

EYEGROUND PHOTOGRAPHY IN CARDIOVASCULAR DISEASE STUDY

心 臓 血 管 疾 患 調 査 に お け る 眼 底 写 真 所 見

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EYEGROUND PHOTOGRAPHY IN CARDIOVASCULAR DISEASE STUDY

心臓血管疾患調査における眼底写真所見

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SUMMARY

A total of six color slides was made of the fundus of both eyes of 458 males, age 40 or over, who were subjects in a program of detailed biennial medical examinations during the past 8 years. A descriptive classification was used to analyze the relationship of eyeground findings to age, blood pressure, and duration of hypertension. In addition, black and white photographic prints were used to measure the caliber of the previously selected arteriole-venule (A-V) pairs for calculation of the A-V ratio. The significance of these findings were reviewed, and the following conclusions were reached.

The results obtained from the evaluation of changes based solely on six color photographs of both eyes were found to be similar to ophthalmoscopic findings, and eyeground photography is felt to be a useful epidemiologic tool.

Examination of the overall grade of changes showed the frequency of abnormal findings to increase significantly with age, blood pressure, and duration of hypertension.

Persons with fundus abnormalities had a significantly higher frequency of cardiomegaly, aortic calcification and tortuosity, and electrocardiogram abnormalities.

Generalized narrowness of arterioles and changes in venule caliber at A-V crossing were the most frequently observed abnormalities. Generalized narrowness is closely related to hypertension.

要約

過去8年間にわたって2年ごとの詳細な医学的検査を受けている40歳以上の男子458人を対象として、1人につき両眼眼底の合計6枚のカラーズライド写真を撮影した。記述的所見を分類して、眼底所見と年齢、血圧および高血圧持続期間との関係を解析した。さらに、その白黒写真を用いて、あらかじめ選定したA-V(細動脈-細静脈)対の血管口径を計測し、A/V比を算出した。これらの所見の意義を検討して次のような結論を得た。

両眼6枚のカラーズライド写真のみから得た判定成績は、検眼鏡による成績とほぼ等しいことが認められ、眼底撮影が疫学的検査として有用であると考えられる。

総合判定度を見ると、年齢、血圧および高血圧持続期間とともに異常所見出現率は有意に高くなる。

眼底異常のある者には、心拡大、大動脈の石灰化と蛇行および心電図異常が有意に多く見られた。

細動脈の瀰漫性狭細と交差部細静脈内径変化は、出現率の最も高い異常であった。瀰漫性狭細は高血圧との関係が強い。

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The A-V ratio, as an objective method of evaluating the findings, was studied in detail. This ratio, calculated for A-V pairs of the same sector, showed a significant relationship to the gross findings of the degree of generalized narrowness, which seemed to be the manifestation of generalized narrowness as reflected in the area about the optic disk. However, the A-V ratio in itself did not show any definite relation to either age, blood pressure, or duration of hypertension. That is, it was found that for certain limited cases, the A-V ratio was meaningful as a method for the numerical expression of generalized narrowness, but no further significance could be found.

No relationship was observed between the frequency of abnormal findings of the eyeground and the estimated radiation dose among A-bomb survivors.

INTRODUCTION

Cardiovascular diseases are increasing as a cause of death in Japan as elsewhere. Studies on circulatory diseases have been conducted at ABCC for several years. In 1956 plans¹ were made to conduct examinations of the eyegrounds including fundus photographs, as part of the ABCC-JNIH Adult Health Study (AHS).² In 1965, Hashimoto et al³ made a preliminary study on AHS subjects concerning the use of color photographs of the eyeground and the measurement of the caliber of retinal vessels from enlarged black and white photographic prints, and reported that such studies were feasible.

The 1962 WHO criteria⁴ for hypertension as well as other classifications for hypertension include lesions of the eyeground in addition to other target organs such as the heart, brain, and kidney. The present study⁵ was an attempt to determine the relations of 1) the degree of hypertension and 2) the duration of hypertension to lesions of the eyegrounds as interpreted from color photographs. It was also planned to determine the relationship of hypertension to the caliber of the retinal vessels.

SUBJECTS AND METHOD

Subjects. Members of the AHS sample² in Hiroshima and Nagasaki, which is comprised of 20,000 males and females living as of 1 October 1950, have had biennial medical examinations, including electrocardiograms (ECG) and chest X-ray, since July 1958. Color photographs of the eyeground were obtained on all male subjects age 40 or over who came for their routine examination over a period of 1 year beginning May 1965, except those who refused, had present or past history of eye disease, or who wore glasses.

客観的所見判定法の一つであるA/V比について詳細な検討を加えた。同一分節同士の細動脈対について算出したA/V比は、肉眼的所見である瀰漫性狭細の程度と有意な関係を示し、それは瀰漫性狭細の乳頭近辺への反映と考えられた。しかし、A/V比自体は、年齢、血圧または高血圧持続期間のいずれとも明確な関係を示さなかった。すなわち、限られた例においては、瀰漫性狭細の数量的表現としては意義があったが、それ以上のものは見いだせなかった。

原爆被爆者における眼底の異常所見出現率と推定放射線量との間の関連は認められなかった。

緒言

死因としての心臓血管疾患は、外国同様、日本においても増加の一途をたどっている。ABCCでは、過去数年間にわたり、循環器疾患に関する調査を行なっている。1956年には、ABCC-予研成人健康調査²の一環として眼底写真撮影を含む眼底検査の実施を計画した。¹ 1965年に橋本ら³は、この成人健康調査集団を対象として眼底カラー写真撮影および拡大した白黒写真による血管口径の計測などについて予備調査を行ない、それらが実施可能であることを報告した。

1962年のWHO高血圧病期分類⁴をはじめ高血圧の重症度区分には、心臓、脳および腎臓に加えて眼底病変も重要な目標臓器として取り上げられている。今回の調査⁵は、1) 高血圧の程度および 2) 高血圧の持続期間と眼底病変との関係をカラースライド写真による判読によって検討することにあった。また、高血圧と眼底血管内径の計測値との関係を決定することを意図したものであった。

対象者および方法

対象者：広島および長崎における成人健康調査対象集団²は、1950年10月1日現在生存していた男女合計20,000人で構成されており、1958年7月以来2年ごとに、心電図検査や胸部X線検査を含む医学的検査を受けている。眼底カラー写真撮影は、1965年5月から1年間にわたって定期検査を受けた40歳以上の男子で、この検査を希望しなかった者、眼疾患有病者と既往歴のある者、あるいは矯正用眼鏡使用者を除いた全員について行なわれた。

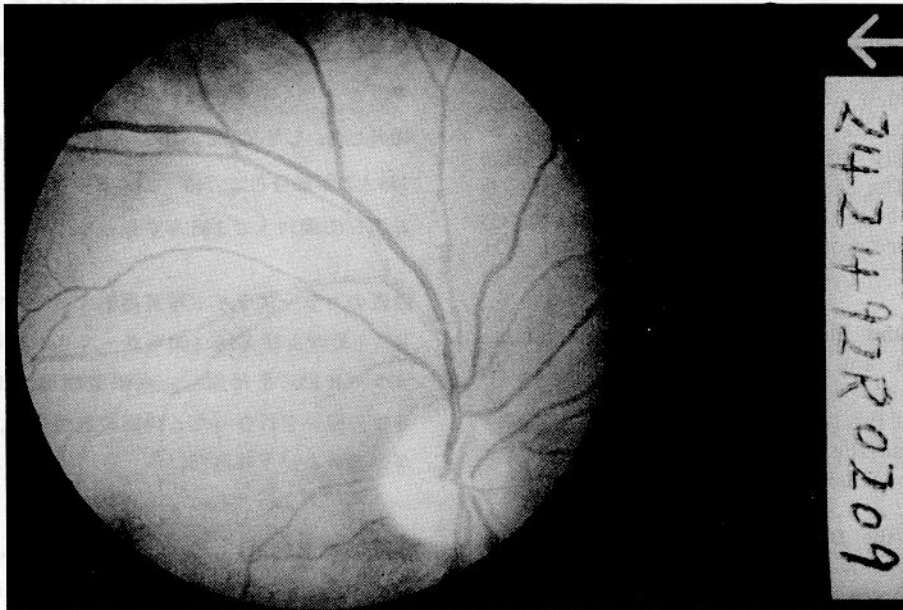


FIGURE 1 EYEGROUND PHOTOGRAPH

図1 眼底写真

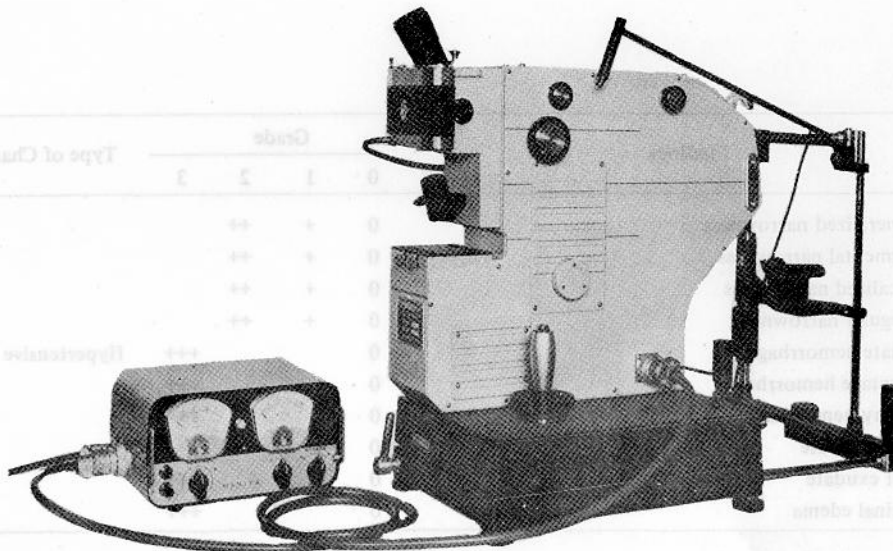


FIGURE 2 MAMIYA MIRROR FUNDUS CAMERA MODEL R1

図2 マミヤ眼底撮影カメラR-1型

Eyeground photographs were obtained for 535 subjects. Of this number 63 were excluded at the time of analysis, because of a history of renal disease, diabetes, or eye disease. Of the remaining 472 subjects, an additional 14 cases were excluded mainly for such reasons as unsatisfactory color photographs or inadequate number of photographs. Thus, ultimately there were 458 subjects available for analysis. The age distribution of the 458 subjects showed 88 to be in the 40-49 age group, 172 subjects in the 50-59 age group, and 198 subjects in the 60+ age group.

Color Eyeground Photography. A fundus camera (Mamiya R-1) and color film (Fujicolor R-100, ASA 100) were used to obtain a total of six photographs of the following sites of the dilated eye: the area around the disc, and the upper and lower temporal fields including the disc of both eyes.

Evaluation of the Description Findings. The gross findings were evaluated using the classification of findings and grades shown in the following table, which is based upon the classification of the 1961-62 Welfare Ministry Adult Disease Survey⁶ and the criteria recommended by the Research Staff on Hypertensive Fundus Committees of the Japanese Ophthalmological Society.⁷ Normal is graded as 0, and the more severe the abnormality the greater is the number of +.

眼底撮影を行ない得たのは535人であった。このうち、腎疾患、糖尿病または眼疾患の既往歴のある者63名を除外した。残りの472人のうち、さらに14人は、主としてカラースライドが不鮮明、写真枚数の不足などの理由で除外した。したがって、結局458人が解析の対象となった。458人の年齢分布は、40-49歳が88人、50-59歳が172人、および60歳以上が198人であった。

眼底のカラースライド写真撮影。マミヤ眼底撮影カメラR-1型およびASA 100カラースライド用フィルム(フジカラーR 100)を使用し、両眼散瞳後、次の部位の合計6枚の撮影を行なった：両眼の乳頭中心、乳頭を含む上耳側部および下耳側部。

記述的所見判読。肉眼的所見の判読は、1961-62年の厚生省成人病基礎調査の分類⁶および日本眼科学会高血圧眼底委員会の基準⁷を参考にして作成した下表のような所見別程度区分表に基づいて行なった。正常は0とし、異常度が強いほど+の数が増える。

| Findings | Grade | | | | Type of Change |
|---|-------|---|----|-----|-------------------------|
| | 0 | 1 | 2 | 3 | |
| I-1 Generalized narrowness | 0 | + | ++ | | |
| 2 Segmental narrowness | 0 | + | ++ | | |
| 3 Localized narrowness | 0 | + | ++ | | |
| 4 Irregular narrowness | 0 | + | ++ | | |
| II-1 Striate hemorrhage | 0 | | | +++ | Hypertensive change |
| 2 Punctate hemorrhage | 0 | | | +++ | |
| 3 Patchy hemorrhage | 0 | | | +++ | |
| III-1 Hard exudate | 0 | | ++ | | |
| 2 Soft exudate | 0 | | | +++ | |
| IV Retinal edema | 0 | | | +++ | |
| V Increased light reflection | 0 | + | ++ | +++ | |
| VI-1 Arteriole-Venule crossing, changes in Venule-caliber | 0 | + | ++ | +++ | Arteriosclerotic change |
| 2 Arteriole-Venule crossing, changes in Venule-course | 0 | + | ++ | +++ | |

Each eye was evaluated separately. The abnormalities of highest grade among findings in groups I to IV were recorded as the degree of hypertensive changes (H grade), and similarly the findings of highest grade among groups V and VI were given as the degree of arteriosclerotic changes (S grade). The higher of the H and S grades of either eye was used as the overall H and S grade for each case.

For practical purposes the H and S grades were classified into the following three groups: " H_0S_0 ", in which H and S grades were both 0; " H_1S_1 ", which included H_1S_0 and H_0S_1 in addition to H_1S_1 ; and " H_2S_2+ " in which either the H or S grade or both had changes of ++ or greater, i.e. " H_2S_2+ " is meant to indicate definite abnormal findings.

Main Arteriole and Venule. In evaluating the descriptive findings, the presence or absence of the main arteriole and venule in the upper and lower temporal fields of each eyeground was also recorded according to the 1964 WHO criteria.

Measurement of Caliber of Blood Vessels. Black and white photographs enlarged approximately 10 times were prepared for all color slides using the Mamiya reverse projector attachment on the camera used in the study. Measurements of the inner caliber of the vessels were made only on those A-V pairs which had been previously marked as suitable for calculation of A-V ratio defined as the ratio of inner caliber of arteriole and those of venule, at the time of evaluation of the findings on color photographs as mentioned below. Measurements were taken to the closest 0.1 mm. The caliber of vessels was, for reasons given later, taken at the point 1.5 disc diameters from the margin of the disc. The transverse diameter of the disc was measured to the nearest mm.

Calculation of A-V Ratio. From the record of the presence or absence of the main arteriole and venule, only the A-V pairs which satisfied WHO criteria were used for the calculation of the A-V ratio.

In a pilot study of 300 cases by the author⁸ in 1966, the primary sector of the main arteriole was found, on the average, to extend 1.75 disc diameters from the margin of the disc and that of the main venule to extend 1.5 disc diameters. (By the WHO criteria, this is the distance from the point 0.25 disc diameters from the margin of the disc to the first point of bifurcation.) Therefore, it was felt that examination at a point 1.5 disc diameters from the margin of the disc would provide a high frequency of pairs of primary sectors of the main arteriole and

判読は両眼左右別に行なった。I から IV までの所見程度の中の最も高い数字を高血圧性変化の程度 (H - grade) とし、V から VI についても同様に最も高い数字を動脈硬化性変化の程度 (S - grade) として記録した。各例の総合判定度としては、両眼のうち H および S grade とともに左右いずれかの高いほうをとった。

実際には、H および S grade を次の 3 区分に分類した: 「 H_0S_0 」, これは H および S grade がともに 0 であったもの; 「 H_1S_1 」, これは H_1S_1 であった者に加えて H_1S_0 および H_0S_1 であった者; 「 H_2S_2+ 」, これは H または S grade のいずれか、あるいはともに ++ 以上の変化を示した者である。すなわち、「 H_2S_2+ 」は明らかな異常所見を意味する。

主細動静脈. 記述的所見の判読に際しては、1964 年の WHO の基準に従い、両眼底の上下耳側部に主細動静脈が存在するかどうかをも記録した。

血管内径の計測. すべてのカラスライドは、今回の調査で使用したカメラに付属する逆投影装置を用いて約 10 倍に拡大し、白黒写真を作成した。後述するような、カラスライドにおける所見の評価にあたっては血管の計測を、細動脈と細静脈との内径の比率である A/V 比の算出に適當であるとしてあらかじめ標識された細動静脈対のみについて行ない、その内径を 0.1mm まで計測した。血管内径の計測は、後述の根拠に基づいて乳頭辺縁から 1.5 乳頭径の点において行なわれた。乳頭横径は mm まで計測した。

A/V 比の算出. 主細動静脈の有無の記録から、WHO の基準をみたす主細動静脈対のみを A/V 比の算出に用いた。

1966 年に著者は、⁸ 300 例の予備調査において主細動脈の第 1 分節長は乳頭辺縁から平均 1.75 乳頭径、および主細静脈のそれは平均 1.5 乳頭径であることを認めた。(WHO の基準では、これは乳頭辺縁から 0.25 乳頭径はなれた点から第 1 分岐点までの距離である。) したがって、乳頭辺縁より 1.5 乳頭径の点では、第 1 分節同士の主細動静脈対が求められやすいと考えられたので、今回の

venule, and thus the calculation of the A-V ratio was done at this point in the present study.

Calculations were made for the upper and the lower temporal fields of each eye in all cases. When two or more A-V ratios could be obtained in any subject, the smallest was taken to represent the ratio.

Blood Pressure at Time of Eyeground Photography.

Blood pressure measurements were taken on the right upper arm with the subject sitting. The values were classified into three groups (normotensive, borderline, and hypertensive) according to the WHO criteria.⁹

Duration of Hypertension. Most of the 458 subjects of study have had blood pressure values recorded on five occasions at the time of their regular biennial physical examinations during the past 8 years. Each of these measurements were classified according to the three groups in the WHO criteria, and scored as 0 if normotensive, 1 if borderline, and 2 if hypertensive. The sum of the scores was used as the index of duration of hypertension. For analytical purposes, a classification was made into the following three groups.

Group 1: 0-2 (Normotensive or hypertension of short duration)

Group 2: 3-6 (Hypertensive of moderate duration)

Group 3: 7+ (Hypertension of long duration)

RESULTS

Blood Pressure and Abnormal Findings. The distribution of the overall HS grades of findings by 10-year age groups and blood pressure is shown in Table 1. The proportions of definite abnormal findings are 78% in the hypertensive group, 52% in the borderline group, and 26% in the normotensive group, indicating that the proportion of abnormals increases with increased blood pressure.

In each age group, the proportion of " H_2S_2+ " is higher the higher the blood pressure. The proportion of " H_2S_2+ " increases with age in each blood pressure group.

Duration of Hypertension and Abnormal Findings.

Study was made to see whether duration of hypertension had any effect on the proportion of " H_2S_2+ " and it was found that the proportion is higher the longer the duration (Table 2).

A/V比算出はこの点において行なった。

全例について、両眼の上下耳側部の計測を行なった。同一対象者においてA/V比が二つ以上得られた場合には、最も小さい値をもって比率を代表させた。

眼底写真撮影時の血圧値。血圧測定は、座位で右上腕で行なった。血圧値はWHOの基準⁹に従い、正常血圧群、境界血圧群および高血圧群の三つに分類した。

高血圧持続期間。458人の調査対象者のほとんどは、過去8年間にわたる2年ごとの定期検診で血圧値が5回記録されている。それぞれの血圧測定値はWHOの基準の3区分に従って分類し、正常血圧値には0、境界血圧値には1、高血圧値には2の評価値を与えた。この評価値の総和を高血圧持続期間の指標とした。統計解析のため、これを次の3区分に分類した。

第1群: 0-2 (正常血圧群または短期高血圧群)

第2群: 3-6 (中等期間高血圧群)

第3群: 7以上 (長期間高血圧群)

成績

血圧値と異常所見。得られた所見の総合HS度の分布を10歳年齢階級別および血圧別に表1に示した。明らかな異常所見を有する者の割合は、高血圧群78%、境界血圧群52%、および正常血圧群26%であり、これは血圧が高いほど高率になることを示している。

各年齢群において血圧が高くなるほど「 H_2S_2+ 」の割合が高くなる。また、各血圧群においても、「 H_2S_2+ 」の割合は年齢とともに増加する。

高血圧持続期間と異常所見。高血圧持続期間が「 H_2S_2+ 」の出現率に影響を及ぼしているかどうかを検討した結果、持続期間が長いほど出現率の高いことが認められた(表2)。

TABLE 1 GRADE OF DESCRIPTIVE FINDINGS OF EYEGROUND BY AGE AT EXAMINATION
AND CASUAL BLOOD PRESSURE

表1 眼底に関する記述的所見の程度：年齢・安静時血圧別

| Age | Blood Pressure | H ₀ S ₀ | | H ₁ S ₁ | | H ₂ S ₂ ⁺ | | Total | | χ ² | Test |
|---------|----------------|-------------------------------|------|-------------------------------|------|--|------|-------|-----|----------------|------|
| | | No. | % | No. | % | No. | % | No. | % | | |
| All age | Normal | 80 | 32.0 | 106 | 42.4 | 64 | 25.6 | 250 | 100 | 109.7 | ** |
| | Borderline | 4 | 4.2 | 42 | 44.2 | 49 | 51.6 | 95 | 100 | | |
| | Hypertensive | 5 | 4.4 | 20 | 17.7 | 88 | 77.9 | 113 | 100 | | |
| | Total | 89 | 19.4 | 168 | 36.7 | 201 | 43.9 | 458 | 100 | | |
| 40-49 | Normal | 33 | 52.4 | 21 | 33.3 | 9 | 14.3 | 63 | 100 | 19.1 | ** |
| | Borderline | 2 | 12.5 | 7 | 43.8 | 7 | 43.8 | 16 | 100 | | |
| | Hypertensive | 2 | 22.2 | 1 | 11.1 | 6 | 66.7 | 9 | 100 | | |
| | Total | 37 | 42.0 | 29 | 33.0 | 22 | 25.0 | 88 | 100 | | |
| 50-59 | Normal | 28 | 27.2 | 46 | 44.7 | 29 | 28.2 | 103 | 100 | 31.4 | ** |
| | Borderline | 1 | 3.0 | 19 | 57.6 | 13 | 39.4 | 33 | 100 | | |
| | Hypertensive | 1 | 2.8 | 9 | 25.0 | 26 | 72.2 | 36 | 100 | | |
| | Total | 30 | 17.4 | 74 | 43.0 | 68 | 39.5 | 172 | 100 | | |
| 60 + | Normal | 19 | 22.6 | 39 | 46.4 | 26 | 31.0 | 84 | 100 | 47.2 | ** |
| | Borderline | 1 | 2.2 | 16 | 34.8 | 29 | 63.0 | 46 | 100 | | |
| | Hypertensive | 2 | 2.9 | 10 | 14.7 | 56 | 82.4 | 68 | 100 | | |
| | Total | 22 | 11.1 | 65 | 32.8 | 111 | 56.1 | 198 | 100 | | |

**Significant at 1% level.

TABLE 2 GRADE OF DESCRIPTIVE FINDINGS OF EYEGROUND BY AGE AND HISTORY OF BLOOD PRESSURE

表2 眼底に関する記述的所見の程度：年齢・高血圧持続期間別

| Age | History of Blood Pressure | H ₀ S ₀ | | H ₁ S ₁ | | H ₂ S ₂ ⁺ | | Total | | χ ² | Test |
|---------|---------------------------|-------------------------------|------|-------------------------------|------|--|------|-------|-----|----------------|------|
| | | No. | % | No. | % | No. | % | No. | % | | |
| All age | 0 - 2 | 80 | 29.5 | 121 | 44.6 | 70 | 25.8 | 271 | 100 | 108.0 | ** |
| | 3 - 6 | 5 | 5.2 | 35 | 36.1 | 57 | 58.8 | 97 | 100 | | |
| | 7 + | 4 | 4.4 | 12 | 13.3 | 74 | 82.2 | 90 | 100 | | |
| | Total | 89 | 19.4 | 168 | 36.7 | 201 | 43.9 | 458 | 100 | | |
| 40-49 | 0 - 2 | 34 | 49.3 | 26 | 37.7 | 9 | 13.0 | 69 | 100 | 25.9 | ** |
| | 3 - 6 | 2 | 15.4 | 3 | 23.1 | 8 | 61.5 | 13 | 100 | | |
| | 7 + | 1 | 16.7 | 0 | 0 | 5 | 83.3 | 6 | 100 | | |
| | Total | 37 | 42.7 | 29 | 33.0 | 22 | 25.0 | 88 | 100 | | |
| 50-59 | 0 - 2 | 27 | 23.7 | 56 | 49.1 | 31 | 27.2 | 114 | 100 | 28.3 | ** |
| | 3 - 6 | 2 | 8.0 | 11 | 44.0 | 12 | 48.0 | 25 | 100 | | |
| | 7 + | 1 | 3.0 | 7 | 21.2 | 25 | 75.8 | 33 | 100 | | |
| | Total | 30 | 17.4 | 74 | 43.0 | 68 | 39.5 | 172 | 100 | | |
| 60 + | 0 - 2 | 19 | 21.6 | 39 | 44.3 | 30 | 34.1 | 88 | 100 | 44.0 | ** |
| | 3 - 6 | 1 | 1.7 | 21 | 35.6 | 37 | 62.7 | 59 | 100 | | |
| | 7 + | 2 | 3.9 | 5 | 9.8 | 44 | 86.3 | 51 | 100 | | |
| | Total | 22 | 11.1 | 65 | 32.8 | 111 | 56.1 | 198 | 100 | | |

**Significant at 1% level.

Other Clinical Findings and Abnormal Findings. The relations between the grade of abnormal findings and the various clinical observations on the cardiovascular system are shown in Figure 3. The proportion of "H₂S₂+" was significantly higher in subjects with cardiomegaly, aortic calcification, and aortic tortuosity ($P < 0.01$). It was also significantly greater in the group with ECG abnormality ($P < 0.05$). Since cases with renal disease and diabetes had been excluded, the number of cases with positive findings for urine sediment, urine protein and urine sugar was small, and although the proportion of "H₂S₂+" tended to be high in the abnormal group, the difference was not statistically significant. No relationships between cholesterol values or 1-hour blood sugar levels following a 50 gm glucose challenge and the grade of eyeground findings were observed.

Distribution of Grades of Descriptive Finding. The distribution of grades of each finding in all 458 cases is summarized in Table 3. The frequency of abnormal findings of 2+ or more is highest for I-1, generalized narrowness, followed by VI-1, changes in venular caliber at A-V crossing.

Thus generalized narrowness which presented the highest frequency was taken as the index of the hypertensive change (H grade), and changes in venular caliber at A-V crossing which presented the next highest frequency was used as the index of the arteriosclerotic change (S grade) for review by age, blood pressure and duration of hypertension. The results are shown in Figure 2. The frequency of "2+" generalized narrowness increases with blood pressure and duration of hypertension. On the other hand, the frequency of "2+" and "3+" abnormalities in venular caliber at A-V crossing seems to become stabilized when hypertension has been present for a certain length of time.

A-V Ratio: The Ratio of Inner Caliber of Arteriole and Those Venule. The A-V ratios do not differ by blood pressure level and also by age as shown in Table 4.

The A-V ratio, however, is smaller the greater the grade of generalized narrowness ($P < 0.01$). This tendency was also noted in every age group.

その他の臨床所見と異常所見. 異常所見の程度と心臓血管系に関する臨床所見との関係は、図3に示すとおりである。心拡大、大動脈石灰化および蛇行のみられるものには、「H₂S₂+'の出現率が有意に高かった ($P < 0.01$)。これはまた、心電図異常群にも有意に高率にみられた ($P < 0.05$)。腎疾患および糖尿病患者は除外したので、尿沈渣、尿蛋白および尿糖の有所見者数は少なく、「H₂S₂+'の出現率はこの異常群に高い傾向を示してはいるが、統計学的に有意な差はなかった。コレステロール値および50 g ブドウ糖投与1時間後の血糖値と眼底所見の程度との間には、関係が認められなかった。

記述的所見の程度の分布. 458人全例における各所見の程度の分布は、表3に要約したとおりである。+以上の異常所見の出現率が最も高いのはI-1の瀰漫性狭細であり、ついでVI-1の交差部細静脈内径変化であった。

したがって、高血圧性変化(H-grade)の指標としては、最も出現率の高かった瀰漫性狭細をとりあげ、動脈硬化性変化(S-grade)の指標としては、次に出現率の高かった交差部内径変化をとりあげて、年齢、血圧および高血圧持続期間別に検討した。その結果は図2に示した。瀰漫性狭細の「+」の出現率は、血圧および高血圧持続期間とともに高くなる。一方、交差部における細静脈の内径変化の「++」および「+++」の出現率は高血圧がある程度長期化すると同じ値を示すようになるものと思われる。

A/V比: 細動脈と細静脈との内径の比率. 表4に示すように、A/V比には血圧値および年齢による差はない。

しかし、瀰漫性狭細が高度になるほどA/V比は小さくなる ($P < 0.01$)。この傾向はどの年齢群にも認められた。

FIGURE 3 PROPORTION OF ABNORMAL FINDINGS OF EYEGROUND BY ASSOCIATED CLINICAL FINDINGS

図 3 眼底の異常所見の割合：関連する臨床所見別

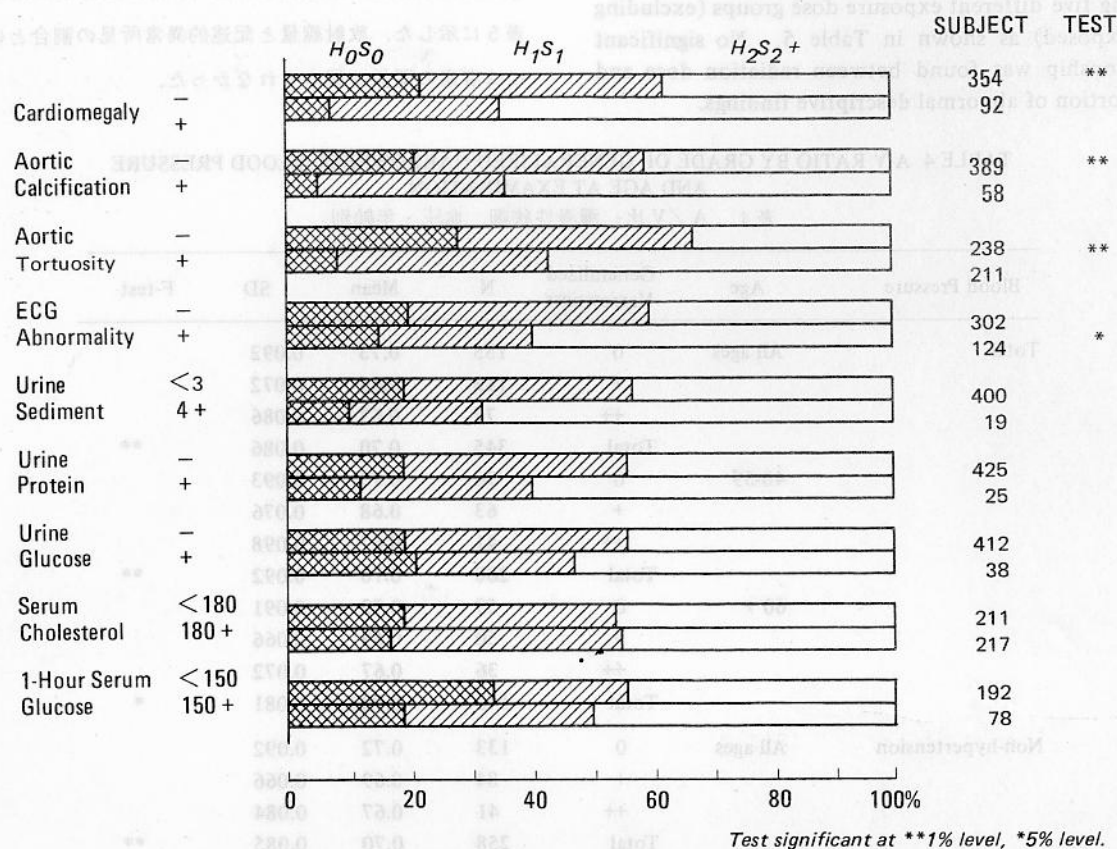


TABLE 3 GRADE OF DESCRIPTIVE FINDINGS (SHEIE'S CLASSIFICATION)

表 3 記述的所見の程度 (Sheie の分類)

| | Total* | | 0 | | + | | ++ | | +++ | | Unknown |
|-------|--------|-----|-----|------|-----|------|-----|------|-----|-----|---------|
| | No. | % | No. | % | No. | % | No. | % | No. | % | |
| I-1 | 454 | 100 | 203 | 44.7 | 148 | 32.6 | 103 | 22.7 | - | - | 4 |
| 2 | 456 | 100 | 338 | 74.1 | 72 | 15.8 | 46 | 10.1 | - | - | 2 |
| 3 | 456 | 100 | 361 | 79.2 | 63 | 13.8 | 32 | 7.0 | - | - | 2 |
| 4 | 456 | 100 | 443 | 97.1 | 10 | 2.2 | 3 | 0.7 | - | - | 2 |
| II-1 | 457 | 100 | 451 | 98.7 | - | - | - | - | 6 | 1.3 | 1 |
| 2 | 457 | 100 | 448 | 98.0 | - | - | - | - | 9 | 2.0 | 1 |
| 3 | 457 | 100 | 445 | 97.4 | - | - | - | - | 12 | 2.6 | 1 |
| III-1 | 457 | 100 | 452 | 98.9 | - | - | 5 | 1.1 | - | - | 1 |
| 2 | 457 | 100 | 453 | 99.1 | - | - | - | - | 4 | 0.9 | 1 |
| IV-1 | 457 | 100 | 448 | 98.0 | - | - | - | - | 9 | 2.0 | 1 |
| V-1 | 456 | 100 | 345 | 75.7 | 39 | 8.6 | 57 | 12.5 | 15 | 3.3 | 2 |
| VI-1 | 451 | 100 | 261 | 57.9 | 113 | 25.1 | 58 | 12.9 | 19 | 4.2 | 7 |
| 2 | 451 | 100 | 393 | 87.1 | 45 | 10.0 | 11 | 2.4 | 2 | 0.4 | 7 |

*Excluding "unknown" cases.

Abnormal Descriptive Findings. The proportion of abnormal descriptive findings (H_2S_2+) was observed among five different exposure dose groups (excluding nonexposed) as shown in Table 5. No significant relationship was found between radiation dose and proportion of abnormal descriptive findings.

記述的異常所見。記述的異常所見(H_2S_2+)の出現率を五つの被爆群(非被爆者は除く)別に検討した結果を表5に示した。放射線量と記述的異常所見の割合との間には有意の関係は認められなかった。

TABLE 4 A-V RATIO BY GRADE OF GENERALIZED NARROWNESS, BLOOD PRESSURE AND AGE AT EXAMINATION

表4 A/V比: 瀰漫性狭細, 血圧・年齢別

| Blood Pressure | Age | Generalized Narrowness | N | Mean | SD | F-test |
|------------------|----------|------------------------|-----|------|-------|--------|
| Total | All ages | 0 | 155 | 0.73 | 0.092 | |
| | | + | 113 | 0.69 | 0.072 | |
| | | ++ | 77 | 0.67 | 0.086 | |
| | 40-59 | Total | 345 | 0.70 | 0.086 | ** |
| | | 0 | 96 | 0.73 | 0.093 | |
| | | + | 63 | 0.68 | 0.076 | |
| | 60 + | ++ | 41 | 0.67 | 0.098 | |
| | | Total | 200 | 0.70 | 0.092 | ** |
| | | 0 | 59 | 0.72 | 0.091 | |
| | | + | 50 | 0.69 | 0.066 | |
| | | ++ | 36 | 0.67 | 0.072 | |
| | | Total | 146 | 0.70 | 0.081 | * |
| Non-hypertension | All ages | 0 | 133 | 0.72 | 0.092 | |
| | | + | 84 | 0.69 | 0.066 | |
| | | ++ | 41 | 0.67 | 0.084 | |
| | 40-59 | Total | 258 | 0.70 | 0.085 | ** |
| | | 0 | 86 | 0.73 | 0.094 | |
| | | + | 52 | 0.69 | 0.073 | |
| | 60 + | ++ | 25 | 0.68 | 0.091 | |
| | | Total | 163 | 0.71 | 0.089 | * |
| | | 0 | 47 | 0.72 | 0.088 | |
| | | + | 32 | 0.69 | 0.055 | |
| | | ++ | 16 | 0.66 | 0.075 | |
| | | Total | 95 | 0.70 | 0.078 | * |
| Hypertension | All ages | 0 | 22 | 0.74 | 0.097 | |
| | | + | 29 | 0.69 | 0.086 | |
| | | ++ | 36 | 0.67 | 0.089 | |
| | 40-59 | Total | 87 | 0.69 | 0.94 | * |
| | | 0 | 10 | 0.73 | 0.093 | |
| | | + | 11 | 0.66 | 0.088 | |
| | 60 + | ++ | 16 | 0.67 | 0.111 | |
| | | Total | 37 | 0.68 | 0.102 | NS |
| | | 0 | 12 | 0.75 | 0.103 | |
| | | + | 18 | 0.70 | 0.084 | |
| | | ++ | 20 | 0.68 | 0.070 | |
| | | Total | 50 | 0.70 | 0.087 | NS |

*Significant at 5% level.

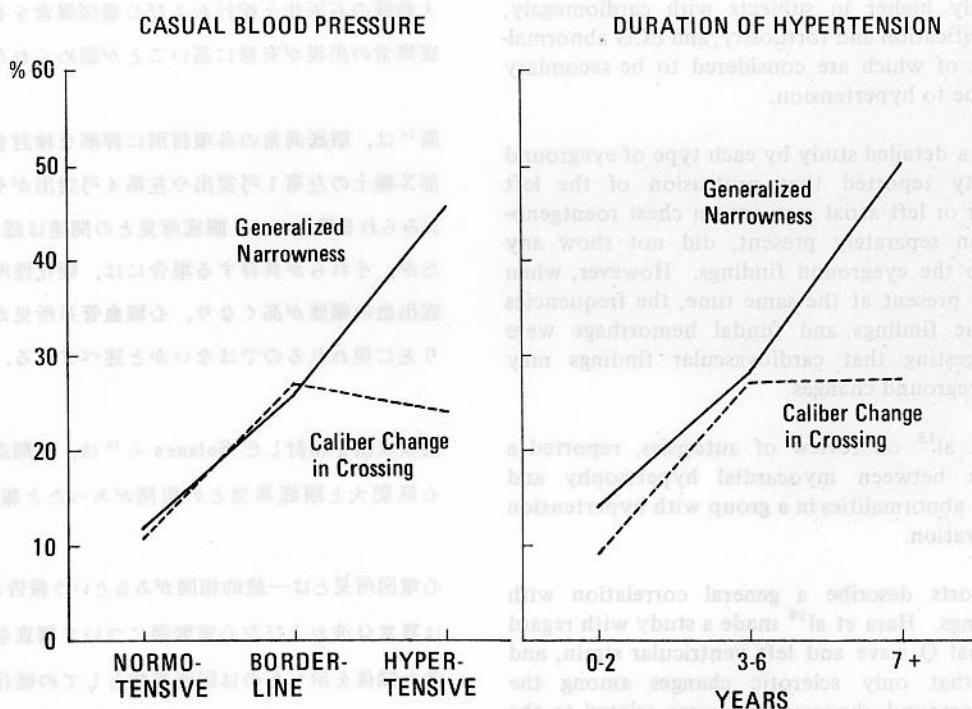
**Significant at 1% level.

TABLE 5 ABNORMAL DESCRIPTIVE FINDINGS (H₂S₂+) BY EXPOSURE DOSE表5 異常記述的所見 (H₂S₂+) : 被曝線量別

| Statistic | T65 Dose (rad) | | | | | | χ^2 -test |
|--|----------------|------|-------|--------|-------|---------|-----------------|
| | Total | 0-9 | 10-39 | 40-179 | 180 + | Unknown | |
| Observed H ₂ S ₂ + | 154 | 61 | 35 | 41 | 13 | 4 | Not significant |
| Expected | 154 | 64.3 | 28.5 | 38.5 | 17.6 | 5.2 | |
| O/E | | 0.95 | 1.23 | 1.07 | 0.74 | 0.78 | |
| Sample | 337 | 141 | 61 | 84 | 39 | 12 | |

FIGURE 4 PROPORTION OF ABNORMAL FINDINGS IN GENERALIZED NARROWNESS (++) & CALIBER CHANGE IN CROSSING (++) & (+++) BY BLOOD PRESSURE LEVEL

図2 瀰漫性狭細(++)および交差部内径変化(++)および(+++)の割合: 血圧値別



DISCUSSION

Most studies utilizing eyeground cameras in the epidemiologic investigation of cardiovascular diseases have used three photographs of one eye (for the same sites as used in the present study).^{10,11} The present authors used a total of six photographs of both eyes because it has been reported¹⁰ that findings of grade 2 or greater by Scheie's classification may be missed at a rate of 22.3% by the examination of three photographs of one eye as compared with ophthalmoscopic examination of both eyes. In addition to this disadvantage, there is considerable disagreement^{10,12} with the ophthalmoscopic evaluation of such findings as color tone, luster, and reflection.

The frequency of definite abnormalities (H_2S_2+) in the overall evaluation of the eyeground changes was found to increase with increasing age and blood pressure. This also has been found in previous reports.¹³

Examination of the relation between abnormal eyeground changes and other clinical findings showed that the frequency of eyeground abnormalities was significantly higher in subjects with cardiomegaly, aortic calcification and tortuosity, and ECG abnormalities, each of which are considered to be secondary changes due to hypertension.

Hara¹⁴ in a detailed study by each type of eyeground abnormality reported that protrusion of the left ventricular or left atrial segment on chest roentgenogram when separately present, did not show any relation to the eyeground findings. However, when they were present at the same time, the frequencies of sclerotic findings and fundal hemorrhage were high, suggesting that cardiovascular findings may precede eyeground changes.

Solanes et al¹⁵ on review of autopsies, reported a correlation between myocardial hypertrophy and eyeground abnormalities in a group with hypertension of long duration.

Many reports describe a general correlation with ECG findings. Hara et al¹⁴ made a study with regard to abnormal Q wave and left ventricular strain, and reported that only sclerotic changes among the various eyeground abnormalities were related to the former. On the other hand, narrowness, irregularity, and hemorrhage which are hypertensive changes, were the most strongly related to ventricular strain. Most reports have found no relation between serum cholesterol levels and eyeground changes.

考 察

循環器疾患を対象とする疫学的調査に眼底カメラを応用する場合、多くは片眼3枚の写真(本調査で採用した部位についての)が用いられている。^{10,11} 片眼3枚の写真的判読と検眼鏡による両眼観察とを比較すると、Scheieの分類による2度以上の所見の見落とし率が22.3%であったという報告¹⁰もあるので、著者らは両眼で合計6枚の写真を用いた。上記の欠点に加えて、色調、光沢、および反射の所見判定では、検眼鏡による判定との間にかんがりの不一致がみられる。^{10,12}

眼底変化の総合判定における明らかな異常(H_2S_2+)の出現率は、年齢および血圧の上昇とともに増加する。これはすでに認められているところである。¹³

眼底の異常変化とその他の臨床検査所見との関係を検討した結果、高血圧による二次的変化と考えられる心拡大、大動脈の石灰化と蛇行および心電図異常を有する者に眼底異常の出現が有意に高いことが認められた。

原¹⁴は、眼底異常の各項目別に詳細な検討を行ない、胸部X線上の左第1弓突出や左第4弓突出がそれぞれ単独にみられる場合には、眼底所見との関連は認められなかったが、それらが共存する場合には、硬化性所見および眼底出血の頻度が高くなり、心臓血管系所見が眼底変化より先に現われるのではないかと述べている。

剖検成績を検討した Solanes ら¹⁵は、長期高血圧群では心筋肥大と眼底異常との相関があったと報告している。

心電図所見とは一般的相関があるという報告が多い。原¹⁴は異常Q波および左心室緊張について調査を行ない、前者と関係を示したのは眼底異常としての硬化性変化のみであり、一方、心室緊張と最も強い関連を示したのは、高血圧性変化である狭細、不整および出血であったと述べている。血清コレステロールについては、大半の報告において眼底変化との関連が認められていない。

It is generally believed that generalized narrowness in the early stage of hypertension consists of functional, reversible "stenosis", and with the persistence of hypertension, organic, irreversible "narrowness" develops, due primarily to thickening of the tunica media of the arterioles.

The findings of the authors showed a relationship between the frequency of 2 plus (++) generalized narrowness and blood pressure.

The frequency of abnormal changes in venular caliber at A-V crossing was less than that of abnormal generalized narrowness and presented a consistent relationship with age rather than with blood pressure. However, further histologic and physiologic evidence is necessary for the interpretation of these findings.

The results of our studies on the relation of age and blood pressure to eyeground changes evaluated solely on the basis of color photographs, show tendencies similar to those reported from ophthalmological studies.¹³ Ito¹⁶ feels that there is no relationship between the degree of sclerotic change and degree of thickening of the arteriolar wall, and that qualitative changes of the tunica media are more important.

Since subjectivity may enter into the evaluation of these findings, studies are being made to develop more objective methods for evaluation. At present the most widely employed method is the measurement of the caliber of the arterioles and venules.¹⁷ Ophthalmological studies have been done in which consecutive measurements were made from the margin of the disc toward the periphery¹⁸ or in which the A-V ratio at a number of points was calculated.¹⁹ Epidemiological studies also have been made using the ratio of the sums of the measurements of the caliber of all arterioles and venules around the disk.²⁰ In order to exclude the effect of the venule, studies have been made using the caliber of the arterioles and the disc diameter.¹⁹ Minsky²¹ obtained the ratio of the measurements of the arteriole before and after their bifurcation, and Minato²⁴ reported that this ratio is highly correlated with blood pressure.

With reference to the relation between the retinal and brachial blood pressure, it is generally accepted that there is a parallel relationship with the ophthalmic arterial pressure.^{23,24} However, the relation may not necessarily be parallel if a stenotic process should occur due to atherosclerosis of the proximal arteries, including the ophthalmic artery.²⁵⁻²⁷

瀰漫性狭細は、高血圧初期においては機能的、可逆的「狭窄」を示し、高血圧の持続とともに主として細動脈中膜の肥厚による器質的、不可逆的「狭細」をきたすと考えられている。

著者らの成績では、瀰漫性狭細の++の出現率は血圧と関係のあることが認められた。

交差部細静脈内径変化の異常出現率は、瀰漫性狭細異常出現率よりも低く、また血圧とよりもむしろ年齢と一定の関連を示した。しかし、これらの所見の解釈については、さらに組織学的および生理学的裏づけが必要である。

カラースライドのみから判読した眼底所見と年齢および血圧との関係について検討した結果、眼科学領域で報告されている成績¹³と同様の傾向が認められた。伊藤¹⁶は、硬化性変化の程度と細動脈壁肥厚度の間には関連がなく、むしろ中膜の質的变化のほうが重要であるとした。

これらの所見の判定には主観が入りやすいので、より客観的な判定法の開発が研究されている。現在最も広く行なわれている方法は、細動静脈内径の計測である。¹⁷ 眼科学領域では、乳頭辺縁から末梢方向へ連続的に計測したものの¹⁸や、あるいはいくつかの点においてA/V比の算出を行なったもの¹⁹がある。疫学分野でも乳頭周囲におけるすべての細動静脈内径の和を比で表わした調査がある。²⁰ また、細静脈の影響を除くために、細動脈内径および乳頭径を用いた調査もある。¹⁹ Minsky²¹は、細動脈の分岐前径と分岐後径の比で求め、また湊²⁴はこの比と血圧とは相関の高いことを報告している。

網膜血管と上腕血圧との関係については、眼動脈圧と平行関係にあることが一般に認められている。^{23,24} しかし、眼動脈をも含めた中枢側の動脈硬化によって狭窄が起これば、この関係はかならずしも平行するとはかぎらない。²⁵⁻²⁷

It cannot be denied that individual variations are present in the response of retinal vessels to changes in brachial blood pressure.^{28,29} It had been felt that the retinal vessels do not have any vasomotoric nerve supply,²⁷ but in 1969 Fukuda et al³⁰ reported that they were able to confirm with almost certainty the presence of adrenergic nerves.

In addition Pickering³¹ has reported that calculation of the A-V ratio had been difficult due to individual variations in the distribution of blood vessels.

In 1966, Stokoe and Turner³² were able to find A-V pairs of the same sector at a frequency of only 32%-48% among study subjects, and they questioned the objectivity of the finding of generalized narrowness.

In 1967, the authors³³ made a review of the frequency of pairs of main arteriole and main venule for which the A-V ratio could be calculated according to the WHO criteria and reported findings similar to the present study.

In 1967, Kagan et al³⁴ reported that the A-V ratio obtained in the upper temporal area showed a significant relation with blood pressure, but no significant difference was found in the lower temporal area. The results of the present study showed that if the mean value and standard deviation are taken into consideration, large variations are present in the A-V ratios for individual cases, and even when the smallest value had been taken to represent the ratio in individual cases, there was no correlation either with age or blood pressure.

Even in cases for which two or more A-V ratios could be calculated, the response of the arterioles in each quadrant to increased blood pressure would not necessarily be consistent.³⁵ Furthermore, fluorescent retinal photography has demonstrated errors in evaluation of the caliber when organic changes extend to the vascular walls and perivascular tissues.³⁶

As previously suggested,^{28,37} observation of the A-V ratio of the same site of the same subject for time changes may be meaningful.

No apparent radiation effect on the cardiovascular diseases has been reported among the A-bomb survivors. Also, no relationship was observed in the present study between the frequency of abnormal findings of the eyeground and the radiation dose among A-bomb survivors.

上腕血圧の変動に対する網膜血管の反応性には個体差があることも否定できない。^{28, 29} 網膜血管には血管運動神経支配がないものと考えられていたが,²⁷ 1969年に福田ら³⁰は、アドレナリン作動性神経の存在をほぼ確認し得たことを報告している。

そのほか Pickering³¹は、血管分布の個人差がA/V比の算出を困難にしていると報告した。

1966年、Stokoe および Turner³²は、同一分節のA/V対をその対象例中の32%-48%にしか認めることができず、瀰漫性狭細所見の客観性を疑問視している。

著者ら³³も、1967年にWHOの基準に基づいてA/V比の算出が可能な主細動静脈対の出現率を検討して、本調査と同様の所見を報告した。

1967年、Kaganら³⁴は、上耳側部で得られたA/V比は血圧と有意な関係を示すことを認めたが、下耳側部では有意差は認められなかったと報告した。本調査の結果では、A/V比の平均値と標準偏差を考慮に入れると、各個人のA/V比には大きなバラツキがあり、たとえその最小値をその個人の比の代表値としても、年齢や血圧のいずれとも相関が認められなかった。

1個人にA/V比が二つ以上算出できた場合でも、各象限における細動脈の昇圧に対する反応が一定であるとはかぎらない。³⁵ また、器質的変化が血管壁や血管周囲組織に及んだ場合、内径判読に誤差のみられることが蛍光眼底写真撮影法によって証明されている。³⁶

A/V比は、すでに指摘されているように、^{28, 37} 同一人の同一部位についての経時的変化について観察する場合に意義があるかもしれない。

原爆被爆者には、心臓血管疾患に対する明瞭な放射線影響は報告されていない。今回の調査でも、原爆被爆者において眼底異常所見の出現率と放射線被曝線量との間になんらの関係も認められなかった。

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