minutes with no further change in an hour's exposure. The loss was about 5 per cent. In the more alkaline solutions the destruction was nearly complete (96 per cent) in 5 minutes. Much of the loss was due to NaCl formed in the reaction. In fact, about 75 per cent of the decreased action observed in the more alkaline solutions may be ascribed to the NaCl effect.

SUMMARY.

1. The inactive principles of an extract of gastric mucosa can be activated to various degrees by varying the degree of original activity.

2. The activity developed at a given degree of acidity can be destroyed by 30 minutes' exposure to a weakly alkaline solution and cannot be restored on acidification to a point below or equivalent to the original H-ion concentration.

3. Further activity can be demonstrated by acidifying to higher degrees than the primary acidity.

4. The proportionate loss in digestive power is greater, upon making the solution alkaline, the higher the degree of preliminary acidity.

5. The activity shown by an acidified extract of gastric mucosa is dependent in part upon the actual amount of active enzyme present.

6. The effect of alkalinity upon the unactivated extract is to lower the resultant activity after acidification. The effect increases rapidly with increasing alkalinity, and all digestive action may be lost around pH 12 to pH 13.

7. Except for the very slight alkalinity of pH 8.00, this destruction by alkali is rapid, reaching its maximum in a few minutes.

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Behavior of Human Gall-Bladder During Fasting and in Response to Food.

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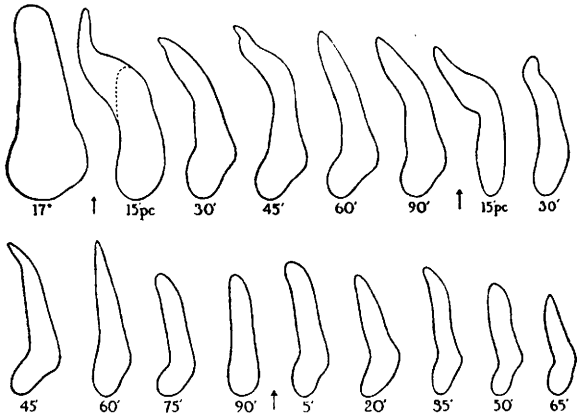
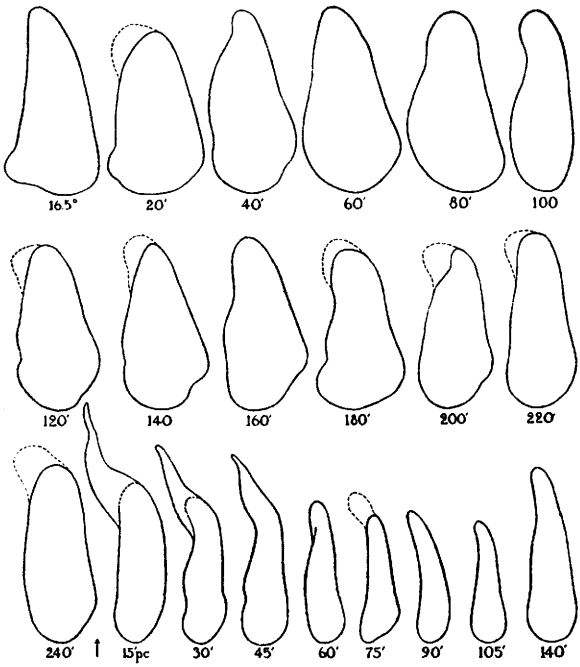
In a recent paper by the author,[1] roentgenological evidence from patients and experimental animals was presented in support of the following conclusions: (1) the mammalian gall bladder, at least in

FIG. 1.



Tracings of human cholecystograms x ¼ (Dr. L. O. Morgan); (three weeks later than those in Fig. 2). 17°-Gall bladder 17 hours after oral administration of iodine salts. Arrows indicate three intervals at which milk was taken.

FIG. 2.



Tracings of human cholecystograms x ¼ (Dr. L. O. Morgan, Sept. 27, 1926). First two rows indicate changing shape of gall bladder during fasting. Dash lines denote ampulla. Note contraction at 100'. Third row shows response to ingestion of half pint of cream. Volume at 240', 2.85 cu. in.; at 60', 0.5 cu. in.; at 105', 0.35 cu. in. of bile.

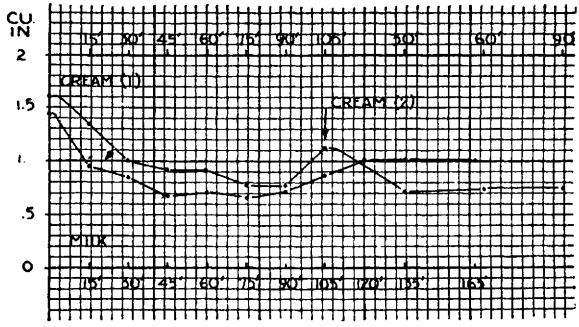
man and in cats, is able to expel all its fluid contents by the contraction of its musculature; (2) after meals this contraction is so timed as to meet the first requirements of digestion—in contrast to hepatic secretion which is designed to meet later needs; (3) in cats the gall bladder responds to such changes in the circulation as are produced by blood transfusions and to such superficial lesions as are caused by shaving and by cutaneous incisions; (4) adrenalin (with its implication of the sympathetic nervous system) is the most powerful excitant of gall bladder contraction yet found.

One of the methods employed was the making of long series of human cholecystograms at 15-minute intervals after meals. In such series it was found that the first X-rays after food showed changes in shape of the human gall bladder which could be interpreted as due only to muscle contraction. In two new series (with Dr. L. O. Morgan as the subject) this fact has been even more strikingly brought out than before (15′ pc., Figs. 1 and 2). During the first 240 minutes (Fig. 2) the gall bladder assumed the shape of a flaccid organ, subject to distortion by external pressure. Fifteen minutes after ingestion of cream the wall tightened and there was revealed an *actual expulsion of iodized bile into the cystic duct.* During the preceding period of fasting, however, there occurred one marked contraction (100′, Fig. 2), as a result of which the volume of the gall bladder shrank from 4.15 cubic inches to 2.17 (for method of calculation, see former paper). This was the only time when Doctor Morgan complained of hunger pangs, and, the coincidence would seem to corroborate Boldireff's statement[2] that during fasting, bladder bile is discharged into the duodenum synchronously with contraction of the stomach. This finding, together with the writer's discovery that certain changes in the circulating blood cause discharge of bladder bile, raises the question as to whether contraction of the gall bladder may not, at times, subserve another function than that of digestion.

Another problem which has puzzled recent workers in this field, relates to the particular elements in the food which cause excretion of hepatic bile and contraction of the gall bladder. Working with dogs, Klodnizki[3] has shown that egg-yolk causes greater acceleration of bile flow from the liver than any other food, and I have found that in cats the same substance induces the most effective contraction of the gall bladder (indeed being the only natural food which consistently empties that viscus).[4] Although Klodnizki has not analyzed the effect of egg-yolk he has given a curve of secretion of hepatic bile following ingestion of milk (*continuous line,*

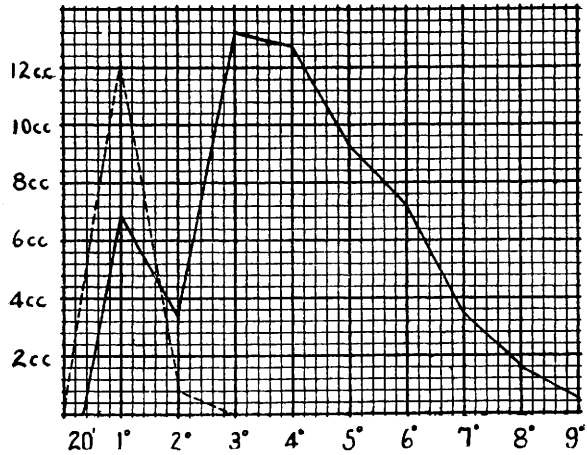
Fig. 4). In analyzing the reaction to this food he correlates the first flow of hepatic bile with the entrance of neutral fat into the duodenum, and the second (which is by far the greater) with the entrance of split products of milk digestion. In order to test the effect of the latter on the gall bladder, another volunteer patient

FIG. 3.



Graphs from two series of human cholecystograms (R. L. Webb: milk series, lower line, Sept. 23, 1926; cream series, upper line, Oct. 14, 1926). Volumes of bile computed from tracings of gall bladder shadows. Abscissas represent time in minutes after a meal; ordinates, volume of bile in cubic inches. Compare with similar graphs in former paper (foot note 1). *Arrow*, second application of cream.

FIG. 4.



Graph illustrating rate of biliary flow after ingestion of milk. *Dash line*, amount of bladder bile leaving the gall bladder in milk series of R. L. Webb (computed from lower line in Fig. 3). (In Dr. Morgan's case, Fig. 3, where we were dealing with a large gall bladder, the discharge of bile in the first hour after milk amounted to 37 cc. *Continuous line*, (after Klodinzki) showing amount of liver bile collected per hour, after diet of milk, in bile fistula dogs.

(Mr. R. L. Webb) was given a pint of milk and then X-rayed at frequent intervals for 3 hours (lower line, Fig. 3). In the first hour, over 12 cc. of bile was expelled from the gall bladder; in the second hour, less than 1 cc.; and in the third hour, none (*dash line*, Fig. 4). Therefore, if the rate at which the split products of milk are formed in man at all resembles that for dogs, we must assume that the split products of milk do not induce effective contraction of the gall bladder. The substance which stimulates the biliary reservoir would thus appear to be some element in undigested food, such as neutral fat. But when a half pint of cream was tried on the same individual (upper line, Fig. 3), no greater effect was produced, in spite of the greater amount of fat in cream. Accordingly a comparison of the effect of these two diets suggests that the distended gall bladder is a trigger mechanism which is set off by a moderate amount of neutral fat, the quantity of which is not important beyond a certain minimum. To confirm this idea, periodic feeding of milk was resorted to (Fig. 1). The first pint induced a marked expulsion of bile, lowering the volume in one hour from 2.8 to 0.55 cu. in.; as the gall bladder began to fill, a second pint was given, lowering the volume in the next hour and a half to .33 cu. in.; finally, a third dose diminished the contents of the gall bladder to .17; and it is not unreasonable to assume that further feedings would have emptied the viscus. The effect of these repeated feedings is to reproduce the successive phases of contraction (and eventual collapse of the gall bladder) which the writer has produced by one feeding of egg yolk and cream. From this we may infer that egg yolk is so effective because successive portions of its fatty substance may continue to be discharged into the duodenum for a long period (egg yolk being retained in the stomach of cats for at least 7 hours); and that after the gall bladder has emptied itself (2 to 3 hours after a meal) the subsequent flow of hepatic bile tends to keep the sphincter papillae open and prevent filling of the reservoir. It is interesting to note, however, that ingestion of food is most effective when the gall bladder is distended. Apparently the response of smooth muscle in this organ is greatest when it is stretched (*cf.*, also with the urinary bladder), to which may be added the auxiliary action of abundant elastic tissue in its wall.

This initial reaction to many foods, containing a moderate amount of fat, emphasizes the importance of the gall bladder as an organ of digestion; and since it plays so consistent a rôle, there should be an end to the indiscriminate cholecystectomy of the last decade. The fact that it is not a vital organ is no argument against its utility.

Also, at present, it is equally indefensible to deny its importance on the ground that certain animals normally reach maturity without developing a storage organ for bile. For in such species a different latent period and modified rate of hepatic flow may yet be found to compensate for loss of the *vesica fellea*.

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[1] Boyden, E. A., *Anat. Rec.*, 1926, xxxiii, 201-256.

[2] Boldireff, W. N., *Diss.*, St. Petersburg, 1904.

[3] In Babkin, "Die äussere Sekretion der Verdauungs-drüsen." Berlin, 1914, p. 345.

[4] Boyden, E. A., *Anat. Rec.*, 1923, xxiv, 388; *ibid.*, 1925, xxx, 333.