MEDICAL PRACTICE

Hospital Topics

The Fibromatoses: A Clinicopathological Concept*

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Adequate treatment of a disease process involves an understanding of the natural history of the disease. It is, of course, highly desirable that the aetiology should also be known and it is useful if terminology is sensible and universally accepted. Ignorance of aetiology and variability of nomenclature, however, are not bars to successful treatment provided that in any given instance the evolution of a disease is fully understood.

This lecture is concerned with a group of conditions of fibroblastic origin which are known collectively as the fibromatoses. Their aetiology is unknown, but their great importance lies, firstly, in the fact that they are often misdiagnosed as true malignant neoplasms and, secondly, in the sad truth that all too frequently they are very badly treated.

Firstly, then, I shall try to define what I mean by a fibromatosis. Secondly, I shall list those conditions which seem to me to justify the label, and, thirdly, I shall deal briefly with selected examples.

Anyone interested in tumours and tumourous conditions of soft tissues knows all too well the vagaries of mesenchymal behaviour, and it is the fibroblastic line of differentiation that I am concerned with here. Terms such as inflammatory, reactive, or neoplastic while appropriate and accurate in many instances are inadequate to define the behaviour patterns of all fibroblastic proliferations. At least one more category is essential, hence the fibromatoses. This concept has been developed largely since the second world war, and most of the main papers have been in the American literature. Nevertheless, the existence of this strange group of fibroblastic disorders has been known for many years, and Janssen (quoted by Touraine and Ruel[1]) wrote of the "diathèse fibroblastique" as long ago as 1902.

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Definition and Nomenclature

A fibromatosis may be defined as an infiltrating fibroblastic proliferation showing none of the features of an inflammatory response and no features of unequivocal neoplasia. These lesions can occur anywhere and to any extent. They can be fatal on very rare occasions or relatively harmless. They are encountered from fetal life to old age. The justification for grouping a wide collection of conditions under one broad heading lies in the fact that regardless of age, site, or extent these conditions have definite features in common. Tissues such as muscle and fat become replaced by or infiltrated with fibrous tissue of varying cellularity. Sometimes this is a diffuse or multifocal process and sometimes a localized nodular one. The fibroblasts are well differentiated, uniform in size, and often devoid of mitotic activity. Inflammatory infiltration is not a feature. These lesions mimic a fibrosarcoma through their infiltrative capacity but do not metastasize. In many cases, however, they show a pronounced tendency to recur and lead to major problems of eradication. I have no doubt at all that the concept of "the fibromatoses" is a valuable one in that it defines within broad limits a definite pattern of behaviour shared by a collection of lesions with many characteristics in common, even if some have individual features as well.

I believe that a wider use of the term fibromatosis is highly desirable. At the moment many patients with a fibromatosis have been diagnosed as suffering from a fibrosarcoma and live under the disturbing impression that they have had cancer. They cannot be blamed if they interpret the assurances of their medical advisors as attempts to hide the fact that they have a potentially lethal disease. Cumbersome labels such as non-metastasizing fibrosarcoma or fibrosarcoma grade I (desmoid type) are undesirable not only because of the suffix sarcoma but because with the passage of time the qualifying words tend to get lost, leaving the plain diagnosis of fibrosarcoma. In my view the term sarcoma should never be used unless a patient is suffering from a neoplasm which in the opinion of a competent pathologist has the ability to metastasize. The suggestion that the terms fibromatosis and well-differentiated fibrosarcoma are interchangeable would if accepted perpetuate a misuse of language and lead to widespread confusion.

Before dealing with some of the fibromatoses individually one other difficulty must be mentioned. Unhappily, universal agreement on those conditions qualifying for the title has not been reached. Over the years conditions such as fasciitis and Peyronie's disease, which seem to me to have a reactive or inflammatory background, have been included. Similarly, the clinicopathological entity of dermatofibrosarcoma protuberans has at times been included with the fibromatoses, whereas in all probability it is a true fibrohistiocytic neoplasm.

Those entities which seem to me to justify the label are listed in Table I. The fibromatoses as a whole have many features in common and the subdivisions result more from clinical than from histopathological differences. It is therefore unnecessary to give detailed descriptions for each sub group.

TABLE I—*The Fibromatoses*

Congenital and juvenile fibromatoses	Fibrous hamartoma of infancy Fibromatosis colli Infantile and juvenile fibromatosis Juvenile aponeurotic fibroma Congenital generalized fibromatosis
Miscellaneous fibromatoses	Palmar and plantar fibromatosis Mesenteric fibromatosis Musculo aponeurotic fibromatosis Generalized multifocal fibromatosis Hereditary gingival fibromatosis Fibrous dysplasia of bone

Time prevents consideration of all these variants and I do not propose to discuss the familiar fibromatosis colli (congenital torticollis), the common palmar fibromatosis (Dupuytren's contracture) and the plantar variant, or fibrous dysplasia of bone. The placing of fibrous dysplasia of bone among the fibromatoses is debatable, and I have discussed this elsewhere.[2]

Congenital and Juvenile Fibromatoses

FIBROUS HAMARTOMA OF INFANCY

In 1956 Reye[3] described six cases under the heading of subdermal fibromatous tumours of infancy. Enzinger[4] described 30 more cases and labelled the lesion fibrous hamartoma of infancy. Seventy-five per cent. of cases are male and in about 20% of cases the lesion is present at birth. The age range extends from birth to 4 years. The patient presents with an ill-defined mass usually less than 10 cm in diameter. The commonest site is the axilla, and about 70% have occurred in the axilla or upper extremity. Histologically there are three components in varying proportions—the fibroblastic one, fat, and islands of cellular tissue resembling primitive mesenchyme (Fig. 1). Recurrences have been reported but these were probably related to inadequate surgery. Complete excision is curative.

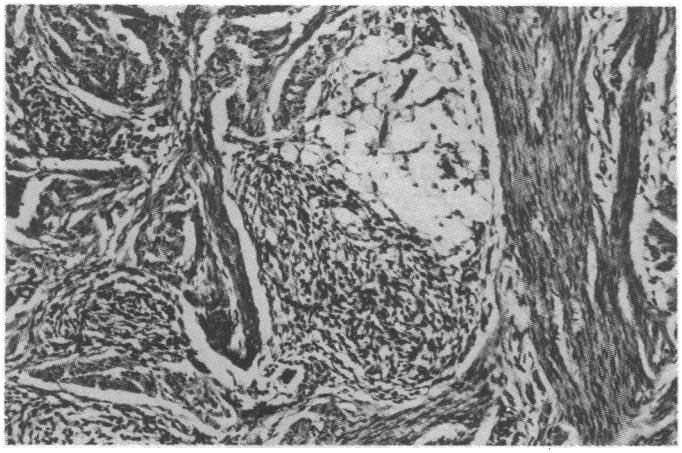

FIG. 1—Fibrous hamartoma of infancy showing primitive mesenchyme, fat, and fibrous tissue. (H. and E. × 100.)

JUVENILE FIBROMATOSES

In 1954 the late Arthur Purdy Stout wrote a classic paper called Juvenile Fibromatosis[5] in which he described 44 cases of fibroblastic lesions of infants and children. Subdivisions have inevitably followed. For example, Enzinger[6] carried out a review of 250 fibrous tumours occurring in infants and in children up to 15 years of age. He found that these fell readily into two large groups—namely, those lesions occurring exclusively as congenital or infantile lesions, and those occurring between 5 and 11 years, where the lesions tended to have a histological counterpart in adult life. He used the term infantile dermal fibromatosis for superficial lesions which were particularly apt to affect the extensor surfaces of the terminal phalanges of the fingers and toes. He used the term diffuse infantile fibromatosis to describe a similar fibroblastic process affecting a variety of muscle groups, mainly in the head, neck, and upper extremity. The term aggressive infantile fibromatosis has also been used for the more cellular forms. In as much as the labels define clinical entities they are useful, but it would be quite wrong to regard them as separate diseases. As stated above, certain fibromatoses have their own individual features, and this is true of some of those occurring on the fingers and toes of infants. Reye[7] noted that these tumourous lesions often contained intracytoplasmic inclusion bodies (Fig. 2). Battifora and Hines[8] studied such a case by electron microscopy and thought the inclusions were reminiscent of the viroplasm of fibroblasts infected with the Shope fibroma virus; however, all attempts to isolate a virus have been unsuccessful. A typical example of congenital fibromatosis affecting the thigh muscles is shown in Fig. 3.

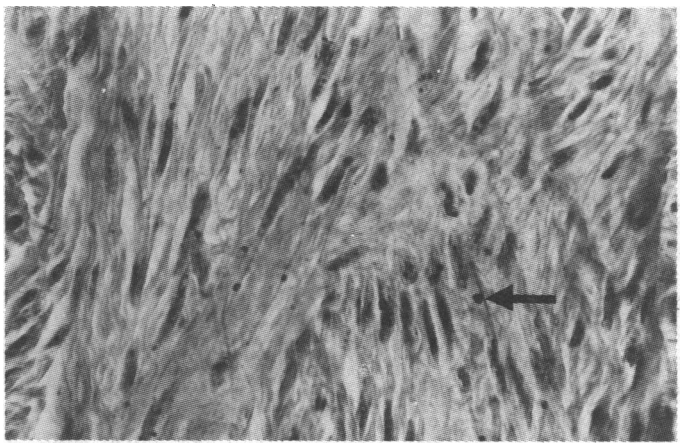

FIG. 2—Digital fibrous tumour of infancy showing intracytoplasmic inclusion bodies. (Phosphotungstic Acid Haematoxycin × 140.)

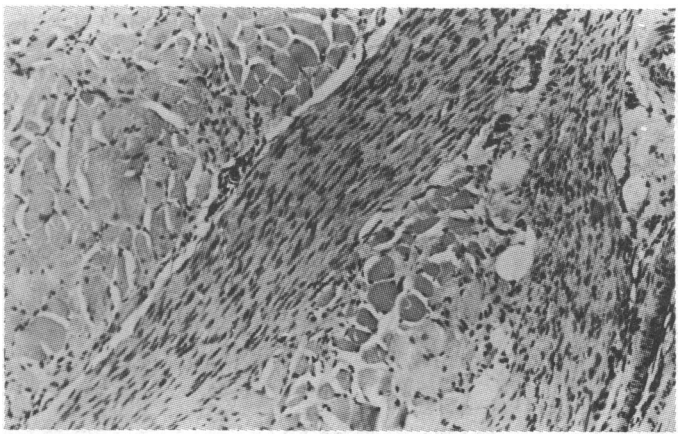

FIG. 3—Congenital fibromatosis of thigh showing infiltration of muscle (H. and E. × 110.)

In spite of individual peculiarities these lesions conform to the fibromatosis pattern of behaviour—that is, they are infiltrative fibroblastic lesions with a high recurrence rate in many instances but with no metastatic potential.

JUVENILE APONEUROTIC FIBROMA

Although the entity juvenile aponeurotic fibroma may correctly be labelled a juvenile fibromatosis there are certain features which render it a distinct entity within the group. Originally described by Keasbey in 1953 there are two interesting papers by Allen and Enzinger and by Goldman, both published in 1970.[10 11] The age range is widening as more cases are recorded but the majority have occurred from birth to 18 years. Most cases have occurred in the hands and feet but lesions occurring in the trunk and limbs are well documented. The patient presents with a lump, usually painless and characteristically less than 4 cm in diameter. This is usually superficial and often lies in intimate relation to tendons—a fact which makes adequate removal difficult, particularly in children. This fact accounts, in part at any rate, for the very high recurrence rate.

Histologically the lesion is made up of small, plump fibroblastic cells which tend to be smaller and less spindle-shaped than those seen in many fibromatoses. They infiltrate surrounding muscle and fat and may engulf nerves and skin adnexial structures. In mature lesions there may be a fine stippling of calcium detectable on radiographs and visible to the naked eye in histological sections (Fig. 4). Keasbey commented on the tendency for all the cells to be orientated in a single direction, but this is not an universal finding. A further feature unique to this condition is the occurrence of focal differentiation of the spindle cells towards a fibrocartilaginous pattern. This chondroid differentiation is not seen in any other fibromatosis.

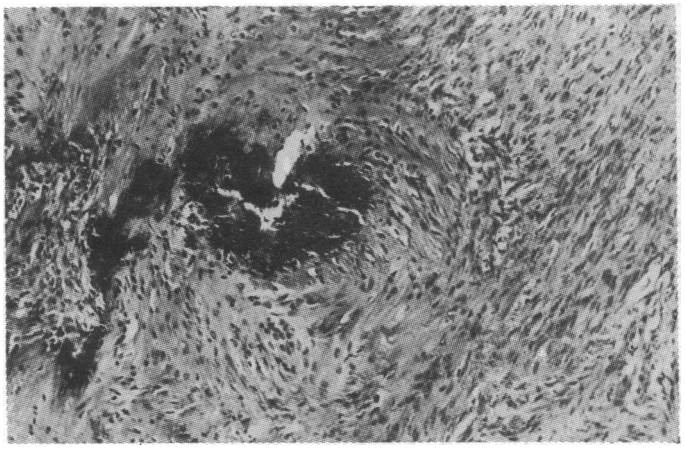

FIG. 4—Focal calcification in juvenile aponeurotic fibroma. (H. and E. × 85.)

CONGENITAL GENERALIZED FIBROMATOSIS

The definitive paper on the rarest and most deadly form of fibromatosis is that of Shnitka *et al.*[12] The babies are usually born with multiple subcutaneous nodules. In addition the intestinal tract, heart, bones, and skeletal muscles may be involved. There is some evidence to suggest that the cellular proliferation in this fibromatosis may include other lines of mesenchymal differentiation. It is, however, predominantly fibroblastic. It has, of course, been suggested occasionally that this condition is really a congenital fibrosarcoma with multiple metastases. Histologically it is a fibromatosis. Cells are never seen in blood vessels or lymphatics and the sites of the lesions would indeed be unusual for metastases.

Miscellaneous Fibromatoses

MESENTERIC FIBROMATOSIS

Fibroblastic proliferations of fibromatosis type occur within coelomic cavities. Localized intra-abdominal involvement is well recognized and usually affects the mesentery or omentum. There are two main types. Firstly, there are cases where the fibroblastic mass or masses constitute the only abnormality, and, secondly, there is a group where intra-abdominal fibromatosis is associated with subcutaneous soft-tissue tumours and, more important, familial intestinal polyposis, the so-called Gardner's syndrome. Gardner and Richards[13 14] studied 51 members of a family, seven of whom manifested familial intestinal polyposis plus a variety of other lesions including osteomas, epidermoid cysts, and multiple ill-defined masses of connective tissue. Simpson *et al.*[15] described seven cases with Gardner's syndrome including mesenteric fibromatosis and reviewed 15 other cases from the literature. The sex incidence was equal and the ages ranged from 20 to 61 years, with an average of 40 years. In six out of seven of their own cases there was a family history of multiple polyposis of the colon. They made the important observation that in 15 of the 22 cases the patients had had previous intestinal surgery. Additional examples were given by McAdam and Golighter.[16] A typical example is shown in Fig. 5.

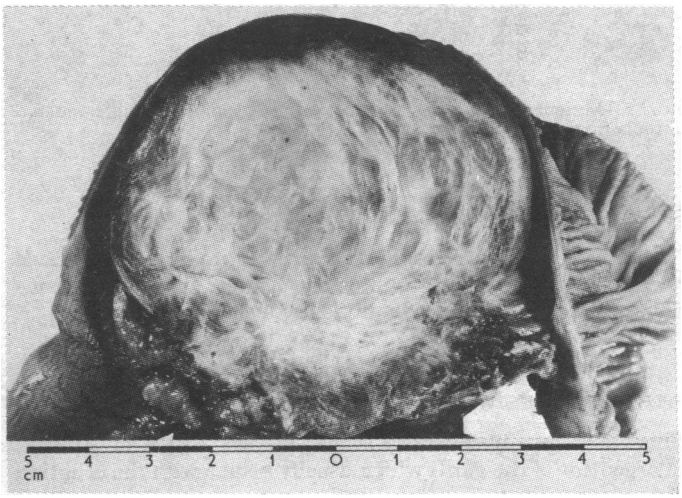

FIG. 5—Mesenteric fibromatosis showing typical whorled appearance and ill-defined margin. Musculoaponeurotic fibromatoses have the same appearance.

MUSCULOAPONEUROTIC FIBROMATOSES

The most important of the fibromatoses are the musculoaponeurotic fibromatoses sometimes known as the desmoid and extra-abdominal desmoid tumours. Though less common than the palmar and plantar variety they are more serious in that the process is not self-limiting. It is indeed in this group where most of the disasters occur, disasters of nomenclature and treatment. Apart from noting that most of the abdominal wall musculoaponeurotic fibromatoses occur in parous women, I see no point in separating the abdominal wall fibromatoses from musculoaponeurotic fibromatoses occurring elsewhere. There were 56 cases in the Westminster series and the sites and age distribution are shown in Tables II and III; there were 31 males and 25 females.

TABLE II—*Sites of Musculoaponeurotic Fibromatoses Among the 56 Patients in the Westminster Hospital Series*

	No. of Cases
Lower limb	18
Chest wall and shoulder region	12
Head and neck	7
Abdominal wall	7
Upper limb	6
Buttock	5
Back	1

TABLE III—*Age Distribution of the 56 Patients in the Westminster Hospital Series with Musculoaponeurotic Fibromatoses*

Age in years	≤10	−20	−30	−40	−50	−60	−70
No. of patients	5	7	20	9	9	1	5

The macroscopic and microscopical appearances of this type of fibromatosis are very characteristic. The masses have ill-defined margins and a typical whorled appearance reminiscent of a uterine fibroid (Fig. 5). Microscopically they show well-differentiated fibroblastic tissue (Fig. 6).

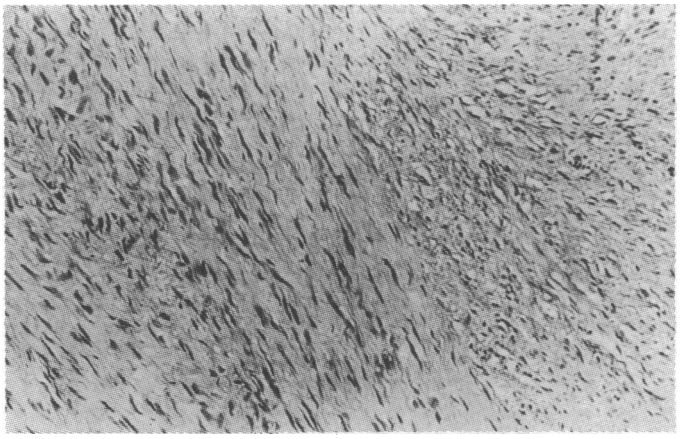

FIG. 6—Musculoaponeurotic fibromatosis showing well-differentiated fibroblastic tissue. (H. and E. × 110.)

GENERALIZED MULTIFOCAL FIBROMATOSIS

In this very rare variant the fibroblastic proliferation spreads relentlessly or arises in a multifocal fashion. The process continues until some vital structure is involved.[17]

HEREDITARY GINGIVAL FIBROMATOSIS

This uncommon fibromatosis is characterized by a firm, painless enlargement of the gums which usually begins with the eruption of the permanent dentition. Very rarely it may be present at birth.[18] The condition is often inherited as a dominant trait but sporadic cases are also encountered. The disease may be associated with hypertricosis, feeble-mindedness, neurofibromatosis, hemifacial hyperplasia, and cherubism.[19]

Recurrences

Although there are variations within the group most fibromatoses have a great capacity for recurrence after surgical removal. In the Westminster series of musculoaponeurotic fibromatoses at least one recurrence was noted in 41% of cases. Two recurrences occurred in 9% and three recurrences in 5% of cases. Many of these cases, however, were referred to Westminster Hospital because the lesion had already recurred at least once. In the series of 30 cases involving the shoulder girdle described by Enzinger and Shiraki[20] local recurrence was observed in 57% of cases. Major surgery including three amputations was necessary to eradicate the disease, but it was indeed eradicated in all cases in the end. In Goldman's review of 34 cases of the aponeurotic fibroma re-excision for recurrent lesions was necessary in 38% of cases.

Treatment

The treatment of choice may be defined as "adequate understanding surgery." This should be carried out by someone who understands the natural history of this group of conditions and who realizes that there are behaviour variations within the group. The infiltrative margins of a musculoaponeurotic fibromatosis may reach 2-3 cm beyond the palpable ones, and this must be taken into account. Any attempt at enucleation will virtually guarantee a recurrence. It is doubtful whether radiotherapy is of any use in the initial treatment, though it may play a part if recurrences have been allowed to reach unmanageable proportions. It is surgery and the quality of that surgery which really matters.

Differential Diagnosis

Fibromatoses must be distinguished from fibrosarcomas on the one hand and from benign processes in which fibroblasts or facultative fibroblasts occur on the other. The former problem is by far the more important of the two. In view of the very variable cellularity of the fibromatoses pathologists may well ask whether this distinction can always be made on the basis of histological studies alone. The truth is that the distinction can be made in the great majority of cases but not in all provided that adequate material is available for study. Biopsy material may indeed be misleading. Given a proper case history, the specimen to look at, and multiple sections difficulty will be encountered in only a tiny minority of cases. I will not deny, however, that this tiny minority of cases exists where the borderline between a fibromatosis and a fibrosarcoma seems dangerously blurred. I get the impression that this is more apt to occur in infancy and childhood—hence the term aggressive infantile fibromatosis. The desmoid type of fibromatosis has a naked-eye appearance, which is pathognomonic. The finger-like processes of infiltration are clearly seen. The sections show the uniform collagen-producing fibroblasts.

Contrary to usual teaching a fibrosarcoma and soft-tissue sarcomas in general may give the impression of genuine encapsulation. The cut surface lacks the whorled fibroid-like appearance of a musculoaponeurotic fibromatosis and the sections show greater cellularity with far less collagen formation even in well-differentiated examples. The case history is vital. For example, the more cellular areas of a palmar fibromatosis are often disturbing seen in isolation but there is no worry when the case is considered as whole. As noted above some fibromatoses such as the fibrous hamartoma of infancy or the aponeurotic fibroma have their own special histological features. Very few benign lesions cause diagnostic problems for people with an average amount of experience of tumours and tumourous conditions of soft tissues. Fasciitis (nodular fasciitis) can be distinguished by its disorderly histological structure, greater vascularity, and inflammatory component. Some atypical Schwann cell tumours may cause confusion but their collagen content tends to be less than that of fibromatosis and their spindle cells are more irregluar in shape. Histiocytomas and fibrous histiocytomas are usually far more cellular and show aggregates of foamy cells or the characteristic storiform arrangements of the fibroblasts. The superficial ones are in any case distinguishable on clinical grounds.

Aetiology

I have left the question of aetiology to the end because so little is known for certain.

Some people undoubtedly have a predisposition for this type of mesenchymal misdemeanour. In the case of the mesenteric fibromatosis of Gardner's syndrome it is probable that the families exhibit a dominant inheritance, and Zayid and Dihmis[17] believe that a dominant autosomal gene may play a part in the development of musculoaponeurotic fibromatoses of desmoid type. A familial incidence of palmar fibromatosis is well known.

A hormonal theory of origin was put forward by Geschickter and Lewis as long ago as 1935.[21] On one occasion they claim to have found 13,000 rat units of gonadotropic substance per kg of tumour in a desmoid type of fibromatosis. They found no oestrogens. They stated that there might be some connexion between these tumours and what they called sex physiology. In this context it may be mentioned that Nadel[22] was able to produce nodular fibroblastic proliferations in the abdominal cavity of guinea-pigs by the use of stilboestrol subcutaneous implants. These had the histological appearances of a fibromatosis. It is tempting to recall at this point that palmar fibromatosis is one of the stigmata of cirrhosis of the liver in which hyperoestrogenism is known to occur. In addition, Pojer *et al.*[23] discussed the increased incidence of palmar fibromatosis in chronic alcoholism and also in epileptics receiving long-term anticonvulsant therapy. They noted increased enzyme abnormalities in patients with liver disease and palmar fibromatosis which were hard to explain. They referred eventually to a fibromatous hereditary tendency.

Trauma has been invoked particularly in the case of fibromatosis colli, palmar fibromatosis, and desmoids of the abdominal wall, but the evidence is on the whole unconvincing for these three variants. Nevertheless, trauma of many kinds does seem able to trigger off the fibromatosis process in some people. Enzinger and Shiraki[20] described cases where the process developed in operation scars and in sites of injury from a variety of agents. In this complex picture, however, only the word predisposition really rings true, with definite familial tendencies in some cases.

Conclusion

This has been a very brief account of a clinicopathological concept of the fibromatoses. The necessity for this third world of fibroblastic behaviour seems to me to be inescapable. This concept, if understood better by clinicians and pathologists alike, must result in better treatment and the removal of the fear of cancer from many lives.

I am indebted to many clinical colleagues for permission to study cases under their care. My thanks are due to Dr. F. M. Enzinger, of the Armed Forces Institute of Pathology in Washington, for the loan of slides, and to the department of medical photography, Westminster Medical School. I am indebted to Blackwell Scientific Publications Ltd., Oxford, for permission to use the data in Table I.

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Clinical Problems

Diagnostic Accuracy of Early Radiology in Acute Gastrointestinal Haemorrhage

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Summary

The accuracy of early radiology in patients with acute gastrointestinal haemorrhage has been studied by a comparison of the radiological opinion with the established diagnosis. A full examination has proved safe and uncomplicated with a high degree of accuracy and no false-positive results.

Analysis of the errors shows that the presence of residue discourages the radiologist from making the correct diagnosis, and modification of the standard barium-meal technique may be needed to overcome this difficulty.

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Introduction

Prompt investigation of patients presenting with acute gastrointestinal haemorrhage is accepted as a method of providing valuable information for their clinical management,[1] and an active policy of early diagnosis is advocated in many units.[2–4] Endoscopy has been widely used in the early phase with results as good as those claimed for radiology in the detection of gastric lesions.[4] Improvements in radiological technique have received little recent emphasis, and clearly it is important to define the current diagnostic accuracy of the best radiological methods available when the value of endoscopy is being considered.