Kirsner and Palmer (1940) and Kirsner (1941) recorded the pH of aspirated gastric samples at hourly intervals in patients with healing duodenal ulcer who were given hourly feeds of milk and cream plus antacids hourly midway between the milk feeds. The gastric contents were aspirated just before each feed—i.e., half an hour after the antacid was given. They found that milk and cream feeds alone (3 oz. total volume, made up of equal parts) had no effect after one hour, although others have found that larger volumes or more frequent feeds were very effective, as described above. A general diet raised the pH somewhat.

A number of antacids in various doses, and atropine, were tested. 2 g. CaCO_3 hourly raised the pH from 1.75 to 4.35, 2 g. magnesium carbonate from pH 1.9 to 5.1, 2 g. magnesium trisilicate from pH 1.95 to 2.57, 2 g. $\text{Ca}_3(\text{PO}_4)_2$ from pH 1.75 to 2.61, 2 g. $\text{Mg}_3(\text{PO}_4)_2$ from pH 1.65 to 3.06, and 30 c.cm. (1 fl. oz.) $\text{Al}(\text{OH})_3$ from pH 1.9 to 3.0. Atropine enhanced the action of CaCO_3 but had little effect on the other drugs.

The order of efficiency of drugs acting alone in equal (2-g.) doses was: (1) calcium carbonate; (2) magnesium carbonate; (3) tribasic magnesium phosphate; (4) tribasic calcium phosphate; (5) magnesium trisilicate. 30 c.cm. (1 fl. oz.) of 5% colloidal aluminium hydroxide is probably little inferior to calcium and magnesium carbonates.

Breuhaus and Eyerly (1941) studied the effects of antacids in man by recording the intragastric pH at 5-minute intervals for two hours. $\text{Ca}_3(\text{PO}_4)_2$, $\text{Mg}_3(\text{PO}_4)_2$, and CaCO_3 in doses of 1–1.3 g. raised the pH more effectively than 1.3 g. of NaHCO_3 , 10 c.cm. of colloidal $\text{Al}(\text{OH})_3$, or 0.65 g. of $\text{Mg}_2\text{Si}_2\text{O}_8$, and the effects were not necessarily proportional to the neutralizing capacity *in vitro*. This was particularly well shown when mucin was compared with the tribasic powders or CaCO_3 : 10 g. of mucin *in vitro* neutralized as much acid as 1 g. CaCO_3 or $\text{Mg}_3(\text{PO}_4)_2$, but in the stomach mucin was much less efficient than either of the salts. This was probably due to the inadequate distribution of the mucin in the stomach—obviously a question of prime importance. It was also shown that 90 c.cm. of milk half-hourly was inferior only to the tribasic powders and CaCO_3 .

Bennett and Gill (1939) have demonstrated the efficiency of colloidal aluminium hydroxide in patients with peptic ulcer (see Fig. 6). Suggestions have also been made by Schiffrin and

FIG. 6.—Milk plus aluminium hydroxide (Bennett and Gill, 1939).

Komarov (1941) that aluminium hydroxide and phosphate inactivate pepsin even at pH 1–2, but their work has been criticized on technical grounds by Schoch and Fogelson (1942).

It is unlikely that methods of treatment in which two-hourly milk feeds are given, with antacids halfway between, would be as efficient in neutralizing free HCl as the hourly administrations of Kirsner and Palmer; so a pH of 4 will probably not be reached for very long, and at night there will be no neutralization on either regime. Since the majority of peptic ulcers heal readily it may well be that complete inactivation of pepsin is unnecessary and that a pH of 2–3 will cause sufficient reduction of proteolytic activity. We do not know the answer to this question, but if an ulcer does not heal it is important to determine free HCl or pH levels of gastric contents to see how much neutralization has occurred. We have seen cases in which free acid levels increased when antacids were added to a two-hourly milk-feed regime, and such patients would probably require continuous drips of milk or colloidal $\text{Al}(\text{OH})_3$ to control free HCl levels adequately.

Summary

The immediate aim of peptic ulcer therapy is to inactivate the pepsin of gastric juice by raising the pH of gastric contents to 3.5–4. Neutralization to pH 7 is unnecessary, and may easily produce alkalosis.

Milk, magnesium carbonate, calcium carbonate, tribasic magnesium and calcium phosphates, colloidal aluminium hydroxide, and magnesium trisilicate are the most efficient and safe neutralizing agents.

Our own observations were made on patients in the Courtauld Research Ward of the Middlesex Hospital before the war, and we are grateful to Dr. T. Izod Bennett for permission to study his patients. We should like to thank Prof. Samson Wright for his advice and criticism.

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A PRECISION METHOD OF CEPHALOMETRY AND PELVIMETRY

BY

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No method of cephalometry in common use hitherto can claim to be a method of precision. Each is based upon a preliminary estimate (not upon exact measurement) of the height of the "greatest circular section" of the skull above the film. Measurements based upon estimates can never be consistently accurate. The essential features of the various methods are as follows:

Reece (1935) palpates the head, makes allowance for the thickness of the abdominal wall, and adds 2 in. to the tube-skull distance. Thoms (1927) estimates the height and inclination of the occipito-frontal diameter with the patient in the supine position, and after exposure of the film makes another exposure with a perforated lead strip placed above the couch at the height and in the plane of the occipito-frontal diameter. Rowden (1935) measures the foetal skull with the patient in the sitting position, using cephalic scale strips placed at the estimated level of the foetal skull. Walton (1931) and McDonogh (1935) take lateral views of the patient lying either prone or supine with lead marks or a graduated lead rule at right angles to the couch in order to determine the height of the skull above the film. Roberts (1935) examines the patient in the prone position without using a Potter-Bucky diaphragm, and measures the suboccipito-bregmatic diameter on the basis that at term the true diameter of $3\frac{1}{4}$ in. results in a film diameter of 4 in. Chassar Moir (1941) uses a lateral view with the tube at 5-ft. distance and with a scale interposed at the mid-plane of the pelvis. He claims that this gives a fairly accurate guide to the size of the foetal head in about 75% of cases.

It is obvious that in all these methods there is a margin of possible error. For instance, the thickness of the abdominal wall can be estimated but it cannot be measured. The taking of a lateral film in breech cases does not definitely establish the depth of the foetal skull, as the foetus may have moved in the interval between the exposure of the A.-P. and lateral views. A serious disadvantage of these methods is that they require the whole-time supervision of a radiologist. No radiologist should be expected to take the responsibility of calculating the size of a foetal skull from factors not estimated by him personally. These are some of the reasons why

cephalometric results are viewed with reserve by obstetricians and radiologists alike.

The method to be described is a modification of one recorded by Portes and Blanche (1924a, 1924b). It derives its accuracy from the fact that the distance of the foetal skull from the film can be ignored. It can be applied with the patient in any position—A.-P., P.-A., lateral, sitting, standing, prone, or supine. The films can be taken by a radiographer in the absence of the radiologist, and the latter can make his calculations with the knowledge that (except from gross carelessness on the part of the radiographer) the results will be accurate.

Technique

An exposure is made with the tube centred over the foetal skull, at a known tube-film distance. Then a second exposure is made with the same centring, but with a different known tube-film distance. The two exposures may be made on one film, or, if preferred, a separate film used for each exposure. The technique is simple and rapid. The resultant film images are measured and applied in a simple formula (Formula 1), which gives the actual length of the diameter under consideration.

For simplicity in working out the formula, it is recommended that the tube-film distance (X and Y) should be simple numbers. I use 60 in. and 30 in., but other combinations such as 50 and 25 or 50 and 30 are equally effective. The choice of these distances depends partly on the power of the apparatus and partly on the facilities for moving the tube away from the film. With the patient lying or sitting, the tube is moved vertically. If the patient stands, the tube is moved horizontally.

Those who wish to test the accuracy of this method before applying it in practice should make the following experiment with an egg as the object for measurement:

Support the egg on a cardboard box placed on the radiographic couch. Centre the tube accurately over the egg with a small plumb-bob suspended from the centre of the tube aperture, and make an exposure with the tube, say, 40 in. above the film in the Potter-Bucky tray. Lower the tube to 20 in. and make a second exposure on the same film. After development measure the "greatest circular section" of both images and apply the formula to obtain the true diameter. Having done this, apply the second formula (Formula 2) $OF = Y - \frac{(DD \times Y)}{D_2 D_1}$, which will give the height of the centre of the egg above the film. Then check the results by direct measurement.

In cephalometry, the biparietal diameter is the most important. Next come the suboccipito-bregmatic and occipito-frontal. No film should be accepted for measurement which

the tube aperture during the exposure. Lower the tube to a second known distance and make another exposure on a second film. Examine the films after processing and make sure that the shadow of the plumb-bob is over the same part of the foetal skull in each film, and that one of the essential diameters is clearly seen. This is all that will be required before measurement when the films are dry.

If the preliminary A.-P. view shows that the position is a breech, note the position and orientation of the foetal skull and decide whether the examination can be continued with the patient supine, or whether a better view will be obtained with the patient in the lateral position. In either event the plumb-bob should be centred over the foetal skull and two separate exposures made. Thus, three films (one 15×12 in. and two 12×10 in.) are required in the average case, unless technical errors in exposure or in centring call for repeats. The length of each exposure differs, of course, in relation to the height of the tube.

Pelvimetry

The method can be applied to obtain any transverse diameter of the inlet or outlet irrespective of its height above the film. There is no need to ensure that the conjugate diameter is parallel with the film. Each pair of films taken in the sitting, prone, or supine position will give data sufficient for measuring accurately the transverse diameter of the brim and the interspinous diameter, in spite of the fact that these diameters are on different planes. Both the intertuberosity and the interspinous diameters can be measured from the pair of films taken in the supine position. The intertuberosity diameter cannot be measured in the films taken with the patient sitting, as the ischial tuberosities are obscured by the pubic bones.

When taking films for transverse measurements it is essential that the pelvis should not be tilted to one side. In other words, the plane or planes that are being measured must be parallel with the film. The method, if applied to measurement of the diagonal conjugates, must be done with the patient sitting. The true conjugate is better measured with a single film in a lateral view, the patient standing with a metal scale placed between the thighs. In the A.-P. view in the sitting position, the upper anterior border of the sacrum is sometimes difficult to identify. In vertex cases it is often possible to measure the foetal skull, the transverse diameter of the pelvic brim, and the interspinous diameter from data supplied by a pair of 10×12-in. films.

In its application to pelvimetry this method has a certain resemblance to that devised by Hastings (1942), who uses a double exposure with a 3-in. horizontal shift. It differs, however, in this important respect: that whereas Hastings first determines the height of the diameter to be measured above the film and then proceeds to its measurement, with my method the true measurement is obtained direct.

Measurement of the transverse diameter by this method is simpler and more accurate than when measurement is based on the height of the symphysis pubis from the film: simpler because there is no need to palpate the symphysis, or to adjust its height so that it is level with the sacral promontory; more accurate because the transverse diameter is at a lower level than the true conjugate. The difference in height may be as much as two inches. In experiments on a dried pelvis I found an appreciable error in measuring the transverse diameter by Thoms's method, owing to the different levels of the true conjugate and transverse diameters in this particular pelvis. With the new method such errors are impossible and the patient's comfort is increased.

The following example illustrates the simple sum involved in calculating a diameter:

The tube-film distances = 30 and 60 in.

The short and long images = 4.8 and 5.3 in.

$$\text{Then (by Formula 1) the true diameter} = \frac{4.8 \times 5.3 \times 30}{(5.3 \times 60) - (4.8 \times 30)} = \frac{763}{174} = 4.4 \text{ in.}$$

Other Uses of the Method

The method can be employed to obtain exact measurements of any opaque circular or oval objects in the body and their depth from the surface. Irregularly shaped objects may require

- $T_1F (X)$ = Long tube-film distance
 $T_2F (Y)$ = Short tube-film distance
 $T_1F - T_2F (Z)$ = Difference of tube-film distances
 DD = True diameter (to be measured)
 D_1D_1 = Short image of diameter
 D_2D_2 = Long image of diameter
 OF = Object-film distance

$$\text{Formula 1: } DD = \frac{D_1 D_1 \times D_2 D_2 \times Z}{(D_2 D_2 \times X) - (D_1 D_1 \times Y)}$$

$$\text{Formula 2: } OF = Y - \frac{(DD \times Y)}{D_2 D_1}$$

does not show clearly one of these diameters, else a source of error will be introduced. The following procedure is recommended for routine examination:

Take an A.-P. view with the patient supine. If the position is a vertex take a vertical view through the pelvic brim with the patient in the sitting position. There is no need to ensure that the plane of the true conjugate is parallel with the film. The tube-film distances must be known, and should be recorded on the film before processing. A small lead plumb-bob should be suspended from the centre of

several separate examinations with the patient rotated in oblique positions in order to bring each diameter in turn parallel with the film. Linear objects can be measured provided that they are parallel with the film.

The calculation of the size of the tumour or cavity in the lung and its depth from any part of the chest wall is a simple matter. A double exposure on one film will suffice, or two separate films may be taken if preferred. The method can be used as a check on tomography. The size and depth of opaque cerebral tumours could be determined in a similar manner. The dimensions of a vesical or biliary calculus, or other opaque object, could be determined and compared with its dimensions at a subsequent examination. The results would be comparable even though the position of the object had changed. No doubt other applications of this method will present themselves.

Summary

A new radiometric method is described.

It is claimed to be a method of precision, as the human factor in first estimating the distance of the object from the film is eliminated.

The application of the method to cephalometry and pelvimetry is described in detail.

Other applications in surgery of the brain, chest, abdomen, and pelvis are indicated.

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INTRAMUSCULAR INJECTION OF MEPACRINE (ATEBRIN): HISTOLOGICAL EFFECT

BY

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This note describes a histological examination of the effect of injecting mepacrine methanesulphonate (atebrin musonate) intramuscularly. Owing to the shortage of quinine, mepacrine will be used more extensively than in the past. When oral administration is impracticable it will be necessary to inject the drug intramuscularly or intravenously; in order to assist the choice between these two routes information is presented about the local effects caused by intramuscular injection.

Literature

Many clinical observations on the subject have been reported, but histological observations have not been described. Field, Niven, and Guest (1937) injected two doses each of 0.375 g. musonate into 284 patients. Local reactions were usually unimportant, but occasionally there was a little tenderness and induration at the site; in one case an abscess with atebrian-stained contents developed. During the Ceylon malaria epidemic (1934-5) 681 patients were treated with similar doses; 21.3% developed pain at the site of injection, and in two cases abscesses occurred. (When quinine was injected 36% of 424 patients suffered from pain, but there were no abscesses.) In a later series of 530 cases treated in the field most patients complained of pain for 2 to 4 days, some suffered from painful swelling and induration at the site, and in two instances abscesses resulted. Pain after the injection of atebrian was less frequent than after the injection of quinine; it might be severe. Abscesses were indolent and slow to heal; they were similar to those caused by quinine, and tracked along the fascial planes in the same way. Hay, Spaar, and Ludovici (1935) treated 3,500 cases; pain was negligible and no abscesses were observed. Simeons (1936) injected two doses each of 0.3 g. into 2,800

people. With good aseptic technique no abscesses occurred; but with a second series of 2,800 cases, in which aseptis was less satisfactory, there were 49 abscesses. Clinical series in which the local reactions were considered as unimportant are also reported by Carman and Cormack (1936), Eckhardt (1933), Kröber (1936), Seelig and Singh (1936), Sicault (1934), Siegenbeek van Henkelom and Overbeek (1938), van Slype (1935), Vardy (1935). Dove (1942) recommends the intramuscular injection of atebrian as being less harmful than quinine. The injection is not painful, and if done with sterile precautions will not cause abscesses; Dove prefers it to intravenous injection of atebrian.

Experimentally Hecht (1933) injected 0.1 c.cm. of a 1% solution of the hydrochloride—i.e., 1 mg.—apparently subcutaneously; it caused hyperaemic swelling, which disappeared in 24 to 48 hours without necrosis. Hicks (1935) injected 10 to 20 mg. atebrian musonate intramuscularly into 8 monkeys, which were killed two days later. In one case he found macroscopically an area of congestion 1×0.5 cm., haemorrhage, and oedema, but the rest showed no gross changes; no histological observations were made.

Summing up the literature, it is generally considered that the intramuscular injection of atebrian is as a rule innocuous, but pain and swelling occur in some patients, and, rarely, abscesses may result.

Experimental Results

The present experiments were made by injecting mepacrine methanesulphonate (quinacrine), 50 mg. in 0.5 c.cm. of distilled water, into rabbits weighing 1.5 to 2 kg. Most of the injections were made into the muscles of the thigh or of the loin, but some were made under the skin of the abdominal wall. If larger quantities—e.g., 70 mg. per kg.—were injected the rabbits were often prostrated in about 5 minutes, and some died; apparently absorption is very rapid. Injections were also made into rats. The rabbits were killed after 1 to 5 days and the rats after 1 to 14 days; the site was excised, fixed in formal-saline, and examined by the usual histological methods.

Naked-eye Appearances.—After intramuscular injection the macroscopic evidence of injury was usually slight. The muscles might be somewhat swollen and small haemorrhages might be present along the needle track. In the thigh, the intermuscular space along the sciatic nerve was often stained yellow from hip to knee. But in most cases there was little to be seen, and the site of injection was often difficult to identify. After subcutaneous injection the skin was usually greatly swollen, sometimes becoming as much as 1 cm. in thickness, the swollen area being 4 cm. in diameter. The swelling occurred in the connective tissue of the skin, which was stained yellow and distended with fluid. After 5 days the affected part was converted into a hard dry necrotic mass. The underlying muscles were little affected.

Microscopical Appearances.—Sections taken 1 to 2 days after intramuscular injection showed areas of necrosis in the muscles. The affected fibres were swollen, structureless, and eosinophilic, and the nuclei were destroyed. A moderate amount of fluid (often albuminous) was present between the fibres, but cell-infiltration was minimal. The areas of necrosis seen on the slide (transverse section) measured 0.5 to 1 cm. across, but they probably extended over a greater distance in the longitudinal direction. In cases in which the site involved an intermuscular space the connective tissue was greatly distended with fluid and a moderate number of cells, most of the cellular elements being necrotic. Nerve trunks showed haemorrhage and degenerative changes, and the outer coats of the larger blood vessels were necrotic. The necrosis also involved the superficial layers of the adjacent muscles. At the edges of the necrotic region there were moderate collections of cells. In the adjacent areas the muscle fibres were often swollen, and stained irregularly. After 4 to 5 days the cellular reaction around the area of necrosis was more pronounced, granulation tissue began to appear, and a zone of demarcation became established.

After subcutaneous injection the appearances were similar. The deeper connective tissue of the skin was greatly swollen with fluid, and towards the edges it was patchily infiltrated with cells, many of which were degenerate; the whole tissue had undergone necrosis over a considerable area. The sub-