M. ASHBY *ET AL.*: RECURRENT TRANSIENT MONOCULAR BLINDNESS

PLATE I

PLATE II

PLATE III

PLATE IV

PLATE V

FIG. 1

Case 4.—For six months this 57-year-old man had been suffering from severe lumbar pain. No abnormality was found on examination. The testes were noted to be normal. Radiographs revealed destruction of the second lumbar vertebra, but further investigations, including blood and marrow examination, electrophoresis of serum proteins, skeletal survey, and an intravenous pyelogram, were all normal. X-ray therapy was given to the affected vertebra. Two months later he complained of enlargement of the right testis. Orchidectomy was performed and a histological diagnosis of malignant lymphoma made. The assumption that the vertebral lesion is a manifestation of the same condition can fairly be made, but the patient has been under review for only a short time.

Case 5.—At the age of 28 this patient noticed a swelling in his left groin. A year later he developed a mass in the left axilla followed within a month by pain in the left loin, jaundice, night sweats, and pyrexia. On examination he was anaemic (Hb 5.3 g./100 ml.) and jaundiced. Both eyes were proptosed, and, as well as the nodes he had noticed, there was a large mass in the left abdomen and a hard swelling of a solitary left scrotal testis. The right testis was presumed to be undescended. Biopsy of the axillary mass and an orchidectomy revealed a lymphosarcomatous type of malignant lymphoma. Local palliative x-ray therapy was given to the orbits and residual masses, but he rapidly developed skin metastases and within a few weeks died of disseminated disease.

Case 6.—In June, 1951, at the age of 58, this man developed a painless swelling of the right testis. In October of that year right orchidectomy was carried out and prophylactic x-ray therapy given to the whole abdomen. Four years later the left testicle became enlarged and was excised. The pathology of both testes was malignant lymphoma. Further x-ray therapy could not be given, but he remains well 11 years after the first operation.

Case 7.—A swelling of the right testis was noticed by this patient at the age of 47. He ignored this until two years later, when his left testis became enlarged. At this time he also had

enlarged right cervical lymph nodes and a tumour of the hard palate (Fig. E). Bilateral orchidectomy and palatal biopsy were carried out and malignant lymphoma of these sites was diagnosed. He was given a course of x-ray therapy to the neck and palatal region, and this was followed three months later, when he developed an upper abdominal mass, by abdominal x-ray treatment. Resolution of the tumours was good at first, but he died of disseminated disease seven months after the orchidectomy had been performed.

FIG. E.—Case 7. Malignant lymphoma of the hard palate.

Case 8.—This 57-year-old man had an orchidectomy for a painless swelling of the left testis of five months' duration. There was no other evidence of disease, and post-operative x-ray therapy was given to the whole abdomen. During his four-weeks course of treatment the right tonsil became enlarged and ulcerated. Local x-ray therapy was given to this area with good response. Six months after this he complained of increasing lassitude and dyspnoea. There were multiple subcutaneous nodules over the chest wall, and radiographs revealed a large mediastinal mass with bilateral pleural effusions. He died shortly afterwards, and at necropsy there was a solid mass of tumour extending continuously from the para-aortic lymph nodes through the diaphragm, occupying most of the mediastinum and thoracic inlet and extending into the neck. The pathology of the testicular and metastatic tumours was malignant lymphoma.

Discussion

The term malignant lymphoma has been used to include all types of malignant lympho-reticular disease, and, in our experience, is the commonest secondary testicular tumour. The existence of primary malignant lymphoma of the testis has been disputed. Chevassu (1906) considered them all to be embryonal tumours or seminomas, while others (Pease and McDonald, 1947; Ficari, 1950) regarded them as being always secondary to disease elsewhere.

When the testis appears to be the only site involved by malignant lymphoma it is impossible to state unequivocally whether a localized or generalized process exists. In this series testicular swelling was the first sign of disease in 30 patients. However, 20 were dead within 18 months, suggesting that the condition was generalized by the time the swelling was noticed. In the first seven cases from Table II it appears that the testis was the primary and sole site. This is certainly so in the first three cases, whose survival, after orchidectomy alone, was longer than that of any of these patients dying of metastases. In Case D from this Table post-mortem examination six months after orchidectomy failed to reveal any residual tumour, although careful search was made. Of the three patients surviving 11, 9, and 6 years after treatment by orchidectomy and

LEGENDS TO SPECIAL PLATE

PLATE I: Left optic fundus $1\frac{1}{2}$ minutes after onset of attack.—The disk and retina are pale and the arteries, containing dark blood, are difficult to distinguish from the veins. The branches of the central artery of the retina, arising out of the disk, are filled with a white material which extends in the superior nasal and superior temporal arteries to just beyond their first major divisions. In the distal portions of the arteries small pieces of white material break up the columns of blood to give a segmented appearance, and the distinct interfaces have various contours. In the superior temporal artery at the edge of the disk a small plug of blood is sandwiched between two columns of white material.

PLATE II: $3\frac{1}{2}$ minutes after onset of attack.—The embolic material is advancing into the superior nasal and temporal arteries, pushing the small plug of blood further up the superior temporal artery, and extending further into the three branches of this vessel. The radiating pattern of nerve fibres is becoming more easily visible in the relatively bloodless zone on either side of the superior temporal artery.

PLATE III: 4 minutes after onset of attack.—The embolus is flowing mainly into the superior temporal artery, carrying upward the attenuated plug of blood towards the first major division of the vessel. Small veins running direct to the disk are now almost empty, although the major venous tributaries do not seem to have changed in calibre.

PLATE IV: $4\frac{1}{2}$ minutes after onset of attack.—Suddenly the embolus has been displaced and oxygenated blood is filling the arterial tree except for the inferior nasal artery, in which a segment of white material remains lodged. The colour has returned to the retina and the veins are dilated. There is no cherry-red spot at the macula.

PLATE V: $4\frac{1}{2}$ minutes after onset of attack.—The embolus in the inferior nasal artery has been dislodged and blood is passing through this artery. Venous dilatation and hyperaemia persist.

FIG. 1: Left carotid angiogram.—Contrast dye, entering the common carotid artery, is filling the external carotid artery and its branches. A total occlusion of the internal carotid artery at its origin prevents filling of this vessel and its branches.

x rays it may be argued that involved abdominal lymph nodes had been cured by the radiotherapy. However, it would still appear probable that the testis had been the primary site. Especially is this so in Case E, still alive seven years from the second orchidectomy, which was not followed by x-ray therapy.

The natural history of these tumours differs from that of other testicular neoplasms. Lymphomas tend to occur in the older age-group. Although our youngest patient was only 28 years old, and sporadic cases have been observed even in children (Turley and Moore, 1952; Waddell, 1961), the majority are in the fifth to seventh decades of life. Bilateral testicular involvement is commoner in lymphoma, more than 50% of recorded bilateral tumours falling into this category (Hotchkiss and Laury, 1950; Abeshouse *et al.*, 1955). In our 665 cases there were six bilateral tumours, of which five were lymphomas. There is, in addition, an association with lesions of the skin and upper respiratory tract. It has been suggested that the occurrence of skin lesions associated with enlargement of the testis is indicative of lymphoma (Altman and Winkelmann, 1960) and that 20% of cases of nasopharyngeal lymphoma are associated with a similar lesion in the testis (Varney, 1955). Genito-urinary symptoms, including testicular swelling, are occasionally the first manifestations of leukaemia (Watson *et al.*, 1949). In none of our cases was a leukaemic blood count obtained even when the disease was widespread. The 11.4% survival rate at five years compares unfavourably with that of other testicular tumours, in which an overall 50% five-year survival may be expected (Boden and Gibb, 1951).

The single case of plasmacytoma we have described has been included for interest. Its occurrence in this site is rare, and it always appears to be part of a generalized process (Hayes *et al.*, 1952; Melicow and Cahill, 1954).

Summary and Conclusions

The pathology of 665 cases of testicular tumour has been reviewed. Of these, 34 have been recognized as malignant lymphoma and one as plasmacytoma.

The pathology, clinical features, and results of treatment of this group are described and illustrative cases presented. The existence of primary malignant lymphoma of the testis is established and the natural history of the disease discussed and compared with that of other testicular tumours.

Primary lymphoma of the testis is a recognizable entity which should be suspected in all cases of testicular tumour occurring over the age of 60. There is a tendency for bilateral involvement and an association with lesions of the skin and upper respiratory tract. The prognosis is poor, although some long-term survivals occur. There appear to be no distinguishing features, either clinical or pathological, which would enable these fortunate few to be recognized.

We wish to thank Dr. Robert Gibb for encouragement and valuable criticism. Material from 32 of our cases has been available for submission to the Testicular Tumour Panel and Registry, of which one of us (J.P.S.) is a member. We wish to acknowledge the help received from the Panel in the study of these cases.

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RECURRENT TRANSIENT MONOCULAR BLINDNESS

BY

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[WITH SPECIAL PLATE]

There are over thirty published descriptions of the ophthalmoscopic appearances during attacks of transient monocular blindness, yet the absence of reliable drawings, photographs, or even detailed descriptions makes it impossible, in the majority of cases, to obtain much useful information about the cause of the condition.

This is well illustrated by Fisher's (1959) difficulty in dividing previous reports into two main aetiological groups; different classifications are assigned to two separate accounts of a single patient (Harbridge, 1906; Zentmayer, 1907), and, in fact, most of the cases end up under a third heading—"miscellaneous." It is further supported by Russell (1961), who includes in his paper retinal photographs showing appearances without clear aetiological

significance, although his text implies that the ophthalmoscopic changes were undoubtedly those of retinal embolism.

The main object of this paper is to present a sequence of retinal photographs taken during one of over twenty attacks of transient monocular blindness experienced by a man with thrombosis of the ipsilateral internal carotid artery, and to discuss the objective findings thus recorded.

Historical Background

Shortly after the introduction of the concept of embolism von Graefe (1859) suggested it as a possible mechanism in cases of monocular blindness; subsequently this aetiology became generally accepted, and when Coverdale (1929) described 11 cases of central retinal artery occlusion he concluded that "the most satisfactory explanation of the great majority of cases . . . is embolism," and that "there

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is evidence that emboli, when arrested, do not lead to early thrombosis, and may subsequently become detached and pass further along the vessel, with or without causing retinal damage."

Shortly before the turn of the century, however, a rival cause for transient and permanent monocular blindness was introduced—spasm (Wagenmann, 1897). The spasm hypothesis clearly represented an active departure from currently held views, and most of the cases attributed to spasm seem to have been regarded as such because of retinal appearances which could not be reconciled with an embolic aetiology.

During the first half of this century spasm figured more prominently than embolism in reported cases of what was often termed "amaurosis fugax"; Sie Boen Lian (1948) confidently diagnosed spasm in a case with ophthalmic appearances strongly suggestive of arterial embolism. In an important paper, in which he reviewed 150 cases of transient monocular blindness from the published literature, Fisher (1952) first drew attention to the significant association between such attacks of blindness and contralateral hemiplegia in cases of occlusion of the carotid artery. It is with this association that recent work, which is discussed later, is mainly concerned.

Case Report

A cinema manager aged 51 was admitted to New End Hospital in April, 1961, after a myocardial infarct; he recovered and was discharged home on long-term anticoagulants.

Eight months later, on December 8, he was admitted to the Whittington Hospital under the care of one of us (M. A.), with a two-weeks history of pleurisy, loss of weight, and pyrexia; there had been no response to tetracycline prescribed by his general practitioner.

He looked very ill and a chest x-ray examination showed miliary mottling. His Mantoux reaction was negative at 1:100, but a liver biopsy, performed after his prothrombin index had been allowed to return to normal, revealed non-caseous granulomatous tubercles. Despite the absence of bacteriological confirmation (which was never obtained), he was regarded as a case of miliary tuberculosis and treated with streptomycin, "pasinah," and cortisone. The clinical course was complicated by a transient meningitis, but he recovered and was discharged home on February 9, 1962. His cortisone was withdrawn under out-patient supervision over the next few weeks.

On April 13 he complained for the first time of clumsiness of the right hand, and on April 17 he developed a severe headache and roaring in the left ear; the clumsiness of the right hand had increased and he was readmitted two days later. No inequality of the carotid pulses was felt on external palpation of the neck at this time, and the signs, which were restricted to the right upper limb, suggested a cortical lesion. While in hospital, however, he developed a transient right facial weakness and increased right knee and ankle reflexes. His Mantoux reaction had become positive at 1:10,000, but neither air encephalography nor examination of the cerebrospinal fluid revealed any abnormality, and the picture seemed to suggest localized cerebral ischaemia. He started to improve without treatment, and was therefore discharged home again to be followed as an out-patient.

On May 28 he presented at the casualty department complaining of transient attacks of blindness affecting the left eye. These attacks had been occurring several times a week for about four weeks, and by the end of May he was having them daily. Each attack would last from one to five minutes, starting as blurring and greying of vision in the left eye, usually associated with flashes of light; often, but not always, complete blindness supervened within 20 to 30 seconds. Recovery of sight was always rapid. Despite over 20 episodes of transient blindness no residual defect in visual fields or loss of acuity

could ever be detected. A typical attack of transient blindness occurred while the patient was being examined in the casualty department. His blood-pressure, which was usually normal, did not fall during the attack. He was admitted to the ward, where further attacks were followed ophthalmoscopically. The appearances were so unusual that a photographic record seemed desirable; he was therefore transferred to Hammersmith Hospital, where he spent 48 hours under the care of Professor Russell Fraser, whose assistant (D. S.) witnessed an episode of blindness which was recorded in a series of 16 colour retinal photographs, starting within one minute of the onset of the attack.

The clinical picture clearly suggested occlusion of the left internal carotid artery, and in view of the danger of permanent blindness the patient was referred to Mr. H. H. G. Eastcott, at St. Mary's Hospital, for surgical assessment. Carotid arteriography showed an obstruction of the left internal carotid artery which was too extensive for surgical treatment (Fig. 1), and he was sent back to the Whittington Hospital. Treatment with anticoagulants was resumed, and he was finally discharged home on June 23.

His right arm continued to improve slowly, and he experienced only two more attacks of blindness over the next six months, during which time anticoagulants were continued under out-patient supervision.

We subsequently heard that he died suddenly in November, 1962, after a further myocardial infarct. A coroner's post-mortem examination was performed, but the head and neck were not examined.

The Retina During Attacks of Transient Blindness

Observations

On each occasion that an attack of blindness was followed ophthalmoscopically the appearances were substantially the same as those recorded in the serial retinal photographs (Plates I-V). These are reproduced from the most significant and technically satisfactory pictures of an original sequence of 16 taken at 15-second intervals.

The actual onset of an attack was never observed, but the first two photographs, taken 60 and 75 seconds after the onset of symptoms, represent closely the earliest appearances seen with the ophthalmoscope (Plate I).

There is retinal pallor. In the particularly bloodless region of the superior temporal vessels the normal featureless retinal ground takes on a striated appearance, possibly due to reduced filling of the capillary network, which may allow the pattern of nerve fibres to become visible. The calibre of the retinal arteries appears to remain normal, but progressive emptying of the veins occurs, some small ones disappearing entirely by four minutes. The blood in the arteries is much darker than normal. There are slight irregularities in the inferior temporal vein, but no venous "cattle-trucking" can be seen. The central retinal artery and the proximal parts of all its main divisions appear to be filled with a pearly-white material which does not mix with blood; these bloodless arterial segments retain their normal calibre, as can be seen from the easily discernible vessel walls. Contact between the blood and pearly-white zones takes various forms. The simplest is the transverse boundary (Chart, A). A second form is represented diagrammatically (Chart, B). Ophthalmoscopically this looks as though a thin streak of blood is remaining adherent to the wall of an artery along which occlusive material is advancing; when this type of boundary is seen at the proximal end of a bloodless segment the appearances are those of arterial blood infiltrating up one side of an obstruction prior to its com-

Chart showing types of boundaries between the blood and the white material in the arteries.

plete displacement. The third diagram (Chart, C) depicts what look like small fragments of white material sticking to the walls of vessels otherwise full of arterial blood.

Allowing for the decrease in arterial calibre towards the periphery of the retina, each bloodless segment appears to maintain a constant volume. Fisher (1959) observed some such segments to be of decreasing size as they moved towards the periphery, and Russell (1961) saw what he interpreted as fragments breaking off the distal end of an embolus and being carried away in the blood-stream. There is no evidence of these phenomena in our photographs, nor were they observed ophthalmoscopically. The rate of progress of the pearly-white segments towards the periphery varies considerably. Sometimes movement is very slow, as indicated by the small plug of blood seen in the superior temporal artery at the edge of the disk in Plates I-III. More often advance is intermittent and extremely rapid, with sudden progress and arrest, the latter often occurring at an arterial bifurcation.

Direct observations showed no relation between the pulse beat and movement of the occlusive material. The photographs taken at 1 minute 15 seconds (Plate I), at 3 minutes 15 seconds (Plate II), and at 4 minutes (Plate III) are clearly quite similar and show few significant differences from the earliest observed appearances. Between 4 minutes and 4 minutes 15 seconds blood suddenly returns to the retina. Plate IV shows the retina at 4 minutes 30 seconds with only the inferior nasal artery remaining bloodless. The veins are now distended and the appearances are those of reactive hyperaemia. Vision returned rapidly at this stage. By 4 minutes 45 seconds (Plate V) even the inferior nasal artery is filled with blood. The hyperaemia persists for several minutes, after which the retina looks completely normal.

Interpretations

The constant calibre of the clearly visible arteries and the apparently unchanging volume of the moving bloodless zones suggest the presence of embolic material. The appearance of the red-white interfaces and ophthalmoscopic observations on the movements of the white zones and their boundaries provide further evidence and suggest that such embolic material must be of a semi-fluid consistency, but incapable of mixing with blood.

On no occasion was venous "cattle-trucking" observed, neither has it been recorded photographically. This may be due to the comparatively short duration of the attacks of this patient—insufficient to cause permanent visual loss. "Cattle-trucking" has been observed by Fisher (1959), Russell (1961), and McBrien *et al.* (1963), but all their patients experienced longer periods of local circulatory arrest.

In summary, therefore, it seems likely that this patient has experienced multiple retinal emboli and not recurrent attacks of retinal-artery spasm. The case differed from those previously reported in that venous "cattle-trucking" was not seen.

Discussion

At least six recently reported cases of transient monocular blindness (Fisher, 1952 (2 cases); Fisher, 1959; Russell, 1961 (2 cases); McBrien *et al.*, 1963) have been associated with contralateral hemiplegic signs and proved occlusion of the internal carotid artery; the literature contains 13 further similar cases in which the diagnosis of occlusion of the internal carotid artery was not firmly established (Fisher, 1952). The best explanation of this association comes from Russell (1961), who suggests that platelet agglutinates break away from the tip of accumulating carotid thrombus and pass into the retinal arteries, causing temporary ischaemia and blindness. Strong support for this view is provided by McBrien *et al.* (1963), who have demonstrated platelet-like material in occluded retinal arteries at necropsy.

The origin of retinal emboli is easier to understand than their ultimate fate, for it must be remembered that even

after over 20 attacks our patient showed neither a permanent visual field defect nor any impairment of visual acuity. Fisher (1959) claims that his patient experienced over 700 such attacks without any permanent visual damage.

Small emboli may either lodge in capillaries or disintegrate and pass through into the venous system. The former seems very unlikely, as it requires the retinal capillary bed to accommodate increasingly large amounts of embolic material without any disturbance of function. Disintegration and passage into the venous system implies that emboli may be held up for a short time in the arterial tree but then pass on without causing any permanent capillary obstruction; this is quite consistent with the present set of observations.

For approximately the first four minutes of an attack the retinal arteries remain of normal calibre but obstructed by embolic material. Hyperaemia is seen to occur during the fifth minute from the start of the ischaemic stimulus and appears to indicate vasodilatation following the restoration of a normal blood supply. There is, however, a more attractive interpretation: this is that ischaemia may cause vasodilatation preceding and responsible for the rapid passage of embolic material, followed by blood, through the almost empty but dilated capillaries and veins. This would account for the surprisingly constant duration of the many attacks.

The internal carotid artery carries blood to the brain as well as to the retina, and although much of the brain is now known to function as a whole it seems likely that were numerous small parts to be rendered temporarily ischaemic by platelet microemboli some transient neurological symptoms would arise. The clinical picture of carotid-artery thrombosis does, in fact, include such episodes, and the possibility of their being due to small cerebral emboli has been suggested by Denny-Brown (1960) following his observations on the development of platelet emboli in traumatized arteries; arguments in favour of this opinion are well summarized by Russell (1961).

Acceptance of the view that many published cases of monocular blindness have not been embolic in origin would explain the scarcity of accounts recording associated transient neurological disturbances; these have, however, been present in most of the recently reported cases.

Fisher (1959) describes his patient as experiencing numerous attacks of transient weakness of the face and both right limbs, and also an episode of aphasia, from which he failed to make a complete recovery. Russell's (1961) first case had intermittent clumsiness and tingling of the right arm and hand, and his second patient had two similar attacks, each lasting about 15 minutes. McBrien *et al.* (1963) state that their patient experienced attacks of numbness and weakness of the face and both left limbs, but the duration of these attacks is not indicated. Our patient had no clear-cut transient disturbances of this kind, although at times minimal facial weakness and pyramidal signs in the right leg were recorded.

These positive neurological findings imply the entrance of platelet agglutinates into both the retinal and the cerebral circulation; this suggests that such emboli arise in the carotid artery itself rather than its ophthalmic branch. Russell (1961), however, indicates that thrombotic extension into the ophthalmic artery occurred in both his cases; in one there was pathological proof, while in the other the retinal arteries failed to pulsate normally on digital compression of the eye, despite the fact that angiography showed only slight narrowing of the origin of the internal carotid artery. A possible explanation is that micro-emboli

may be breaking away from two thrombi—one in the carotid artery itself, the other in its ophthalmic branch.

Treatment of Blindness Due to Retinal Emboli

There are two objectives in the treatment of occlusion of the carotid artery. First is the prevention of transient episodes—both neurological and visual—which are probably due to platelet emboli; second is the prevention and, if possible, reversal of persistent ischaemic damage. It has recently been pointed out that such damage is probably not caused by platelet agglutinates but by a reduction in cerebral blood flow, due either to sudden carotid narrowing or to large solid emboli (Crompton, 1963).

The two major therapeutic approaches to the carotid-artery syndrome are disobliteration of the artery and anticoagulation. In the small group of cases under review, surgery was undertaken in two patients (Russell, 1961; McBrien *et al.*, 1963); both died during the post-operative period. Platelet emboli were seen by McBrien *et al.* after thromboendarterectomy, but it is not clear whether the operation was technically successful or whether thrombosis had recurred. The failure of surgery may perhaps be explained by the fact that while surgery achieves its best results in cases of localized atheromatous narrowing (Edwards and Gordon, 1962), retinal emboli can be associated with complete arterial thrombosis.

The visual symptoms responded satisfactorily to anticoagulants in our case, in that of Fisher (1959), and in the second case of Russell (1961); in Russell's first case phenindione started two days after operation failed to prevent further extensive and ultimately fatal thrombosis, although no further visual episodes were observed.

These findings suggest that transient blindness, in association with occlusion of the carotid artery, may respond to

anticoagulation, and that this, rather than surgery, is the treatment of choice. What is more, the threat of permanent blindness and of hemiplegia (if it has not already occurred) seems to be so great that anticoagulants should seldom, if ever, be withheld.

Summary

Recurrent monocular blindness is described in a 51-year-old man suffering from occlusion of the internal carotid artery.

Serial retinal photographs of a typical attack are presented.

The appearances seen and photographed are consistent with the view that such attacks of blindness are due to platelet micro-emboli temporarily obstructing the retinal arteries.

The natural history of such emboli, and the treatment of patients in whom they occur, are discussed.

We wish to express our thanks to the Wellcome Trust for a generous grant towards the cost of printing Plates I and IV in colour; and we are indebted to Mrs. Morag Engel, S.R.N., for taking the retinal photographs.

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ASPIRIN AND THE EXFOLIATION OF GASTRIC EPITHELIAL CELLS CYTOLOGICAL AND BIOCHEMICAL OBSERVATIONS

BY

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[WITH SPECIAL PLATE]

It is now firmly established that oral aspirin can cause occult gastro-intestinal blood loss (Stubbé, 1958; Pierson *et al.*, 1961; Wood, 1963), but the mechanism of this phenomenon is not known. There is evidence that particles of aspirin tablets can cause macroscopic erosions in the gastric mucosa (Douthwaite and Lintott, 1938; Muir and Cossar, 1955), but macroscopic particle erosion does not explain the bleeding which occurs after the administration of dispersions and solutions of aspirin (Stubbé, 1958; Wood *et al.*, 1962).

This paper describes the results of an investigation into the mechanism of occult salicylate bleeding into the gut, with particular reference to calcium and soluble aspirin. The macroscopic and microscopical features of human gastric washouts before and after the administration of dispersions of aspirin in saline are described. The cellular content of gastric washouts has been assessed by estimating the deoxyribonucleic acid (D.N.A.) content. The method is based on the assumption that all somatic human nuclei contain the same amount of D.N.A., which is the essential constituent of the genes and is present only in the nuclei

of cells. Davidson *et al.* (1951) find that the measure of agreement of the D.N.A. content of the nuclei of human prostate, kidney, and marrow is good, and there is no reason to think that the D.N.A. content of the nuclei present in gastric washouts is significantly different from the D.N.A. content of the nuclei of other human tissues. The quantity of D.N.A. in a cellular specimen, such as a gastric washout, is therefore proportional to the number of nuclei, and thus the number of cells, present.

Methods

Gastric Washout Technique.—The subject, who had fasted for 5 to 12 hours, lay inclined to the left with a latex gastric tube passed into the stomach. He was asked not to swallow during the investigation and to expectorate all saliva and sputum. Each gastric washout specimen was obtained by injecting into the stomach, and withdrawing, five volumes of saline (0.9 g./100 ml.), using a 100-ml. syringe. For the fasting gastric washout (specimen A) 500 ml. of saline was used, and for all other washouts 450 ml. Immediately after specimen A had been obtained 50 ml. of saline was injected into the stomach, and after it had

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