239	22	9.2
Total	1334	112	8.4	687	41	6.0	647	71	11.0

** $P<0.01$　　*** $P<0.05$　　NS $P>0.1$

Combination of PCA, DB, and Serum Pepsin Analyses. All three of the basic stomach cancer screening tests were received by 508 subjects. The appropriate data are given in Table 5 and it is again apparent that while most of the PCA positives were within the normal serum pepsin range, the prevalence of PCA positives were higher in the high pepsin group ($P<0.05$). Also, the largest number of PCA-positive DB-negative subjects were within the normal serum pepsin range.

Relationship Between Parietal Cell Antibody and Findings on GI Series. Upper GI series were performed on 283 individuals with PCA determinations. Of these PCA tests 30 were positive for antibody, with half appearing in the normal GI series group and 12 in those with the X-ray diagnosis of gastritis, gastric atrophy, or prominent rugae. The PCA test was positive in none of the cases with X-ray suspicion of gastric carcinoma and of these there were two, both negative (i.e., "achlorhydria") on DB test, who were later shown to have documented cancer and the others were benign polyp and erosion. Of those with normal GI series 90.5% were PCA negative.

Regarding the important question as to whether a positive test for parietal cell antibody helps in identifying individuals with atrophic gastritis, it is of interest that, as seen in Table 6, whereas 15 of 158 (9.5%) individuals with normal GI series had circulating antibodies, a higher percentage (19.4%) of those with X-ray demonstrated gastritis had this laboratory abnormality ($P<0.05$).

胃側壁細胞抗体，DBおよび血清ペプシン検査の組み合わせ． 基本的な胃癌スクリーニング検査3種類全部を受けたのは508名で，その資料は表5に示してある．これによっても，ほとんどの胃側壁細胞抗体検査陽性者の血清ペプシン値が正常範囲内でありながら，同抗体検査陽性の頻度は高ペプシン群の方が高かった（$P<0.05$）．また，同抗体検査陽性でかつDB陰性者の多くは血清ペプシン値が正常範囲内であった．

胃側壁細胞抗体と上部消化管X線検査結果の関係． 上部消化管X線検査は，胃側壁細胞抗体検査を受けた者の中から283名について行った．そのうち30名が抗体陽性で，その半分は上部消化管X線検査結果が正常で，12名は胃炎，胃萎縮，または，胃褶隆起と診断されていた．X線検査で胃癌の疑いのあった症例には胃側壁細胞抗体検査の結果が陽性であった者はなかった．この中にはDB検査が陰性（無酸症）で，後に癌であることが分かった症例が2例あった．その他は良性ポリープおよび糜爛例であった．上部消化管X線検査の結果が正常であった者の90.5%の胃側壁細胞抗体検査結果は陰性であった．

萎縮性胃炎の患者を見分ける上で胃側壁細胞抗体陽性の結果が利用できるかどうかという重要な問題に関連して，表6にみられるとおり，158名中15名（9.5%）の上部消化管X線検査正常者に循環抗体が認められたが，X線検査の結果胃炎が証明された者では，もっと高い割合（19.4%）で抗体検査の異常が認められた（$P<0.05$）という興味ある所見が得られた．

TABLE 5 RELATION OF POSITIVE PARIETAL CELL ANTIBODY (PCA) FINDINGS TO DIAGNEX BLUE (DB) TEST & PEPSINOGEN LEVEL, ALL AGES

表 5　胃側壁細胞抗体検査結果と DB 検査結果およびペプシノーゲン値との関係，全年齢

Pepsinogen Level	Total			Result of DB Test								
				Normal			Hypochlorhydria			Achlorhydria		
	Total	Positive PCA		Total	Positive PCA		Total	Positive PCA		Total	Positive PCA	
		No.	%		No.	%		No.	%		No.	%
Low (<880)	92	9	9.8***	29	0	0.0	12	0	0.0	51	9	17.7
Normal (880-1969)	340	32	9.4***	106	7	6.6	46	3	6.5	188	22	11.7
High (1970+)	76	14	18.4***	19	4	21.1	8	0	0.0	49	10	20.4
Total	508	55	10.8	154	11	7.1	66	3	4.5	288	41	14.2

*** $P < 0.05$

TABLE 6 RESULTS OF X-RAY EXAMINATION OF UPPER GASTROINTESTINAL (GI) SERIES BY PARIETAL CELL ANTIBODY (PCA) FINDINGS

表 6　上部消化管 X 線検査結果；胃側壁細胞抗体検査結果別

X-ray Diagnosis of Upper GI Series ACR†	Total		Positive PCA	
	No.	%	No.	%
Normal (110, 140)	158	54.1	15	9.5***
Stomach ulcer, niche or erosion (251, 254, 255)	19	6.5	1	5.3***
Stomach polyp (311)	23	7.9	1	4.3***
Stomach cancer (321)	7	2.4	0	0***
Gastritis, gastric atrophy, prominent rugae (290)	62	21.2	12	19.4***
Other	23	7.9	3	13.0
Total	292‡	100.0	32	11.0
Persons	283		30	10.6

† American College of Radiology Code

‡ Total number of diagnoses

*** $P < 0.05$

Relationship Between Results of GI Series, PCA Analysis, and DB Test. There were 243 individuals who underwent X-ray examination, for which abnormal DB tests were one indication for referral. Of these, 222 had abnormal DB tests and of this group 23.0% had X-ray evidence of gastritis (Table 7). On the other hand, among 21 X-rayed subjects with normal DB tests 3 (14.3%) had evidence of gastritis. The added impact of the documentation of circulating antibodies is again noted with the observation that the percentage of those with atrophic gastritis rises to 32.0% among those DB abnormals with a positive PCA test.

上部消化管 X 線検査，胃側壁細胞抗体検査および DB 検査の結果の間における関係．X 線検査を受けたのは 243 名であって，その検査が要求された理由の一つは DB 検査の異常であった．このうち DB 検査で異常を示したのは 222 名で，そのうち X 線検査の結果胃炎の認められたのは23.0%であった（表 7）．一方，DB 検査の結果が正常であった者で X 線検査を受けた21名のうち，胃炎が明らかになったのは 3 名，14.3%であった．循環抗体の検査を一つ加えたところ，DB 検査結果が異常で胃側壁細胞抗体検査が陽性を示す者における萎縮性胃炎患者の割合がこの場合も32.0%に上昇した．

TABLE 7 RESULTS OF X-RAY EXAMINATION OF UPPER GASTROINTESTINAL (GI) SERIES BY PARIETAL CELL ANTIBODY (PCA) FINDING & DIAGNEX BLUE (DB) TEST

表 7　上部消化管X線検査結果；胃側壁細胞抗体検査およびDB検査結果別

X-ray Diagnosis of Upper GI Series (ACR Code)	Result of DB Test									
	Total		Normal		Hypochlorhydria		Achlorhydria		Hypochlorhydria + Achlorhydria	
	No.	%	No.	%	No.	%	No.	%	No.	%
Total										
Normal (110, 140)	141	56.4	14	63.6	13	54.2	114	55.9	127	55.7
Stomach, ulcer, niche or erosion (251, 254, 255)	12	4.8	3	13.6	2	8.3	7	3.4	9	3.9
Stomach polyp (311)	18	7.2	1	4.5	1	4.2	16	7.8	17	7.5
Stomach cancer (321)	6	2.4	1	4.5	1	4.2	4	2.0	5	2.2
Gastritis, gastric atrophy, prominent rugae (290)	56	22.4	3	13.6	5	20.8	48	23.5	53	23.2
Other	17	6.8	0	0.0	2	8.3	15	7.4	17	7.5
Total	250*	100.0	22	100.0	24	100.0	204	100.0	228	100.0
Persons	243		21		23		199		222	
Positive PCA										
Normal (110, 140)	15	53.6	2	66.7			13	56.5	13	52.0
Stomach, ulcer, niche or erosion (251, 254, 255)	1	3.6	0	0.0			1	4.3	1	4.0
Stomach polyp (311)	1	3.6	0	0.0			1	4.3	1	4.0
Stomach cancer (321)	0	0.0	0	0.0					0	0.0
Gastritis, gastric atrophy, prominent rugae (290)	9	32.1	1	33.3	1	50.0	7	30.4	8	32.0
Other	2	7.1	0	0.0	1	50.0	1	4.3	2	8.0
Total	28*	100.0	3	100.0	2		23	100.0	25	100.0
Persons	26		3		2		21		23	
Negative PCA										
Normal (110, 140)	126	56.8	12	63.2	13	59.1	101	55.8	114	56.2
Stomach, ulcer, niche or erosion (251,254, 255)	11	5.0	3	15.8	2	9.1	6	3.3	8	3.9
Stomach polyp (311)	17	7.7	1	5.3	1	4.5	15	8.3	16	7.9
Stomach cancer (321)	6	2.7	1	5.3	1	4.5	4	2.2	5	2.5
Gastritis, gastric atrophy, prominent rugae (290)	47	21.2	2	10.5	4	18.2	41	22.7	45	22.2
Other	15	6.8	0	0.0	1	4.5	14	7.7	15	7.4
Total	222*	100.0	19	100.0	22	100.0	181	100.0	203	100.0
Persons	217		18		21		178		199	

*Total number of diagnoses

Relationship Between GI Series and Serum Pepsin Results. As noted in Table 8 serum pepsin determinations did not help in identifying individuals with X-ray evidence of atrophic gastritis, nor was there any indication that pepsin results were related to the presence of gastric ulcer by X-ray.

上部消化管X線検査と血清ペプシン検査結果との関係．表8にみられるように，血清ペプシン測定は，X線検査で萎縮性胃炎が認められた者を見分ける上では役に立たなかった．また，ペプシン検査の結果がX線で発見された胃潰瘍と関係があるという徴候も示さなかった．

Comparison Between Findings on GI Series and at Gastroscopy. Almost all 35 cases who had

上部消化管X線所見と胃鏡検法による結果の比較．表9にみられるように，35名が胃鏡検査を受けた．

TABLE 8 RELATIONSHIP BETWEEN X-RAY EXAMINATION OF GASTROINTESTINAL SERIES & PEPSINOGEN LEVEL

表8　上部消化管X線検査結果と血清ペプシノーゲン値の関係

X-ray Diagnosis	Pepsinogen Level		
	Low (<880)	Normal (880-1961)	High (1970+)
Normal	35	21	8
Atrophic gastritis	7	7	6
Ulcer niche or erosion	3	7	1

TABLE 9 RELATIONSHIP BETWEEN X-RAY EXAMINATION OF UPPER GASTROINTESTINAL (GI) SERIES & GASTROSCOPY FINDINGS

表9　上部消化管X線結果と胃鏡検査結果の関係

X-ray Diagnosis of Upper GI Series (ACR Code)	Gastroscopy				
	Atrophic gastritis, atrophic hyperplastic gastritis	Gastric polyp	Gastric ulcer	Gastric cancer	Normal
Gastritis, gastric atrophy, prominent rugae (290)	23 (65.7)	-	1 (50.0)	-	2 (33.3)
Gastric polyp (311)	4 (11.4)	12 (92.3)	-	1	2 (33.3)
Gastric ulcer, niche, or erosion (251, 254, 255)	4 (11.4)	-	1 (50.0)	-	1 (16.7)
Gastric cancer (321)	2 (5.7)	-	-	-	1 (16.7)
Normal	1 (2.9)	-	-	-	
Other	1 (2.9)	1 (7.7)	-	-	
Total	35 (100%)	13 (100%)	2 (100%)	1	6 (100%)

abnormal GI series, underwent subsequent gastroscopy, as seen in Table 9. This group included 26 of the group with gastritis, atrophy, and rugae diagnosed by X-ray, and it should be noted that diagnosis was confirmed in 23 by gastroscopy.

この35名のほとんどに上部消化管X線検査上異常があった．この中にはX線検査で診断された胃炎，萎縮および胃襞隆起を有する者26名が含まれていたが，そのうち23名が胃鏡検査によって確認されたことは注目に値する．

DISCUSSION

It is emphasized that the acceptance rate for DB and the other tests used in this screening process may well have been influenced by presence of GI symptoms and that these cases were not excluded from the study. Also, referral for GI series and gastroscopy may have been influenced by subjective complaints or the physicians' diagnostic impressions. Any extrapolation of the above results to the general AHS population would therefore not be warranted, and even the interrelationship between the test results should be interpreted with these facts in mind.

考　察

このスクリーニング検査のもとで用いられたDB検査およびその他の検査の受諾率は，胃腸の症状があった者を除外しなかったために影響されたかも知れないことを強調したい．また，上部消化管X線検査および胃鏡検査を要求したことは，自覚症状や医師の診断所感に影響されているかも知れない．したがって，上記の検査結果を用いて成人健康調査対象集団への外挿はすべきではなく，また，検査結果間の相互関係を解釈する場合も，上記のことを念頭におくべきである．

In 1972 Pastore et al described the late follow-up of a large number of AHS subjects who had undergone two tests of presumed gastric function (tubeless gastric analysis and blood pepsin determinations) approximately 10 years earlier.[1] It was found that gastric cancer was three times more frequent in males who had low pepsin levels on initial evaluation, a higher incidence of stomach cancer in both sexes among individuals with an abnormal DB test, and that risk prediction was greatly strengthened when both abnormalities were detected in a smaller subgroup. In that study the "end point" was documented cases of cancer as determined in a retrospective search for that disease among the original study group.

There were several obvious reasons for proceeding to a prospective examination of the AHS population from a similar standpoint. First of all it was hoped that closer observation of a defined high risk group would provide greater opportunity for operative cure in those individuals with very early cancer. There seems little question that a striking increase in therapeutic success is possible under such circumstances, a fact of especial importance in this population in which gastric carcinoma is so common.[5,6] Because the relationship between both an abnormal DB test and subnormal pepsin levels and gastric malignancy is thought to be through the identification of the precancerous lesion of atrophic gastritis, it has been hoped that by such screening tests a high risk group of individuals could be revealed and followed more closely. The diagnosis of atrophic gastritis can be established by upper GI X-ray and gastroscopic methods, and the modern gastroscopes available here provide biopsy capability for confirmation of both the precancerous lesion as well as early carcinoma. It was felt that a continuing investigation of gastric cancer risk factors would be useful in evaluating the importance of circulating anti-parietal cell antibodies, an immunologic response which has also been thought to be associated with the presence of atrophic gastritis.[7]

While the diagnosis of early gastric cancer is of obvious importance to the individual who may thereby benefit therapeutically, accurate clinical diagnosis is of importance also in the epidemiologic search for a possible relationship between atomic radiation and stomach cancer. In a population where this neoplasm is so common

Pastore らは1972年に，約10年前2種類の胃機能検査，すなわちDB測定および血中ペプシン検査を受けた多数の成人健康調査対象者について行ったその後の再調査について報告した.[1] この調査によって初回検査時のペプシン値が低かった男性では胃癌頻度が3倍高いこと，DB検査結果が異常であった者は男女共に胃癌発生率が高いこと，副次調査集団において両方の異常が発見された場合には危険の可能性が非常に高くなることが明らかとなった．この調査における最終目的は，最初の調査時の集団における癌を遡及的に研究，調査して，癌症例について記録を作ることにあった．

成人健康調査対象集団について同様の観点から計画調査を実施するのには，いくつかの明白な理由があった．まず第一には，高危険率群を限定して，これを注意深く観察することによって極く初期の癌を有する者の場合，外科的に治癒をもたらす機会が大きくなることが期待される．このような状況では，胃癌の発生頻度の高いこの集団にとって重要な問題である治療の成功が著しく増加することは疑う余地がない.[5,6] DB検査が異常でペプシン値が正常以下の場合の胃の悪性腫瘍との関係は，前癌病変である萎縮性胃炎の形で認められると考えられたことから，このようなスクリーニング検査の採用によって高危険率群を識別し，より注意深く追跡調査ができることが期待される．萎縮性胃炎の診断は上部消化管X線および胃鏡検査によって確定することができる．当所で使用している最新の胃鏡では前癌病変ならびに初期癌の確認のための組織切片の採取を行うことができる．最後に，胃癌危険因子を引き続き調査することによって循環胃側壁細胞抗体，すなわち萎縮性胃炎の存在と関係があると考えられている免疫反応[7]の重要性を評価する上で役に立つと考えられた．

早期胃癌の診断は，それによって治療による恩恵に浴すことができる本人にとっては明らかに重要であるが，同時に正確な臨床診断は，原爆被爆と胃癌の関係について疫学的調査を行う上でも重要である．この集団において新生物の頻度が高く，しかもその

and with the realization that there are probably multiple etiologic factors responsible for its occurrence, it is quite essential that accurate incidence data are available to relate to measured risk factors. While there is a high autopsy confirmation rate of death certification of gastric carcinoma, the possibility remains that there may be significant underdiagnosis of this malignancy on death certificates.[8] With our autopsy percentage presently at a level somewhat lower than 30.0% it is clear that every effort should be made to establish the diagnosis in living patients.

The earlier ABCC publications have outlined various controversies concerned with the physiologic interpretations and implications of the DB and serum pepsin tests, such as the question whether the "tubeless gastric analysis" really provides an estimate of gastric acid secretion. These problems will not be considered again here. On the other hand, some of the background concerning the parietal cell antibody requires comment.

It has been possible to demonstrate circulatory autoantibodies to gastric parietal cells in normal humans, with the frequency of positives increasing with age and in females.[9,10] The explanation for the presence of these antibodies is not known. It has also been evident for some years that such antibodies occur with greater frequency in paitents with pernicious anemia, diabetes mellitus, and thyroiditis.[11-19] While it might be proposed that an autoimmune process effected through parietal cell antibody could explain the development of atrophic gastritis, a lesion consistently present in pernicious anemia, the theory is inconsistent with the finding that PCA is found no more frequently in association with the gastritis or gastric carcinoma than in normal individuals.[20] Despite this uncertainty regarding the mechanism of PCA production it is important to characterize the relationship between the presence of circulating PCA, serum pepsin levels, and the results of the tubeless gastric analysis.

The results of the present study cannot be correlated closely to the publication by Pastore et al,[1] for the diagnosis of gastric cancer was the end point in that paper, and the sample of the present study was small and therefore contained only two stomach cancer cases. The identification of the cancer risk factor, atrophic gastritis,

発生の原因となる病因が多数存在するであろうと考えられる場合は，調査した危険因子との関係を明らかにするために正確な発生率資料を入手することが絶対必要である．死亡診断書記載の胃癌の剖検確認率は高いが，死亡診断書ではこの悪性腫瘍について相当の見落しがある可能性がある．[8] 現在当所の剖検率は30.0%より幾分低いので，生存中の対象者の診断を確立するためあらゆる努力を払わなければならないことは明白である．

ABCCの初期の報告では，DB検査や血清ペプシン検査の生理学的解釈や意味に関する様々な論議，例えばDB測定によって本当に胃酸分泌が推定できるかというような問題について略述している．これらの問題はここでは再度取り上げない．しかし，胃側壁細胞抗体に関する背景については説明が必要である．

正常人における胃側壁細胞に対する循環自家抗体は，年齢と共に陽性頻度が増加し，また女性において高いことが認められている．[9,10] これらの抗体の存在する理由は不明である．このような抗体の認められる頻度は，ここ数年来再生不良性貧血ならびに糖尿病および甲状腺炎の患者において高いことも認められている．[11-19] 胃側壁細胞抗体によって生じた自家免疫作用で再生不良性貧血と共に常に認められる萎縮性胃炎の発現が説明できるかも知れないが，この説は，胃炎または胃癌患者において胃側壁細胞抗体が正常人より高い頻度で起こらないという所見と矛盾する．[20] 胃側壁細胞抗体産生の機序についてはまだ不明ではあるが，循環胃側壁細胞抗体の存在と血清ペプシン値ならびにDB測定結果の間の関係について特徴を明らかにすることは重要である．

本調査結果と Pastore ら[1] による報告を密接に関係づけることは不可能である．その理由は，Pastore の報告では胃癌の診断が最終的な目的であった反面，本調査の集団が小さく胃癌の症例が2例しかなかっ

was the primary goal in the study described herein.

As noted there is an indication that in the group of individuals who took the test the DB determination assisted in identifying a number with X-ray evidence of gastritis, and combining DB and PCA screening tests further identified those with this risk factor. There is no means for estimating false negatives without subjecting a sample to X-ray examination irrespective of DB and PCA test results. On the other hand, it is seen that we failed to find parietal cell antibodies in 45 of 53 individuals (85.0%) with abnormal DB results and X-ray demonstrated atrophic gastritis. It is also of interest, though it cannot be examined statistically, that one individual with gastritis and circulating antibodies had a normal DB test. Serum pepsin determiantion were not useful in the identification of atrophic gastritis.

たからである．癌の危険因子である萎縮性胃炎を確認することが，本調査の主要な目的であった．

検査を受けた者では，DB測定が，X線検査所見で胃炎と認められた者数例を確認する上で役に立ち，DB検査および胃側壁細胞抗体検査の組み合わせで，この危険要因を持つ者をさらに多く確認することができた．DB検査および胃側壁細胞抗体検査の結果に関係なく調査対象者にX線検査を受けさせる以外には偽陰性例を識別する方法はない．反面DB検査結果が異常で，X線検査で萎縮性胃炎が認められた53名のうち45名(85.0%)に胃側壁細胞抗体を発見することができなかった．また，統計的に検討を加えることはできないが，興味深いことに，胃炎にかかっており循環抗体があるにもかかわらずDB検査の結果が正常を示した者が1名いた．血清ペプシン測定値は，萎縮性胃炎を確認する上で役に立たなかった．

APPENDIX
付　録

NORMAL RANGE OF PEPSINOGEN VALUES

A normal range of serum pepsinogen as a standard method was determined by assuming that the value of pepsinogen is normally distributed with a mean and a variance.[1,2] The distribution of serum pepsinogen is considered as log-normal, because a big difference in the relation between observed and expected values of actual serum pepsinogen was noted. Certainly, log-values transferred the actual values of pepsinogen for 1341 subjects who were examined between 1 September 1971 and 1 June 1972 for the AHS in both cities[3] give a good fit in the association between observed and theoretical values (Figure 1). Accordingly, we can assume that the log-values transferred are normally distributed with mean 7.2 and variance 0.17.

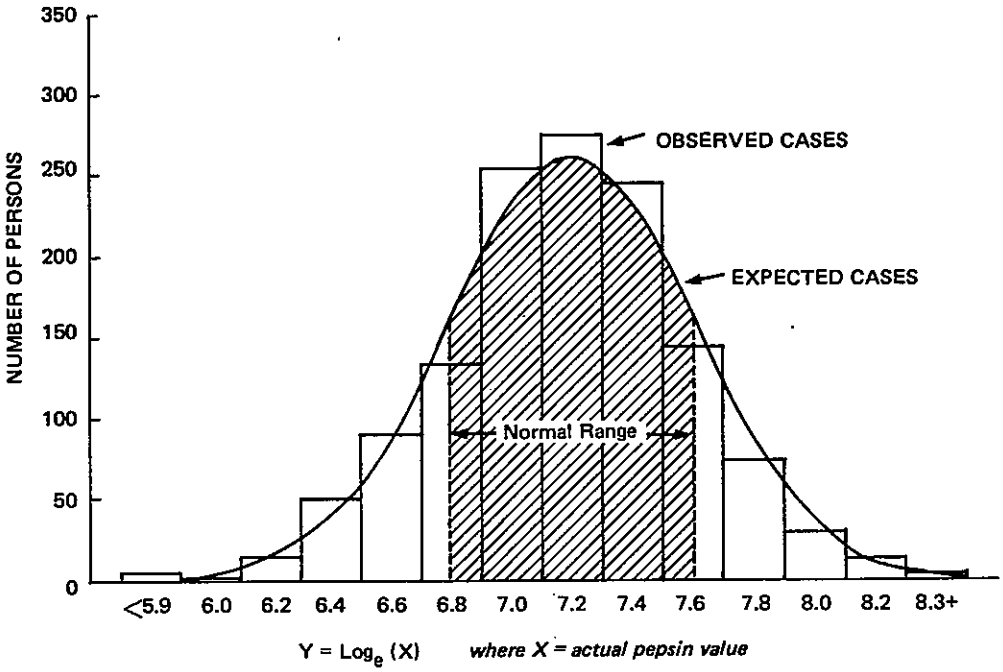
The results of serum pepsinogen were divided into three categories with low, normal, and high levels. The normal range was defined within the limits from 6.8 to 7.6 (mean ± standard deviation) with actual values of pepsinogen from 880 to 1969 tyrosine units. The low level was defined by less than 880 tyrosine units. Similarly, high level was determined with 1970 tyrosine and over.

ペプシノーゲン値の正常範囲

標準方法での血清ペプシノーゲン値の正常範囲は，ペプシノーゲン値が平均値と分散をもって正規分布すると仮定して定められた．[1,2] 血清ペプシノーゲンの観察値と期待値の間には大きな相違が認められることからみて，血清ペプシノーゲンの分布は対数正規であるとみなされる．確かに，両市の成人健康調査集団において，1971年9月1日から1972年6月1日の期間中に検査を受けた対象者1,341例に対する測定ペプシノーゲン値を変換した対数測定値は，測定値と理論値との関係においてよい適合性を認めた(図1)．[3] したがって，対数変換値は平均値7.2，分散0.17をもって正規分布すると仮定することができる．

血清ペプシノーゲン値は，低値，正常値，高値の三つに分類した．正常範囲は6.8－7.6（平均値±標準偏差）内と定め，その場合のペプシノーゲンの実際の値は880－1969チロジン単位であった．低値は880チロジン単位以下とし，同様に，高値は1970チロジン以上と定めた．

FIGURE 1 LOG-NORMAL DISTRIBUTION OF SERUM PEPSINOGEN
図 1 血清ペプシノーゲン値の対数正規分布



1. *Knittle JL: Achlorhydria in the ABCC-JNIH Adult Health Study sample, Hiroshima 1959. ABCC TR 11-60*

2. *Wenger J, Munro M: Semiautomated method for serum pepsinogen determination. Clin Chem 16:207-11, 1970*

3. *Otake M: Normal range of serum pepsinogen values and relationship of three tests for 1st D.B., Serum pepsinogen and anti-PCA, Hiroshima and Nagasaki.*
Memorandum to JL Belsky, 14 June 1972. Department of Epidemiology and Statistics Files

REFERENCES
参考文献

1. PASTORE JO, KATO H, BELSKY JL: Serum pepsin and tubeless gastric analysis as predictors of stomach cancer; A 10-year follow-up study, Hiroshima. N Engl J Med 286:279-84, 1972. (ABCC TR 19-71)

2. PASTORE JO, BELSKY JL, OTAKE M, OKAWA T, HAMILTON HB: Screening for stomach cancer in the ABCC-JNIH Adult Health Study population, Hiroshima. ABCC TR 4-72

3. KNITTLE JL: Serum pepsin levels in the ABCC-JNIH Adult Health Study sample, Hiroshima. Relation to radiation, ABO blood groups, and gastrointestinal disease. ABCC TR 12-60

4. COONS AH, KAPLAN MH: Localization of antigen in tissue cells. II. Improvements in a method for the detection of antigen by means of fluorescent antibody. J Exp Med 91:1-13, 1950

5. MURPHY ES, YASUDA A: Carcinoma of the stomach in Hiroshima, Japan. Am J Pathol 34:531-42, 1958

6. YAMAMOTO T, KATO H, ISHIDA K, TAHARA E, MCGREGOR DH: Gastric carcinoma in a fixed population, Hiroshima-Nagasaki 1961-68. ABCC TR 6-70

7. CHELI R, SANTI L, CIANCAMERLA G, CANCIANI G: A clinical and statistical follow-up study of atrophic gastritis. Digestive Disease 18:1061-65, 1973

8. BEEBE GW, YAMAMOTO T, MATSUMOTO YS, GOULD SE: ABCC-JNIH pathology studies, Hiroshima and Nagasaki. Report 2. October 1950-December 1965. ABCC TR 8-67

9. ROITT IM, DONIACH D, SHAPLAND C: Autoimmunity in pernicious anemia and atrophic gastritis. Ann NY Acad Sci 124:644-56, 1965

10. WHITTINGHAM S, IRWIN J, MACKAY IR, MARSH S, COWLING DC: Autoantibodies in healthy subjects. Aust Ann Med 18:130-4, 1969

11. IRVINE WJ, DAVIES SH, DELAMORE IW, WILLIAMS AW: Immunological relationship between pernicious anemia and thyroid disease. Br Med J 2:454-6, 1962

12. TAYLOR KB, ROITT IM, DONIACH D, COUCHMAN KG, SHAPLAND C: Autoimmune phenomena in pernicious anemia gastric antibodies. Br Med J 2:1347-52, 1962

13. DONIACH D, ROITT IM, TAYLOR KB: Autoimmune phenomena in pernicious anemia. Serological overlap with thyroiditis, thyrotoxicosis, and systemic lupus erythematosus. Br Med J 1:1374-9, 1963

14. MACKAY IR: Autoimmune serological studies in chronic gastritis and pernicious anaemia. Gut 5:23-6, 1964

15. FISHER JM, TAYLOR KB: A comparison of autoimmune phenomena in pernicious anemia and chronic atrophic gastritis. N Engl J Med 272:499-503, 1965

16. MIYOSHI A: Chronic gastritis and autoimmunity. Gendai Naikagaku Dainenkan Tsuiho (Ann Rep Mod Med, Sup) 1967-a, 68-106, 1968

17. MOORE JM, NEILSON JM: Antibodies to gastric mucosa and thyroid in diabetes mellitus. Lancet 2:645-7, 1963

18. UNGAR BA, STOCKS AE, MARTIN FIR, WHITTINGHAM S, MACKAY IR: Intrinsic factor antibody, parietal-cell antibody, and latent pernicious anaemia in diabetes mellitus. Lancet 2:415-8, 1968

19. UCHINO H, NAKATSUI T, NIIMI M, OOMAE K, SHIMIZU N: A case of pernicious anemia accompanying Hashimoto's disease. Nippon Rinsho-Jap J Clin Med 25:2779-84, 1967

20. SPIRO HM: Clinical Gastroenterology. London, Collier-MacMillan Limited, 1970. p 160