75% of of the predicted value, whereas 6 (40%) of the patients in the inoperable group and 3 (25%) of the patients in the lobectomy group did so.

Several mechanisms are probably responsible for the defects in perfusion. Bronchial obstruction is known to reduce blood flow to the affected region (Wagner *et al.*, 1965). In this series perfusion of the affected lobe was moderately or greatly reduced in 11 out of 14 patients with a narrow or obstructed bronchus. Ten of these patients, however, also had impaired perfusion of the adjacent unobstructed lobe, and five patients with normal bronchoscopies had large defects in perfusion, indicating other mechanisms.

The pulmonary arteries may be invaded by tumour, which is unusual, or thrombosed (Hatch *et al.*, 1965 ; Garnett *et al.*, 1968). The pulmonary veins are more often invaded, but the most frequently observed mechanism in our patients was distortion or compression of the pulmonary vessels by the primary tumour or by enlarged lymph nodes along the bronchi and at the hilum.

In patients with clinically and bronchoscopically operable carcinoma of the bronchus preoperative lung scans make it possible to predict with some confidence when a tumour is unresectable. They also give some indication when a pneumonectomy will be required or a lobectomy possible. Fifteen patients in this series (35%) were found to have unresectable tumours. In 10 of these perfusion of the affected lung was less than one-third of the total perfusion. If thoracotomy had not been advised in these 10 patients on the basis of their lung scan findings, then the unresectable rate would have been 15% (5 out of 33)—a reduction of 20%.

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Failure of Intravenous Aspirin to Increase Gastrointestinal Blood Loss

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Summary: Studies of the effect of intravenous sodium acetylsalicylate (aspirin) on gastrointestinal blood loss with ^{51}Cr-labelled red cells were made on 15 healthy male volunteers. After a control period of five days 1 g. of sodium acetylsalicylate was infused over a period of 100 minutes twice daily for three days. Faecal blood loss was not increased.

In a further six subjects 3 g. of sodium acetylsalicylate was infused over a period of 120 minutes. No salicylate or acetylsalicylate was detected in saliva or gastric washings from these six subjects. Hence gastrointestinal blood loss induced by aspirin may be explained by a local effect on mucosa and not by any systemic effect.

Introduction

Most subjects ingesting about 3 g. of unbuffered aspirin daily develop occult gastrointestinal bleeding (Grossman, Matsumoto, and Lichter, 1961 ; Goulston and Skyring, 1964 ; Smith and Smith, 1966 ; Beeken, 1968). Systemic administration of aspirin has been reported to cause occult gastrointestinal blood loss in man (Grossman *et al.*, 1961) and gastric erosions with bleeding in animals (Barbour and Dickerson, 1938 ; Clark and Adams, 1947 ; Lynch, Shaw, and Milton, 1964 ; Brodie and Chase, 1967). The doses used to show a systemic effect in man and animals were large, and were given in so short a period that it was possible that aspirin may have had a general toxic effect, or diffused into upper gastrointestinal secretions and acted by a local mechanism. There have not been any studies in man using smaller and more usual doses of aspirin.

The aim of the present study was to measure faecal blood loss in response to a dose of intravenous aspirin known to cause gastrointestinal bleeding when given orally.

Methods

Studies were made on 15 healthy male volunteers aged 21 to 23 years. All subjects ate an unrestricted diet and did not ingest any compound containing salicylates during the study. Faecal blood loss was measured by a chromium-51 red blood cell labelling method (Goulston and Skyring, 1964). Collection of faeces was started 48 hours after labelling of red blood cells, and a disposable paint tin was used for each 24-hour faecal

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specimen. Faeces were collected for 10 consecutive days. On the fifth, sixth, and seventh days sodium acetylsalicylate was given twice daily by a continuous intravenous infusion. Sodium acetylsalicylate was prepared by dissolving 1 g. of aspirin (acetylsalicylic acid powder, *B.P.*) in 150 ml. of normal saline in which 1 g. of sodium bicarbonate (AR, Univar) had been dissolved. This solution was filtered through a Seitz pad, pressure being used, into a bottle containing 300 ml. of sterile normal saline. The solution of 1 g. of sodium acetylsalicylate was given twice daily (8 a.m. and 4 p.m.) over a period of 100 minutes. Each infusion was started within 30 minutes after adding aspirin.

Each specimen of faeces and of whole blood was counted for radioactivity in a high geometry counter having a liquid phosphor (Armac, Packard Instrument Co., Illinois). The first five days served as the control period. Day 5 was included in the control period even though infusions began on this day. This was done to allow for the usual delayed appearance of blood in the faeces from upper gastrointestinal bleeding. The mean faecal blood loss for this day was 0·3 ml. (S.E.M. ±0·07 ml.). The statistical difference between the control period and the following five-day period was tested by the paired *t* test (Snedecor and Cochran, 1967).

In a further study 3 g. of sodium acetylsalicylate was infused intravenously over two hours into six other subjects. Saliva was collected continuously. Gastric washings were done at one hour and two hours, 50 ml. of tap-water being used to lavage the stomach. A blood sample was taken at two hours. Samples of gastric washings, saliva, and plasma were tested for salicylate and acetylsalicylate (Trinder, 1954 ; Schanker, Shore, Brodie, and Hogben, 1957). The lower unit for detection of salicylates in gastric juice was 1 mg./100 ml. Faecal blood loss was not studied in these subjects.

Results

Mean daily faecal blood loss for each subject during control and experimental periods is given in Table I. Mean daily faecal blood loss for all 15 subjects during the control period was 0·4 ml. (S.E.M. ±0·09 ml.) and after intravenous acetylsalicylic acid was 0·6 ml. (±0·09 ml.) ($P>0·2$). Subject 14 had 1·5 ml. blood loss per day in the control period and Subject 9 had a mean daily loss of 1·7 ml. during the experimental period. The mean daily faecal blood loss for each day for all 15 subjects for days 1 to 10 was: 0·58, 0·26, 0·35, 0·68, 0·30, 0·74, 0·50, 0·49, 0·58, and 0·52 ml.

TABLE I.—*Mean Daily Faecal Blood Loss in Response to Intravenous Aspirin (ml. of Blood/Day)*

Subject	Control	I.V. Aspirin	Subject	Control	I.V. Aspirin
1	0·1	0·4	10	0·5	0·4
2	0·4	0·7	11	0·6	0·5
3	0·2	0·5	12	0·4	0·4
4	0·2	0·8	13	0·2	0·8
5	0·2	0·3	14	1·5	0·1
6	0·4	0·8	15	0·4	0·4
7	0·9	0·7			
8	0·2	0·6	Mean	0·43	0·60
9	0·3	1·7	S.E.M.	±0·09	±0·09

In the experiments in which 3 g. of sodium acetylsalicylate was infused intravenously for two hours no salicylate was detected in the gastric washings or saliva in any subject. In four subjects plasma acetylsalicylates at the end of two hours were 13, 22, 15, and 12 mg./100 ml. and plasma salicylates were 14·5, 19·5, 18, and 14 mg./100 ml. respectively. No clinical evidence of salicylism was noticed in any subject.

Discussion

There has been abundant evidence in man and animals that unbuffered salicylates cause gastrointestinal bleeding by a local effect. This was reviewed recently (Smith and Smith, 1966). The evidence for a systemic effect rests mainly on animal studies (Barbour and Dickerson, 1938 ; Clark and Adams, 1947 ; Lynch *et al.*, 1964 ; Brodie and Chase, 1967) and one study in man (Grossman *et al.*, 1961). In the animal studies large and often fatal doses were given (Table II). Furthermore, there have been studies in animals in which systemic salicylates did not cause gastric erosions or bleeding (Anderson, 1964 ; Hurley and Crandall, 1964 ; Davison, Hertig, and DeVine, 1966) (Table II). In the only previous study in man a large dose (3 g. of sodium acetylsalicylate) was given in a two-hour period.

TABLE II.—*Effect of Systemic Salicylates on the Gastrointestinal Tract*

Animal	Dose/kg. (mg.)	Route	Method of Administration	Response	Reference
Rat ..	64–128	Intra-peritoneal	One dose	Gastric erosions + bleeding	Brodie and Chase (1967)
Rat ..	500–600	Sub-cutaneous	One dose daily for 10 days	„ „	Barbour and Dickerson (1938)
Cat ..	475–950	Intra-duodenal*	One dose	„ „	Lynch *et al.* (1964)
Dog ..	20–30	Oral†	Three doses daily for 5 days	Bleeding	Clark and Adams (1947)
Dog ..	30–40	Intra-venous + sub-cutaneous	500 mg. loading dose intravenous then 100 mg./hr. sub-cutaneous for 2 hr.	No effect	Davison *et al.* (1966)
Dog ..	80	Intra-venous	One dose twice daily for 8 days	No effect	Hurley and Crandall (1964)
Guinea-pig	150–500	Intra-peritoneal or sub-cutaneous	One dose	No effect	Anderson (1964)
Rabbit	200	Intra-venous	One dose	No effect	Anderson (1964)
Man‡	40	Intra-venous	One dose in 2 hr. daily for 3 days	Bleeding	Grossman *et a* . (1961)
Man ..	13	Intra-venous	One dose in 1·7 hr. twice daily for 3 days	No effect	Present study

* Aspirin placed in duodenum.
† Aspirin given orally and response assessed in gastric pouches.
‡ Assuming a mean weight of 75 kg.

In the present experiments intravenous sodium acetylsalicylate infused over 100 minutes (1 g. b.d. for three days) did not increase gastrointestinal blood loss (Table I). In only one subject did faecal blood loss exceed 1·5 ml., the accepted upper limit of normal (Grossman *et al.*, 1961) (Table I). This dose of aspirin when given orally has been found to increase significantly gastrointestinal blood loss (Goulston and Skyring, 1964 ; Beeken, 1968 ; Goulston and Cooke, 1968). Thus this study does not support a systemic mode of action for salicylate-induced gastrointestinal blood loss. Recently Weiss, Aledort, and Kochwa (1968) found in normal subjects that acetylsalicylic acid (1·5 g.) impaired platelet aggregation and release of platelet adenosine diphosphate by connective tissue. A modest increase in bleeding-time also occurred. Thus there is little doubt that acetylsalicylic acid has a systemic effect on some platelet functions, but this effect does not cause faecal blood loss.

It has been postulated that large intravenous doses of salicylate may diffuse across gastric mucosa into the contents of the lumen and thus produce a local effect (Smith and Smith, 1966). Although this would be unlikely (Schanker *et al.*, 1957) owing to the pKa of acetylsalicylate, this hypothesis was examined in the present study and no salicylate was detected in the gastric contents. Caravati and Cosgrove (1946) reported similar findings but did not fully describe their methods. Furthermore, no salicylate was detected in saliva despite the more favourable *p*H conditions. These findings do not exclude the possibility of salicylates diffusing into the cells of the gastric mucosa but make it unlikely that they reach the lumen.

The results of the present experiments differ from those reported by Grossman *et al.* (1961). The blood loss reported by those workers, however, was of borderline statistical significance ; the dose used was large and was infused over a short period. If these factors (amount of blood loss, dose, and dura-

tion of infusion) are considered, the results of the experiments of Grossman *et al.* (1961) may not be at variance with those of the present study. Thus we suggest on the basis of the present studies that gastrointestinal blood loss associated with the usual doses of unbuffered acetylsalicylic acid can be fully explained by a local action on gastric mucosa, and that a systemic mechanism need not be postulated.

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Chest *X*-ray Film in Acute Myocardial Infarction

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Summary: A total of 185 chest x-ray films taken on 50 consecutive admissions to a coronary care unit were assessed independently for specific abnormalities by three observers. The commonest abnormality was upper lobe pulmonary venous congestion. When this was present by itself it did not appear to affect prognosis. Pulmonary oedema occurred in 12 of the patients, was associated with more pronounced pulmonary venous congestion (but not necessarily with cardiac enlargement), and usually cleared within five days. Generalized cardiac enlargement and septal lines were rarely seen. Clinically silent non-segmental shadows were found in six patients.

No consistent change in radiological abnormality was found in the first three days after infarction, but thereafter a gradual improvement occurred, so that before discharge the x-ray picture was nearly normal. There was good correlation between the presence and extent of lung crepitations and the presence of pulmonary oedema on the chest x-ray film.

It is suggested that the chest x-ray film is a useful additional index of the severity of heart failure in myocardial infarction.

Introduction

The chest *x*-ray film is helpful in the diagnosis of left heart failure, but its value as a routine investigation in myocardial infarction has not been established. Florid pulmonary oedema is uncommon, but the majority of patients have some signs of left heart failure (MacKenzie *et al.*, 1964; McNicol *et al.*, 1965; Fluck *et al.*, 1967), and lesser radiological signs would be expected to be common. We have therefore reviewed the chest *x*-ray films routinely taken of the first 50 patients admitted to the coronary care unit at Central Middlesex Hospital in an attempt to evaluate the diagnostic use of portable chest *x*-ray films in myocardial infarction and to assess the frequency and significance of individual signs of left heart failure.

Patients

The subjects reviewed were the first 50 patients admitted to the coronary care unit with a definite myocardial infarction (typical history with characteristic electrocardiographic (E.C.G.) changes or fewer E.C.G. signs (W.H.O., 1959) and a diagnostic rise in serum enzymes: serum hydroxybutyrate dehydrogenase exceeding 150 i.u./litre). The patients were selected only to the extent that men under the age of 65 years and older men or women with complicated infarctions were preferentially admitted, and in that they survived long enough to have a chest *x*-ray film taken. There were 49 men and one woman. The age range was 38 to 68 (mean 54) years. None of the patients had cardiogenic shock.

The patients were assessed by detailed physical examination on admission, with particular reference to clinical evidence of cardiac failure. Note was also made of any history of chronic bronchitis or hypertension (diastolic blood pressure known at any time to have exceeded 110 mm. Hg or settling above this level in convalescence).

Treatment depended on the overall assessment of the patient's condition and policy in the coronary care unit. Heart failure was treated vigorously; 39 patients received diuretics and 16 received digitalis. As treatment for heart failure was in part

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