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ERENCE TO SECRETION.

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IN a previous paper<sup>2</sup> on the "Influence of Alcohol and Alcoholic Drinks upon the Chemical Processes of Digestion" it was carefully pointed out that any complete and satisfactory answer to the question "How do alcoholic fluids affect digestion?" cannot be obtained by any single line of experimentation, since the rate and extent of digestion may be modified in a variety of ways and through a variety of channels. Thus, due consideration must be given not only to the direct influence of alcoholic fluids upon the solvent or digestive power of the several digestive juices, but heed must also be given to the quantitative and qualitative modifications which the secretions themselves may undergo, as well as to variations in the rate of absorption and to the possible interaction of these and other factors. In our earlier paper, the data presented threw light only upon the character and extent of the influence exerted by various alcoholic fluids upon the purely chemical processes of digestion, *i. e.*, upon amylolysis and proteolysis. In the continuation of these studies during the past year our efforts have been directed mainly to acquiring a fuller knowledge of the action of alcoholic beverages upon secretion; and in so doing new data have been obtained which, it is hoped, will prove of value in explaining more fully the action of these fluids upon the whole process of digestion.

SALIVARY SECRETION.

The current statements regarding the influence of alcohol on the secretion of saliva are confined to a brief reference to the direct

<sup>1</sup> Being a statement of some research work done for the Committee of Fifty for the Investigation of the Liquor Problem, and to be regarded as a preliminary report, contributing facts upon which a general discussion may in the future be undertaken by the Committee as a whole.

<sup>2</sup> CHITTENDEN and MENDEL: American journal of the medical sciences. 1896, January-April.



action on the flow into the mouth. Thus it is stated that almost coincident with the burning sensation caused by alcohol taken into the mouth, a copious flow of saliva begins, due to reflex stimulation of the glands through the nervous system.<sup>1</sup> We have performed experiments with the object of ascertaining (1) the possible variations in the amount of salivary flow due to the presence of alcoholic fluids in the mouth, psychical influences being eliminated so far as possible; (2) the character of the saliva thus secreted; (3) the influence upon secretion of alcoholic beverages introduced into the stomach. It seemed particularly desirable to investigate this latter phase in view of the asserted influence of irritating substances (vinegar, alcoholic extract of pepper, etc.) when introduced directly into the alimentary tract through a fistula. There is said to result under such conditions a reflex flow of saliva, the nervous impulses being transmitted through the vagus.<sup>2</sup>

**The Influence of Alcoholic Fluids introduced into the Mouth.**—In the following experiments the attempt was made to ascertain something as to the character and extent of the direct stimulation of the salivary glands provoked by the presence of alcoholic fluids in the mouth, as well as to determine what quantitative changes, if any, may be called forth in the composition of the secretion in this way. These experiments were made on both man and dogs. The method, in the first instance, consisted in taking into the mouth 10 c.c. of the fluid studied, and allowing it to remain there for an instant previous to swallowing it. The normal conditions were thus closely imitated, and reflex influences from the stomach not excluded. The head was now turned to one side and rested upon the arm, the saliva being allowed to collect in the cavity of the mouth. As the fluid accumulated it was from time to time, during fifteen to twenty minutes, allowed to flow out of a corner of the mouth into a measuring vessel. Movements of the jaws and tongue were carefully avoided and psychic stimulation was excluded as far as possible. The method, already recommended by Hofbauer,<sup>3</sup> was found to be reasonably satisfactory, and control trials showed that the quantities of saliva obtained within periods of fifteen or twenty minutes could be appropriately compared.

<sup>1</sup> Compare, for example, KÜHNE: *Lehrbuch der physiol. Chemie*, 1868, p. 2; LAUDER BRUNTON: *Disorders of digestion*, 1886, p. 143.

<sup>2</sup> OEHL: *Comptes rendus*, lix, p. 336, quoted by HEIDENHAIN, *Hermann's Handbuch der Physiologie*, 1883, v, p. 83.

<sup>3</sup> HOFBAUER: *Archiv für die ges. Physiol.*, 1897, lxxv, p. 503.

Of the saliva thus collected, 3-4 c.c. were taken for analysis. A weighed quantity was dried in a tared crucible on a water-bath and then for four or five hours at 105°C., this time being found sufficient to bring crucible and contents to a constant weight. Total solids were thus determined. The crucible was then ignited, care being taken to prevent loss by volatilization of salts. The ash thus obtained is given as salts in the protocols, while the organic constituents were obtained by subtracting the amount of salts from the total solids. In some cases the amount of Cl in the ash was determined by the usual method of titration with weak silver nitrate solution. The analytical results are all expressed in percentages. The following figures serve to illustrate the results of a typical duplicate analysis:—

SUBMAXILLARY SALIVA OF DOG.

	Water.	Total solids.	Organic constituents.	Salts.	Chlorine.
A.	98.99	1.01	0.80	0.21	0.042
B.	98.99	1.01	0.78	0.23	0.040

It is an observation easily verified, that the presence of a small quantity of strong alcohol or alcoholic beverage in the mouth excites a sudden flow of saliva. This acceleration in flow is, at most, a very brief one, and the rate of flow quickly returns to that pertaining to normal conditions, *i. e.*, absence of stimuli in the mouth. The stimulation in this case is not due merely to the mechanical action of the fluid introduced, nor is it a form of stimulation specific for alcohol alone, as our experiments on dogs have demonstrated. Thus, animals were anaesthetized with ether and chloroform through a tracheal cannula (thereby avoiding direct stimulation of salivary flow), a small dose of morphine, or a larger one of chloral, having been previously administered. A cannula was then introduced into one or both ducts of the submaxillary glands. A small wad of absorbent cotton moistened with the fluid to be studied was introduced with a forceps into the back of the mouth upon the tongue, and the flow of saliva from the ends of the cannulas noted. It was found by this method that water or weak sodium chloride solution (0.7 per cent) produced no further effect than the secretion of a drop or two of

## SALIVARY EXPERIMENTS ON MAN.

	I.		II.		III.		IV.		V.		VI.		VI.		VIII.	
	water a	water b	water a	water b	water a	water b	water a	water b	water a	water b	water a	water b	water a	water b	water a	sherry b
Amount collected in c.c. per 10 minutes.	4.0	4.0	4.4	3.7	2.7	5.3	3.8	4.4	4.7	8.0	4.4	7.1	4.0	4.6	3.5	4.4
Water, per cent.	99.49	99.57	99.52	99.54	99.51	99.49	99.50	99.40	99.57	99.19	99.56	99.45	99.57	99.51	99.41	99.39
Total solids, per cent.	0.51	0.43	0.48	0.46	0.49	0.51	0.50	0.60	0.43	0.81	0.44	0.55	0.43	0.49	0.59	0.61
Organic constituents, per cent.	0.36	0.31	0.35	0.33	0.33	0.35	0.35	0.45	0.31	0.58	0.30	0.38	0.31	0.35	0.41	0.43
Salts, per cent.	0.15	0.12	0.13	0.13	0.16	0.16	0.15	0.15	0.12	0.23	0.14	0.17	0.12	0.14	0.18	0.18
Salts calculated on total solids, per cent.	29.0	29.0	28.0	28.0	32.0	32.0	30.0	25.0	29.0	28.0	31.0	31.0	28.0	28.0	30.0	29.0

saliva due to the mere mechanical action of introducing the wad; with increasing strengths of salt the secretion was decidedly accelerated, flowing readily after application of 20 per cent salt solution, the acceleration, however, being very brief in duration (5 min.). The buccal cavity could be swabbed out with water occasionally, the effect being a minimal one. It was found that *weak* alcohol, introduced in this way, provoked little, if any, flow; while stronger alcohol (50 per cent) gave rise to a transitory secretion, the stimulation in this case, however, being far more marked than can be produced by the indirect action of alcohol through the stomach. Thus, in one animal, in which the activity of the glands was found pronounced when a drop of dilute acetic acid was applied to the tongue, injection of 100 c.c. 50 per cent alcohol directly into the stomach, failed to provoke any reflex salivary flow in half an hour.

Turning now to the influence of alcoholic fluids upon the rate of flow and composition of the saliva in man, the accompanying experiments, by the method above indicated, may be cited (p. 167). The first two (I. and II.) show the results obtained with successive portions of water; in the following ones, a control experiment with water in each instance preceded the trial with the alcoholic fluid.

The alcoholic content of the fluids employed was as follows: Brandy, 47 per cent by vol.; gin, 51 per cent; sherry, 21 per cent.

From these figures it is seen that the results obtained with two successive portions of water scarcely differ from each other, the tendency however being towards decreased flow accompanied by decrease in dissolved material in the saliva. Interpreted in physiological terms, these results indicate that the second stimulation with water is, if anything, weaker than its predecessor. In decided contrast appear the results obtained with the alcoholic liquors. Here may be observed an increased flow of saliva, not pronounced, but accompanied by an increase in both organic and inorganic constituents. The effect is precisely analogous, both in composition and rate of flow, to that brought about by an increase in intensity of stimulation, when the salivary glands are electrically excited through their nerves.<sup>1</sup>

The following diagram represents in graphic form the results given in the preceding table, *i. e.* (1) the relative rate of flow induced by water and by the alcoholic fluid; (2) the content of solid matter,

<sup>1</sup> Cf. HEIDENHAIN: Archiv für die ges. Physiol., 1878, xvii, p. 7, and Hermann's Handbuch der Physiologie, v, p. 52.



together with the relative proportion of ash or inorganic matter and of organic matter as indicated by the loss on ignition.

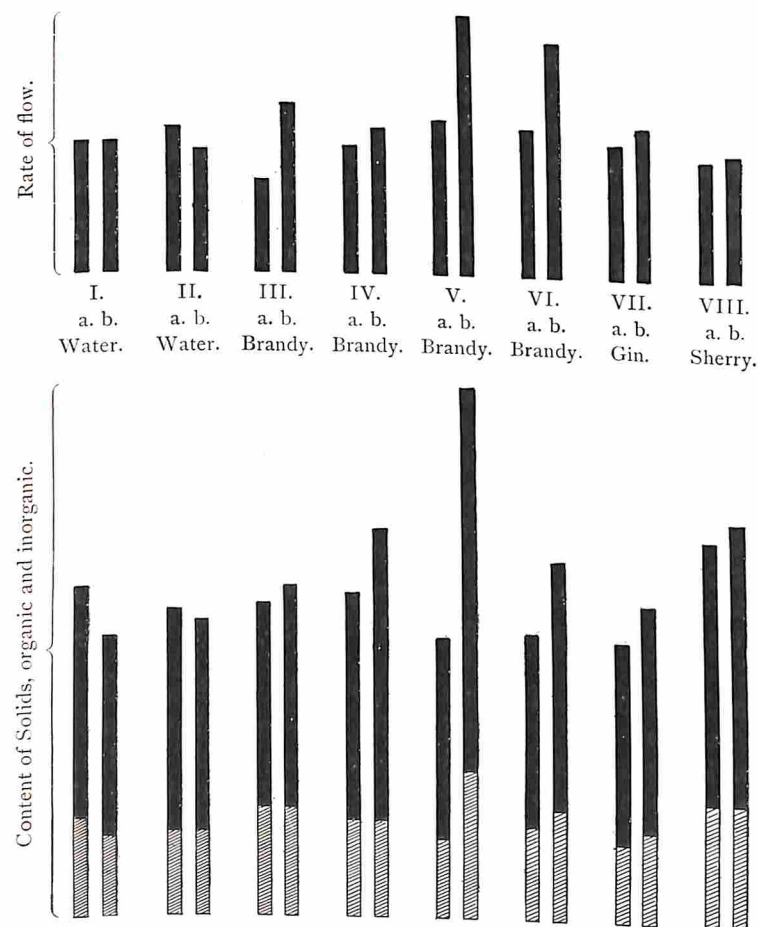


Diagram illustrating the relative influence of alcoholic fluids on the rate of secretion and composition of human saliva.

**The Influence of Alcoholic Liquors introduced directly into the Stomach.**

— In our experiments on the reflex stimulation of salivary flow, the attempt to produce a persisting secretion due to the presence of alcohol in the stomach was unsuccessful; nor have we been able to obtain evidence of an unusual flow of saliva under such circumstances in dogs with gastric fistulæ. It seemed desirable, however, to examine the possible direct influence of alcoholic fluids on the salivary glands

and the resulting secretion, when other factors were excluded as far as possible. In these experiments dogs of 10 to 18 kilos were used. Chloroform-ether mixture was employed to produce anæsthesia, and was administered through a tracheal tube in part of the experiments, the danger of respiratory difficulties resulting from salivary flow induced in the glands as a result of the ether stimulation being thus avoided. In the later stages of the experiments the alcohol introduced usually sufficed to maintain the animal in perfect quiet. Fredericq<sup>1</sup> has recommended the use of alcohol for producing narcosis in rabbits; it has been found quite satisfactory for this purpose in the dog, the effects passing off with relative rapidity.

A glass cannula, bent at the end, was tied in Wharton's duct (and occasionally a second cannula into the duct of the sublingual gland). The chordo-lingual nerve was ligatured and cut at some distance centrally to the point where the chorda tympani branches off to the glands. All secretion in the corresponding gland was thus stopped except during stimulation of the chorda, which was accomplished through raising the peripheral end of the cut nerve by the ligature and slipping hook electrodes under it. The interrupted current of a du Bois induction-coil with a single element was used as the stimulus. Saliva was collected in small graduated cylinders. Alcohol was introduced into the stomach by making an incision through the linea alba, etc., and injecting the fluid directly into the organ thus exposed by means of a large needle-pointed syringe. By careful avoidance of the larger gastric vessels, bleeding was minimal. The general course of the experiments was as follows: A distance between the primary and secondary coil of the inductorium was selected such as a preliminary trial showed to give a medium rate of flow. This stimulus was, so far as possible, kept constant throughout the experiment. The chorda was repeatedly stimulated for periods of one minute, followed by pauses of two minutes, during which the nerve was kept covered. In this way sufficient quantities of saliva for analysis were collected. Before collecting a sample of saliva under any given conditions, the six or seven drops first discharged were thrown away, and thus the fluid stored up from previous stimulation in the gland lumina, ducts, and cannula was avoided.<sup>2</sup> After collecting two or three control samples, the fluid to be considered (usually warmed slightly) was injected

<sup>1</sup> FREDERICQ: *Manipulations de physiologie*, p. 19.

<sup>2</sup> Cf. HEIDENHAIN: *Hermann's Handbuch der Physiologie*, v, p. 53; LANGLEY and FLETCHER: *Philosophical transactions*, 1889, clxxx, B., p. 112.

into the stomach in the manner already described, and this was followed by a pause of five minutes. The pulse was observed at frequent intervals to detect any possible influence on the heart's action and consequent blood-flow. The samples of saliva collected were analyzed in the manner already described. At the conclusion of the experiment, the animal was killed by bleeding, and the condition of the glands, as well as of the stomach and other organs, examined. The protocols of three typical experiments are given below.

I, iii, 1897. Dog. Weight 14 kilos. Chloroform and ether administered through tracheal tube during part of the experiment. Distance of secondary coil = 200 mm. Period of stimulation = 1 min., followed by a pause of 2 min.

	Time.	Amount saliva collected c.c.	Rate of secretion per min. c.c.	Water. per cent.	Total solids. per cent.	Organic matter. per cent.	Salts. per cent.	Chlorine. per cent.
I	10.35	5.3	0.7	98.76	1.24	0.94	0.30	0.026
II	11.08	5.4	0.6	98.94	1.06	0.73	0.33	0.036
III	11.38	5.2	0.8	98.95	1.05	0.69	0.36	0.044
IV	11.56	4.0	0.8	98.90	1.10	....	....	0.048
	12.20	80 c.c. 50 per cent alcohol injected into stomach.						
V	12.35	4.8	0.8	98.96	1.04	0.69	0.35	0.047
VI	12.55	4.8	0.8	99.01	0.99	0.59	0.40	0.076
	1.15	100 c.c. 50 per cent alcohol injected into stomach.						
VII	1.21	4.9	0.8	99.05	0.95	0.59	0.36	0.055
VIII	1.42	6.0	1.0	99.05	0.95	0.60	0.35	0.060
IX	2.02	5.5	0.9	99.14	0.86	0.52	0.34	0.048
X	2.24	5.2	0.8	99.17	0.83	0.47	0.36	0.042
	2.53	100 c.c. 50 per cent alcohol injected into stomach.						
XI	2.58	4.5	0.6	99.07	0.93	0.63	0.30	0.034
XII	3.27	6.0	0.6	99.18	0.82	0.53	0.29	0.037
XIII	4.10	5.0	0.7	99.17	0.83	0.49	0.34	0.038

Dog killed. Stomach mucosa normal in appearance. Urinary bladder and gall bladder greatly distended. Stomach contents = 450 c.c., faintly acid in reaction, and containing 24.6 grams of alcohol. No food present.

<sup>1</sup> In this first period the distance of the secondary coil was 280 mm., but the stimulation was unsatisfactory.

22, iii, 1897. Bitch. Weight 10 kilos. Chloroform and ether administered during operation. Tracheotomy performed after operation. Distance of secondary coil = 240 mm. Period of stimulation = 1 min., followed by 2 min. pause.

	Time.	Amount saliva collected c.c.	Rate of secretion per min. c.c.	Water. per cent.	Total solids. per cent.	Organic matter. per cent.	Salts. per cent.	Chlorine. per cent.
I	11.30	4.6	1.1	98.68	1.32	1.03	0.29	0.032
II	11.42	4.7	0.9	98.70	1.30	0.96	0.34	0.074
III	11.57	4.0	0.7	98.84	1.16	0.73	0.43	0.146
	12.35	150 c.c. burgundy injected into stomach.						
IV	12.41	4.9	0.8	98.72	1.28	0.91	0.37	0.092
V	12.59	5.5	0.6	98.78	1.22	0.87	0.35	0.096
VI	1.29	4.7	0.7	98.91	1.09	0.82	0.27	0.071
	2.00	200 c.c. burgundy injected into stomach.						
VII	2.06	4.7	0.6	98.88	1.12	0.82	0.30	0.058
VIII	2.32	....	....	98.98	1.02	0.69	0.33	0.099

Dog killed; stomach contents = 190 c.c.; claret color; mucosa not inflamed. Contents contained 13.1 grams of alcohol. The burgundy used contained 5.2 per cent of alcohol.

Experiments of the character indicated by these protocols were carried out with alcohol in varying doses, whiskey, brandy, and wine, and control experiments with water were also made. In attempting to interpret the analytical data thus obtained in experiments extending over several hours it is necessary to bear in mind facts regarding salivary secretion which seem to be sufficiently established. Ludwig<sup>1</sup> showed that the submaxillary saliva secreted during stimulation of the chorda tympani undergoes a change in composition varying with the duration of the flow, the content of organic solids decreasing in far greater degree than the dissolved salts. Heidenhain<sup>2</sup> found that the percentage of salts in the saliva varies directly with the rate of secretion, quite independently of the state of the gland, the organic constituents, however, being influenced by the condition of the secreting organ as well as by the strength of stimulus and

<sup>1</sup> LUDWIG and BECHER: Zeitschr. f. rat. Med., 1851, N. F. i, p. 278. Cf. also HEIDENHAIN: Hermann's Handbuch der Physiologie, v, pp. 47-49.

<sup>2</sup> HEIDENHAIN: Archiv für die ges. Physiol., 1878, xvii, pp. 4 and 6.



12, iv, 1897. Bitch. Weight 9 kilos. Chloroform and ether during operation. Distance of secondary coil = 190 mm. Stimulation 1 min., followed by a pause of 2 min.

	Time.	Amount saliva collected c.c.	Rate of secretion per min. c.c.	Water. per cent.	Total solids. per cent.	Organic matter. per cent.	Salts. per cent.	Chlorine. per cent.
I	9.24	4.5	0.9	98.76	1.24	0.97	0.27	0.062
II	9.40	4.6	0.7	98.89	1.11	0.81	0.30	0.054
	10.40	100 c.c. distilled water injected into stomach.						
III	10.53	4.7	0.6	99.04	0.96	0.66	0.30	0.049
IV	11.21	5.0	0.5	99.09	0.91	0.60	0.31	0.060
	11.50	100 c.c. distilled water injected into stomach.						
V	11.56	4.5	0.5	99.30	0.70	0.54	0.16	0.024
VI	12.25	4.5	0.6	99.33	0.67	0.36	0.31	0.078
VII	12.51	4.6	0.7	99.39	0.61	0.36	0.25	0.063
	1.18	100 c.c. 50 per cent alcohol injected into stomach.						
VIII	1.23	5.7	0.7	99.35	0.65	0.36	0.29	0.067
IX	1.44	4.8	0.8	99.38	0.62	0.32	0.30	0.087
X	2.03	4.7	0.7	99.47	0.53	0.29	0.24	0.087
XI	2.25	4.7	0.6	99.47	0.53	0.22	0.31	0.097

Dog killed. Stomach mucosa normal. Contents = 100 c.c. No odor of alcohol.

resulting rate of secretion. These observations, verified by Werther<sup>1</sup> and by Langley and Fletcher,<sup>2</sup> have been extended by the latter investigators, who formulated the opinion that "the secretion of organic substances depends wholly, or almost wholly, upon the strength of the stimulus, whilst the secretion of water and of salts depends also upon the amount of blood flowing through the gland."<sup>3</sup> In view of the well-known fact that changes in the strength of the stimulus immediately bring about a change in both rate of secretion and composition of the saliva, we have attempted to maintain a constant stimulus throughout each series of observations by selecting some satisfactory distance of the secondary coil of the inductorium and by applying the electrodes as uniformly as possible. Owing to

<sup>1</sup> WERTHER: *Archiv f. d. ges. Physiol.*, 1886, xxxviii, p. 293.

<sup>2</sup> LANGLEY and FLETCHER: *loc. cit.*, p. 152.

<sup>3</sup> *Ibid.*, p. 132.

the gradual decline in the irritability of the exposed nerve, the impossibility of applying the electrodes constantly in one position, and other unavoidable difficulties, ideal results cannot be obtained. However, the difficulties were present in every experiment and the results are therefore more or less comparable.

An examination of the data obtained in the manner above indicated shows no constant appreciable influence of alcohol or alcoholic fluids upon the *rate of secretion* of submaxillary (or sublingual) saliva under the influence of a constant external stimulus. Even large doses of alcohol, sufficient to produce prolonged narcosis, fail to check the salivary flow, a result in striking contrast to the effects which morphine may bring about when used in moderately large doses. We have not infrequently observed, in other experiments, an entire absence of salivary flow even with very strong stimuli, when morphine was unintentionally given in doses larger than were necessary to produce a mild narcosis. On the other hand, there is likewise an absence of any stimulating action on the glands, in our experiments; at least the slight variations in the rate of flow after alcohol is administered are no greater than those brought about by water alone (cf. third protocol above). On the *total solids* likewise, the presence of alcohol seems to exercise no noticeable influence. There is a tendency toward decrease in amount as the experiments progress; this decrease, however, is entirely confined to the *organic constituents* of the saliva, the *salts* remaining comparatively constant in amount, as can be seen in the protocols above. The decrease in organic substances is in no way to be attributed to alcohol, since it may be obtained with water alone (cf. protocol third), or in the course of any protracted salivary secretion. Nor is this decrease remarkable when it is remembered that a small gland weighing a few grams has furnished 50 to 75 grams of saliva in the course of three or four hours. The organic constituents of the cells must thus be exhausted somewhat more rapidly than the anabolic processes of the gland can replace them, while the salts are obtained with relative ease from the blood. Any effect upon the secretion of inorganic salts such as might result in accordance with Langley's law (cf. p. 173) was not observed. A large number of determinations of the alkalinity of the saliva (towards lacmoid) likewise failed to show any constant relations. It is interesting in this connection to note that the submaxillary saliva of the



dog was always found alkaline to phenolphthalëin, litmus, lacmoid, and methyloange. Mixed human saliva, like the bile of a number of animals, is almost always acid toward phenolphthalëin.<sup>1</sup>

#### GASTRIC SECRETION.

It has already been pointed out that in an accurate and complete study of the influence of alcohol and alcoholic drinks upon gastric digestion, no single line of experimentation can lead to full and concise results covering the whole ground of inquiry. It was therefore deemed advisable, for experimental purposes, to study the subject under several distinct heads, as (1) the influence of alcohol and alcoholic drinks upon the process of secretion; (2) upon the processes of absorption; (3) upon the motor functions of the alimentary canal; and (4) upon the purely chemical processes of gastric digestion. The last phase has already been considered at some length.<sup>2</sup>

The older announcements regarding the influence of alcohol are summarized in the statement that it is a strong stimulant of gastric secretion, and alcohol is recommended as a means of obtaining gastric juice from fistulæ in animals.<sup>3</sup> Larger doses are regarded as detrimental to the stomach, giving rise to transudation of alkaline fluid, — a process evidently pathological.<sup>4</sup> Gluzinski<sup>5</sup> found in experiments on man with brandy and dilute alcohol that these liquors gave rise, after a brief preliminary period, to the formation of a very active secretion rich in hydrochloric acid.

Likewise Wolff<sup>6</sup> states that cognac in small doses increases the secretion of hydrochloric acid, while in larger quantity it decreases the acidity of the gastric juice and retards peptone formation. The stomach fails to respond in a positive way, however, after the continued use of alcohol. While Klemperer<sup>7</sup> failed to note more than

<sup>1</sup> CHITTENDEN: The reactions of some animal fluids. *Science*, N. S., v, p. 902.

<sup>2</sup> CHITTENDEN and MENDEL: *loc. cit.*

<sup>3</sup> Cf. FRERICHS: Wagner's Handwörterbuch der Physiologie, 1846, iii, (1), p. 788; KÜHNE: Lehrbuch, pp. 28, 30; HEIDENHAIN: Hermann's Handbuch der Physiologie, v, p. 115.

<sup>4</sup> Cf. HEIDENHAIN: *loc. cit.*; LAUDER BRUNTON: Disorders of digestion, 1886, p. 144.

<sup>5</sup> GLUZINSKI: Deutsches Archiv f. klin. Med., 1886, xxxix, p. 405. See Jahresbericht für Thierchemie, 1886, xvi, p. 263.

<sup>6</sup> WOLFF: Zeitschr. f. klin. Med., 1889, xvi, p. 222; Jahresbericht f. Thierchemie, 1889, xix, p. 266.

<sup>7</sup> KLEMPERER: Zeitschr. f. klin. Med., 1890, xvii, Supp., p. 324; Centralbl. f. med. Wissen., 1891, p. 751.

a very slight increase in secretion resulting from moderate doses of alcohol, Blumenau<sup>1</sup> observed that 25–50 per cent alcohol introduced into the healthy human stomach acts as a secretory stimulant, bringing about an increased flow of gastric juice with rise of acidity after a period of 2–3 hours. More recently Brandl<sup>2</sup> has found in experiments on fistulous dogs that alcohol — as contrasted with water introduced with food stuffs into the stomach — brings about an unfailing, though not particularly large, increase in gastric secretion. With repeated and increasing doses of alcohol, Haan<sup>3</sup> has further observed an augmentation of acidity in the dog, followed by a diminution in the amount of secretion and a gradual decline in acidity after several doses.

In our first series of experiments on gastric secretion, attention was directed to the volume and acidity resulting from the introduction of alcoholic fluids into the stomach, independently of any stimulating action due to food simultaneously introduced. Dogs in fasting condition were employed in every instance, and morphine sulphate (introduced subcutaneously) followed by chloroform-ether was used preparatory to operative interference. The method consisted in ligating the duodenum just beyond the pylorus and then introducing a definite volume of the fluid to be examined into the empty stomach in the manner already indicated in previous experiments. In several cases, dogs with gastric fistulæ were employed. The abdomen was quickly sewed up after this operation, chloroform-ether stopped, and the animal allowed entire freedom of movement. The liquid employed was ordinarily warmed gently to avoid the asserted stimulating action of cold fluids on the gastric mucosa.<sup>4</sup> Ligations of the œsophagus and œsophageal fistulæ were avoided, since a somewhat extended experience with gastric fistula dogs, as well as the experiments about to be described, have convinced us, in agreement with Heidenhain's observations,<sup>5</sup> that under ordinary circumstances, *i. e.* in the absence of unusual stimuli (and with slightly narcotized animals) the amount of saliva secreted is small at most, and fails to induce any pronounced secretion in the stomach.<sup>6</sup> Further, we have

<sup>1</sup> BLUMENAU: Therapeutische Monatshefte, 1890, v, p. 504; Jahresbericht f. Thierchemie, 1891, xxi, p. 212.

<sup>2</sup> BRANDL: Zeitschr. f. Biologie, 1892, xxix, p. 304.

<sup>3</sup> HAAN: Comptes rendus de la société de biologie, 1895, ii, p. 817.

<sup>4</sup> Cf. KÜHNE: Lehrbuch der physiol. Chemie, p. 28.

<sup>5</sup> Hermann's Handbuch, v, p. 112.

<sup>6</sup> Compare also the experiment described on page 168.



found that an unusual flow of saliva is at once readily detected by the physical character of the stomach contents, *e. g.* frothing, etc. Furthermore, the conditions of our experiments were intended to approach those normally obtaining in the body as nearly as possible; and finally, a sufficient number of control experiments in which water was introduced into the stomach, have left no doubt as to the validity of the method. At the end of three to four hours—a period shown by our experiments to cover the digestion time of a test meal for the dog—the animal was bled to death, the œsophagus ligated at the lower end, the stomach removed from the body, wiped free from blood, and the contents discharged into a graduated vessel. In the fluid thus obtained total acidity, free and combined HCl, and acid reacting salts were determined by the method of Töpfer;<sup>1</sup> alcohol was estimated, when present, in the distillate from a definite portion of the gastric contents, by the pycnometer method; total solids were determined by drying a weighed quantity of fluid in a tared crucible at 100–105 C°. Protocols follow:—

**A. Control Experiments with Water:—**

I. 31 v, 1897. Dog, with gastric fistula, well healed. Weight 21 kilos. Fluid removed completely through fistula.

Introduced 200 c.c. *distilled water* at 10.50 A. M.

Contents removed at 1.55 P. M. = 3½ hrs.

Volume of fluid recovered from stomach = 160 c.c. = **80 per cent** of original volume.

Analysis of the contents gave:

Total acidity . . . . .	0.203 per cent. <sup>2</sup>
Free HCl . . . . .	0.192
Loosely combined HCl . . . .	0.002
Salts . . . . .	0.009
Total solids . . . . .	0.624

II. 28 vi, 1897. Dog, with gastric fistula, well healed. Weight 25 kilos. Fluid removed completely through fistula.

Introduced 135 c.c. *distilled water* at 11 A. M.

Contents removed at 1.45 P. M. = 2¾ hrs.

Volume of fluid recovered from stomach = 110 c.c. = **81 per cent** of original volume.

Analysis of the contents gave:

Total acidity . . . . .	0.274 per cent.
Free HCl . . . . .	0.241
Loosely combined HCl . . . .	0.018
Salts . . . . .	0.015
Total solids . . . . .	0.77

<sup>1</sup> TÖPFER: Zeitschr. f. physiol. Chemie, 1894, xix, p. 104.

<sup>2</sup> Expressed as HCl in all the experiments.

III. 24 v, 1897. Dog. Weight 7.7 kilos.

Introduced 125 c.c. *distilled water* at 10 A. M.

Contents removed at 1.50 P. M. = 3½ hours.

Volume of fluid recovered from stomach = 114 c.c. = **91 per cent** of original volume.

Analysis of the contents gave:

Total acidity . . . . .	0.094 per cent.
Free HCl . . . . .	0.065
Loosely combined HCl . . . .	0.004
Salts . . . . .	0.025
Total solids . . . . .	0.47

IV. 29 v, 1897. Dog. Weight 14.5 kilos.

Introduced 200 c.c. *distilled water* at 9.30 A. M.

Contents removed at 1.15 P. M. = 3¾ hrs.

Volume of fluid recovered from stomach = 206 c.c. = **103 per cent** of original volume.<sup>1</sup>

Analysis of the contents gave:

Total acidity . . . . .	0.047 per cent.
Free HCl . . . . .	0.040
Loosely combined HCl . . . .	0.004
Salts . . . . .	0.003
Total solids . . . . .	0.50

V. 2 vi, 1897. Dog. Weight 10.5 kilos.

Introduced 125 c.c. *carbonated water* at 9 A. M.

Contents removed at 12.45 P. M. = 3¾ hrs.

Volume of fluid recovered from stomach = 125 c.c. = **100 per cent** of original volume.

Analysis of the contents gave:

Total acidity . . . . .	0.191 per cent.
Free HCl . . . . .	0.152
Loosely combined HCl . . . .	0.014
Salts . . . . .	0.025
Total solids . . . . .	0.55

In this experiment the CO<sub>2</sub> was completely absorbed.

VI. 1 vii, 1897. Dog. Weight 10 kilos.

Introduced 76 c.c. of 2 per cent *dextrose* solution at 9.10 A. M.

Contents removed at 12.40 P. M. = 3½ hrs.

Volume of fluid recovered from stomach = 68 c. c. = **90 per cent** of original volume.

Analysis of the contents gave:

Total acidity . . . . .	0.072 per cent.
Free HCl . . . . .	0.047
Loosely combined HCl . . . .	0.007
Salts . . . . .	0.018

<sup>1</sup> A small quantity of saliva doubtless found its way into the stomach, as the dog salivated somewhat at the beginning of the operation and the stomach contents had a frothy appearance.

## B. Experiments with strong Ethyl Alcohol: —

## VII. 17 v, 1897. Dog. Weight 23 kilos.

Introduced 200 c.c. of 37 per cent *alcohol* at 10.45 A. M.Contents removed at 2.15 P. M. =  $3\frac{1}{2}$  hrs.Volume of fluid recovered from stomach = 407 c.c. = **203 per cent** of original volume.

Analysis of the contents gave:

Total acidity . . . . .	0.164 per cent.
Free HCl . . . . .	0.112
Loosely combined HCl . . .	0.043
Salts . . . . .	0.009

## VIII. 31 v, 1897. Dog. Weight 21 kilos. Gastric fistula well healed.

*Contrast experiment with water and alcohol.**a.* The first part of this experiment has been described under I. p. 177.*β.* After discharge of previous stomach contents completely through fistula, 200 c.c.  $37\frac{1}{2}$  per cent *alcohol* were introduced into the stomach through fistula at 1.55 P. M.  
Contents removed at 5 P. M. =  $3\frac{1}{2}$  hrs.Volume of fluid recovered from stomach = 460 c.c. = **230 per cent** of original volume.<sup>1</sup>

Analysis of the contents gave:

Total acidity . . . . .	0.220 per cent.
Free HCl . . . . .	0.164
Loosely combined HCl . . .	0.011
Salts . . . . .	0.045
Total solids . . . . .	0.987

## C. Experiments with weak (5 per cent) Ethyl Alcohol: —

## IX. 24 vi, 1897. Bitch. Weight 8 kilos.

Introduced 100 c.c. 5 per cent *alcohol* at 10.45 A. M.Contents removed at 2 P. M. =  $3\frac{1}{4}$  hrs.Volume of fluid recovered from stomach = 110 c.c. = **110 per cent** of original volume.

Analysis of the stomach contents gave:

Total acidity . . . . .	0.119 per cent.
Free HCl . . . . .	0.086
Loosely combined HCl . . .	0.011
Salts . . . . .	0.022
Total solids . . . . .	0.69

## X. 8 vi, 1897. Bitch. Weight 7.3 kilos.

Introduced 110 c.c. 4.8 per cent *alcohol* at 9 A. M.Contents removed at 12.45 P. M. =  $3\frac{3}{4}$  hrs.Volume of fluid recovered from stomach = 135 c.c. = **123 per cent** of original volume.

Analysis of the stomach contents gave:

Total acidity . . . . .	0.202 per cent.
Free HCl . . . . .	0.148
Loosely combined HCl . . .	0.021
Salts . . . . .	0.033

<sup>1</sup> A post-mortem examination showed that the stomach contents could be completely discharged through the fistula by the method adopted.

The results of the foregoing experiments, expressed in percentages, are combined in the following table.

A. With water.	Relative volume of fluid at end of experiment.	Total acidity.	Loosely combined HCl.	Free HCl.	Salts.	Total solids.
I	80	0.203	0.002	0.192	0.009	0.62
II	81	0.274	0.018	0.241	0.015	0.77
III	91	0.094	0.004	0.065	0.025	0.47
IV	103	0.047	0.004	0.040	0.003	0.50
V	100	0.191	0.014	0.152	0.025	0.55
VI	90	0.072	0.007	0.047	0.018	....
Average.	90.8	0.147	0.008	0.123	0.016	0.58

B. With strong alcohol.	Relative volume of fluid at end of experiment.	Total acidity.	Loosely combined HCl.	Free HCl.	Salts.	Total solids.
VII	203	0.164	0.043	0.112	0.009	....
VIII	230	0.220	0.011	0.164	0.045	0.99
Average.	216.5	0.192	0.027	0.138	0.026	0.99

C. With weak alcohol.	Relative volume of fluid at end of experiment.	Total acidity.	Loosely combined HCl.	Free HCl.	Salts.	Total solids.
IX	110	0.119	0.011	0.086	0.022	0.69
X	123	0.202	0.021	0.148	0.033	....
Average.	116.5	0.160	0.016	0.117	0.027	0.69

A glance at the data presented leaves little doubt as to the pronounced stimulating action of pure ethyl alcohol upon gastric secre-



tion, even with solutions of only five per cent strength. The effect is not merely one characterized by the discharge of water into the stomach cavity, but gives evidence of a true secretory process. Thus, the volume of fluid found after introduction of water into the stomach is not increased, there being rather a tendency in the opposite direction. Edkins,<sup>1</sup> v. Mering,<sup>2</sup> and others have shown that the absorption of water from the stomach is practically *nil*, while the absorption of alcohol goes on quite rapidly. In our own experiments, the alcohol used had entirely disappeared from the stomach in the course of the experiments; the question of absorption will, however, be referred to in another connection. With five per cent alcohol the increase in the volume of the gastric contents is noticeable, becoming very pronounced with the stronger percentages of alcohol. The increase in total solids gives confirmation of stimulated secretion, as does also the increase in acidity. It must be remembered, further, that the increase in acidity shown by the figures is a relative one; expressed absolutely in grams, the total acid secreted is obviously increased in far greater degree than the percentage figures indicate. The specific action of alcohol is strikingly shown in Experiment VIII., in which the conditions permitted of comparative experiments with water and alcohol on the same animal, with the following results:—

COMPARISON OF THE TWO EXPERIMENTS (VIII. *a*, *β*).

Fluid introduced in stomach.	Fluid recovered from stomach after 3 hours.	Relative volume. per cent.	Total acidity.	Free HCl.	Loosely combined HCl.	Salts.	Total solids.
200 c.c. water	160 c.c.	80	0.203	0.192	0.002	0.009	0.624
200 c.c. alcohol { (37½ per cent.) }	460 c.c.	230	0.220	0.164	0.011	0.045	0.987

A comparison of the proteolytic activity of the two secretions by Grützner's carmine-fibrin method showed a decidedly greater digestive power in the case of the "water" secretion. Much stress cannot be placed, however, on a single experiment. The gastric fluids obtained in the experiments with alcohol possessed strong proteolytic properties in every case examined.

<sup>1</sup> EDKINS: *Journal of physiology*, 1892, xiii, p. 445.

<sup>2</sup> v. MERING: *Verhandlungen des XII. Congresses f. innere Medicin*, Wiesbaden, 1893; *Therapeutische Monatshefte*, 1893, vii, p. 201.

In view of this pronounced action of alcohol on gastric secretion it seemed desirable to ascertain something more definite regarding the way in which this process is provoked. The control experiments with water gave evidence that the mere contact of the fluid with the stomach mucosa could not be the cause of gastric stimulation. It will be remembered that even vigorous mechanical stimulation or irritation ordinarily fails to yield more than a few grams of secretion,<sup>1</sup>—an observation in decided contrast to the phenomena of gastric flow during the presence of digestible materials in the stomach. The following experiments throw light on the question raised:—

**XI.** 25 v, 1897. Dog. Weight 23 kilos. The intestine was ligatured just beyond the pylorus. Another ligature was applied below the point of entrance of the duct of Wirsung. 20 c.c. of 60 per cent alcohol were injected into the lumen of the intestine between these ligatures, while 105 c.c. of 60 per cent alcohol were introduced into the intestine beyond the second ligature. Then

Introduced 200 c.c. *water* into stomach at 10.45 A. M.  
Contents removed at 2.30 P. M. = 3¾ hrs.

Volume of fluid recovered from stomach = 260 c.c. = **130 per cent** of original volume.

Analysis of stomach contents gave:

Total acidity . . . . . 0.241 per cent.  
Free HCl . . . . . 0.213  
Loosely combined HCl . . . 0.002  
Salts . . . . . 0.026

**XII.** 28 v, 1897. Bitch. Weight 28 kilos. Intestine ligatured just beyond the pylorus. Another ligature was applied below the point of entrance of the duct of Wirsung. 125 c.c. of 60 per cent alcohol were injected into the lumen of the intestine below the second ligature,<sup>2</sup> then

Introduced 200 c.c. *water* into stomach at 11 A. M.  
Contents removed at 2.45 P. M. = 3¾ hours.

Volume of fluid recovered from stomach = 375 c.c. = **187.5 per cent** of original volume.

Analysis of stomach contents gave:

Total acidity . . . . . 0.333 per cent.  
Free HCl . . . . . 0.306  
Loosely combined HCl . . . 0.004  
Salts . . . . . 0.023  
Total solids . . . . . 0.30

<sup>1</sup> Cf. TIEDEMANN and GMELIN: *Die Verdauung nach Versuchen*, 1831, p. 92; SCHIFF: *Leçons sur la physiologie de la digestion*, ii, p. 244.

<sup>2</sup> The return of alcoholic fluid into the stomach was thus absolutely prevented.

## SUMMARY OF RESULTS OF EXPERIMENTS.

No.	Relative volume of fluid at end of experiment.	Total acidity.	Loosely combined HCl.	Free HCl.	Salts.	Total solids.
XI	130.0	0.241	0.002	0.213	0.026	...
XII	187.5	0.333	0.004	0.306	0.023	0.30
Average.	158.5	0.287	0.003	0.259	0.024	0.30

From these data it seems clear that a stimulation of the gastric glands may take place, independently of any *direct* gastric irritation, in consequence of the influence of alcohol absorbed from the intestine. The volume of the fluid in the stomach increased relatively far more than when five per cent alcohol was introduced directly into the stomach (cf. Experiments IX., X., p. 179). The composition of the fluid (high acidity, free HCl, total solids) likewise gives evidence of active secretion, while the fluid was found to be strongly proteolytic. The absorption of the alcohol was complete in these experiments; and when it is remembered how quickly alcohol is distributed and disappears in the body, the actual amount reaching the gastric glands must have been relatively small, or at least must have acted during a brief period only. It seems probable, therefore, that there occurs here an indirect stimulation quite comparable to that resulting after absorption of peptone from the alimentary tract, and it is interesting to note by way of comparison that Khigine,<sup>1</sup> in his experiments upon the isolated fundus of the dog, found that the acidity of the secretion after absorption of digestion products runs parallel to a certain degree with the increase in volume. Whether the absorbed alcohol acts directly upon elements of the gastric mucosa (Heidenhain's "secondary secretion"), or becomes a stimulus to specific secretory nerve fibres (Khigine), we are unable at present to decide.<sup>2</sup>

In connection with this "secondary" secretion of gastric juice due to the presence of alcohol in the small intestine, it is to be noted that Macfadyen, Nencki, and Sieber<sup>3</sup> found among the bacteria normally

<sup>1</sup> KHIGINE: Archives des sciences biologiques, St. Petersburg, 1895, iii, p. 461.

<sup>2</sup> Cf. HOWELL: American text-book of physiology, 1896, p. 182.

<sup>3</sup> MACFADYEN, NENCKI, and SIEBER: Archiv f. experimentelle Pathologie und Pharmakologie, 1891, xxviii, p. 311.

present in this portion of the alimentary canal species which give rise to a production of ethyl alcohol from carbohydrates ingested.

D. **Experiments with Alcoholic Beverages.**—It might naturally be assumed that the action of the various alcoholic beverages on gastric secretion would be similar, qualitatively, to that of their common constituent ethyl alcohol. Previous investigation, however, has shown that the influence of these liquors on the purely chemical processes of digestion is not necessarily proportionate to their content of alcohol,<sup>1</sup> hence it seemed desirable to study the effect of a number of typical liquors on secretion, by the method of the previous experiments. This we have done with the following results:—

## XIII. 21 vi, 1897. Dog. Weight 10.7 kilos.

Introduced 50 c.c. **sherry** + 25 c.c. *water* (14 per cent alcohol) at 10.20 A. M.  
Contents removed at 2.15 P. M. = 3½ hrs.

Volume of fluid recovered from stomach = 160 c.c. = **213 per cent** original volume.

Analysis of stomach contents gave:

Total acidity . . . . .	0.367 per cent.
Free HCl . . . . .	0.300
Loosely combined HCl . . .	0.020
Salts . . . . .	0.047
Total solids . . . . .	1.72

## XIV. 2 vi, 1897. Dog. Weight 18.5 kilos.

Introduced 50 c.c. **whiskey** + 100 c.c. *water* (16 per cent alcohol) at 11.15 A. M.  
Contents removed at 3 P. M. = 3¾ hours.

Volume of fluid recovered from stomach = 320 c.c. = **213 per cent** original volume.

Analysis of stomach contents gave:

Total acidity . . . . .	0.382 per cent.
Free HCl . . . . .	0.346
Loosely combined HCl . . .	0.011
Salts . . . . .	0.025
Total solids . . . . .	0.42

## XV. 3 vi, 1897. Bitch. Weight 8 kilos.

Introduced 125 c.c. **Hochheimer** (13.3 per cent alcohol) at 10 A. M.  
Contents removed at 1.45 P. M. = 3¾ hrs.

Volume of fluid recovered from stomach = 140 c.c. = **112 per cent** original volume.

Analysis of stomach contents gave:

Total acidity . . . . .	0.230 per cent.
Free HCl . . . . .	0.165
Loosely combined HCl . . .	0.038
Salts . . . . .	0.027

<sup>1</sup> CHITTENDEN and MENDEL: *loc. cit.*



- XVI.** 28 vi, 1897. Dog. Weight 25 kilos. Gastric fistula well healed.  
*Contrast experiment with water and wine.*  
 a. The first part of this experiment has been described under II. p. 177.  
 β. After complete discharge of previous stomach contents through the fistula, 135 c.c. **white wine** were introduced into stomach through fistula at 1.45 P. M.  
 Contents removed at 4.30 P. M. = 2¾ hrs.  
 Volume of fluid recovered from stomach = 170 c.c. = **126 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.425 per cent.  
 Free HCl . . . . . 0.342  
 Loosely combined HCl . . . 0.018  
 Salts . . . . . 0.065  
 Total solids . . . . . 1.79
- XVII.** 23 vi, 1897. Dog. Weight 12.3 kilos.  
 Introduced 125 c.c. **claret** (5.15 per cent alcohol) at 9.30 A. M.  
 Contents removed at 1.30 P. M. = 4 hrs.  
 Volume of fluid recovered from stomach = 225 c.c. = **180 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.373 per cent.  
 Free HCl . . . . . 0.324  
 Loosely combined HCl . . . 0.025  
 Salts . . . . . 0.024  
 Total solids . . . . . 1.90
- XVIII.** 18 vi, 1897. Bitch. Weight 10.2 kilos.  
 Introduced 100 c.c. **lager beer** (4 to 5 per cent alcohol) at 10.20 A. M.  
 Contents removed at 2.15 P. M. = 3½ hours.  
 Volume of fluid recovered from stomach = 110 c.c. = **110 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.357 per cent.  
 Free HCl . . . . . 0.241  
 Loosely combined HCl . . . 0.064  
 Salts . . . . . 0.052  
 Total solids . . . . . 9.26
- XIX.** 23 vi, 1897. Dog. Weight 10 kilos.  
 Introduced 100 c.c. **lager beer** (4.5 per cent alcohol) at 10.10 A. M.  
 Contents removed at 2 P. M. = 3¾ hrs.  
 Volume of fluid recovered from stomach = 125 c.c. = **125 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.241 per cent.  
 Free HCl . . . . . 0.169  
 Loosely combined HCl . . . 0.032  
 Salts . . . . . 0.040  
 Total solids . . . . . 5.51

- XX.** 14 vi, 1897. Dog. Weight 14 kilos.  
 Introduced 150 c.c. **porter** (3.75 per cent. alcohol) at 9.45 A. M.  
 Contents removed at 1.30 P. M. = 3¾ hrs.  
 Volume of fluid recovered from stomach = 195 c.c. = **127 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.371 per cent.  
 Free HCl . . . . . 0.320  
 Loosely combined HCl . . . 0.036  
 Salts . . . . . 0.015  
 Total solids . . . . . 2.19
- XXI.** 7 vi, 1897. Bitch. Weight 8.5 kilos.  
 Introduced 125 c.c. **lager beer** (4.7 per cent alcohol) at 10.15 A. M.  
 Contents removed at 2.10 P. M. = 3½ hrs.  
 Volume of fluid recovered from stomach = 285 c.c. = **228 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.378 per cent.  
 Free HCl . . . . . 0.308  
 Loosely combined HCl . . . 0.016  
 Salts . . . . . 0.054  
 Total solids . . . . . 2.88
- XXII.** 14 vi, 1897. Dog. Weight 8.2 kilos.  
 Introduced 150 c.c. **porter residue**<sup>1</sup> at 11.30 A. M.  
 Contents removed at 3.15 P. M. = 3¾ hrs.  
 Volume of fluid recovered from stomach = 135 c.c. = **90 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.352 per cent.  
 Free HCl . . . . . 0.280  
 Loosely combined HCl . . . 0.014  
 Salts . . . . . 0.058  
 Total solids . . . . . 2.29
- XXIII.** 9 vi, 1897. Dog. Weight 10 kilos.  
 Introduced 130 c.c. **lager beer residue**<sup>2</sup> at 10.30 A. M.  
 Contents removed at 2.30 P. M. = 4 hrs.  
 Volume of fluid recovered from stomach = 175 c.c. = **134 per cent** original volume.  
 Analysis of stomach contents gave:  
 Total acidity . . . . . 0.346 per cent.  
 Free HCl . . . . . 0.270  
 Loosely combined HCl . . . 0.038  
 Salts . . . . . 0.038  
 Total solids . . . . . 6.80

<sup>1</sup> The residue left on evaporation of 150 c.c. porter, dissolved in 150 c.c. distilled water.

<sup>2</sup> Residue from evaporation of 130 c.c. beer, dissolved in 130 c.c. water.

For the sake of comparison these data are contrasted in the following table: —

	Relative volume of fluid at end of experiment.	Total acidity.	Loosely combined HCl.	Free HCl.	Salts.	Total solids.
XIV. Whiskey + H <sub>2</sub> O (16% alcohol)	213	0.382	0.011	0.346	0.025	0.42
XIII. Sherry + H <sub>2</sub> O (13% alcohol)	213	0.367	0.020	0.300	0.047	1.72
XV. White wine (13% alcohol)	112	0.230	0.038	0.165	0.027	....
XVI. White wine (13% alcohol)	126	0.425	0.018	0.342	0.065	1.79
XVII. Claret (10% alcohol)	180	0.373	0.025	0.324	0.024	1.90
XVIII. Beer (4.7% alcohol)	110	0.357	0.064	0.241	0.052	9.26
XIX. Beer (4% alcohol)	125	0.241	0.032	0.169	0.040	5.51
XXI. Beer (4.7% alcohol)	228	0.378	0.016	0.308	0.054	2.88
XXIII. Residue of Beer (like XXI.)	134	0.346	0.038	0.270	0.038	6.80
XX. Porter (5.3% alcohol)	127	0.371	0.036	0.320	0.015	2.19
XXII. Residue of porter (like XX.)	90	0.352	0.014	0.280	0.058	2.29

These results afford tangible evidence of the stimulating action of the liquors examined, as shown in the increased volume of gastric contents, accompanied by increase in acidity. That alcohol is an important factor in the production of these phenomena seems certain. Contrast, for example, Experiment XX. with XXII., which differs only in the absence of the alcohol. But the wines and organic acids,<sup>1</sup> which perhaps contribute to increase the stimulating effect, and are doubtless partly responsible in a number of experiments for the high acidity observed. The contrast between the action of water and wine is strikingly shown in Experiments XVI.  $\alpha$  and  $\beta$  carried out on the same animal.

<sup>1</sup> Cf. CHITTENDEN and MENDEL: *loc. cit.*, pp. 56, 80.

COMPARISON OF THE TWO EXPERIMENTS (XVI.  $\alpha$ ,  $\beta$ ).

Fluid introduced in stomach.	Fluid removed from stomach after 3 hours.	Relative volume. per cent.	Total acidity.	Free HCl.	Loosely combined HCl.	Salts.	Total solids.
135 c.c. water	110 c.c.	81	0.274	0.241	0.018	0.015	0.77
135 c.c. white wine	170 c.c.	126	0.425	0.342	0.018	0.065	1.79

The marked increase in total solids in many of these experiments, however, is not to be attributed, as it is in the case of pure alcohol, entirely to the increased secretion; it is rather in part accounted for by the unabsorbed constituents of the liquor employed. The following table, compiled from analyses at hand, shows that a large portion of the total solids in the gastric juices obtained may be derived from other sources than the secretion itself: —

TABLE SHOWING TOTAL SOLIDS OF GASTRIC CONTENTS.

Nature of fluid introduced into stomach.	Total solids introduced into stomach.	Total solids in gastric contents at end of experiment.
II. Water . . . . .	0 grams.	0.84 grams.
IX. Weak alcohol . .	0 “	0.69 “
VIII. Strong alcohol . .	0 “	4.50 “
XIV. Whiskey . . . . .	0.15 “	1.34 “
XVI. White wine . . .	2.8 “	2.41 “
XVII. Claret . . . . .	3.9 “	4.28 “
XIII. Sherry . . . . .	2.35 “	2.78 “
XVIII. Beer . . . . .	7.0 “	10.00 “
XXIII. Beer residue . . .	9.1 “	11.56 “
XX. Porter . . . . .	6.6 “	4.16 “
XXII. Porter residue . .	6.6 “	3.10 “

**E. Character of the Gastric Juice obtained by Stimulation with Alcohol.** — The gastric juice obtained as a result of the stimulating influence of alcohol and alcoholic liquors resembles that ordinarily



procured from gastric fistulæ in its physical characters; it is a thin, colorless, or very faintly yellow fluid containing occasional flocks of mucus in suspension. There was no evidence of irritation or hyperæmia of the mucosa, and all traces of blood were absent. After the doses used, the gastric lining was of a pale or faintly pink color when removed after bleeding the animal. When colored alcoholic liquors were employed, the gastric contents retained the characteristic coloring matter, the latter not being absorbed, while the alcohol entirely disappeared. In chemical composition, the gastric juice appeared somewhat more acid than that ordinarily secreted. It likewise contained a larger amount of solid matter, and in harmony with this fact the proportion of combined hydrochloric acid was increased, which in turn suggests the presence of a somewhat larger amount of proteid or other like matter. The fluids were repeatedly tested with boiled fibrin for proteolytic action, and this was always found vigorous. In the experiments in which alcohol was introduced directly into the intestine (Experiments XI., XII., p. 182), the intestinal lining was not abnormal in appearance, the reaction being alkaline to litmus in the upper duodenum and neutral or faintly alkaline further along the alimentary canal. This corresponds with the observations on the normal reaction of the intestinal contents of the dog, by Moore and Rockwood,<sup>1</sup> whose statements we have repeatedly verified.

#### GASTRIC DIGESTION.

Since chemical, mechanical, and physiological processes go on side by side during digestion, we have carried out a series of experiments to determine in what way and to what extent the factors already investigated combine or coöperate under the influence of alcohol and alcoholic liquors. Our method has included the examination of the stomach contents after test meals were given. The statements current in the literature on this subject are by no means concordant.

In experiments on a woman having a gastric fistula Kretschy<sup>2</sup> observed that alcohol retarded digestion. Buchner<sup>3</sup> found that in

<sup>1</sup> MOORE and ROCKWOOD: *Journal of physiology*, 1897, xxi, p. 373.

<sup>2</sup> KRETSCHY: *Deutsches Arch. f. klin. Med.*, xviii, p. 527; *Jahresbericht f. Thierchemie*, 1876, vi, p. 173.

<sup>3</sup> BUCHNER: *Deutsches Arch. f. klin. Med.*, xxix, p. 537; *Jahresbericht f. Thierchemie*, 1881, xi, p. 286.

the human stomach alcohol, wine, and beer all retarded digestion, though not so markedly as in artificial digestion. Bikfalvi,<sup>1</sup> in observations on dogs, obtained a retardation of digestion with even small quantities of alcohol. Beer and wine showed no favorable influence, the latter even retarding digestion when given in large quantities. Ogáta<sup>2</sup> states that beer, wine, and brandy retard gastric digestion noticeably. Schelhaas<sup>3</sup> observed that in the living stomach wine did not retard digestion so long as there was free HCl present; pathological conditions (carcinoma ventriculi) formed the only exceptions. In an extensive series of experiments, Gluzinski<sup>4</sup> distinguishes two phases occurring during digestion in the stomach in the presence of alcohol, (1) a retardation of proteid digestion, and (2) secretion of a very active, strongly acid gastric juice. Henczinski<sup>5</sup> found no bad effect on digestion following the use of beer. Blumenau<sup>6</sup> states that 25-50 per cent alcohol introduced into the healthy stomach induces a decrease in digestive action during the first two or three hours. Wolffhardt,<sup>7</sup> experimenting on a healthy man, concluded that 15-20 grams of absolute alcohol interfere with proteid digestion, while the effect of cognac varies with the period of digestion during which it is taken; he found that wines tend to promote digestion.

With reference to the motor functions of the stomach Lauder Brunton states that alcohol taken into this organ increases its movements as well as its secretory activity, and by mixing its contents more thoroughly with the gastric juice accelerates digestion.<sup>8</sup> Likewise Klemperer<sup>9</sup> states as a result of his experiments that the motor

<sup>1</sup> BIKFALVI: *Jahresbericht f. Thierchemie*, 1885, xv, p. 273.

<sup>2</sup> OGÁTA: *Jahresbericht f. Thierchemie*, 1885, xv, p. 274; *Arch. f. Hygiene*, 1885, iii, p. 204.

<sup>3</sup> SCHELHAAS: *Deutsches Arch. f. klin. Med.*, xxxvi, p. 427; *Jahresbericht f. Thierchemie*, 1885, xv, p. 271.

<sup>4</sup> GLUZINSKI: *Deutsches Arch. f. klin. Med.*, 1886, xxxix, p. 405; *Jahresbericht f. Thierchemie*, 1886, xvi, p. 263.

<sup>5</sup> HENCZINSKI: *Dissertation*, 1886. Quoted by MUNK: *Die Ernährung*, p. 327.

<sup>6</sup> BLUMENAU: *Therapeutische Monatshefte*, 1890, v, p. 504; *Jahresbericht f. Thierchemie*, 1891, xxi, p. 212.

<sup>7</sup> WOLFFHARDT: *Münchn. med. Wochenschr.*, 1890, xxxvii, p. 608; *Centralbl. f. med. Wissen.*, 1891, p. 47.

<sup>8</sup> BRUNTON: *Disorders of digestion*, 1886, p. 146.

<sup>9</sup> KLEMPERER: *Zeitschr. f. klin. Med.*, 1890, xvii, Supp., p. 324; *Centralbl. f. med. Wissen*, 1891, p. 751.

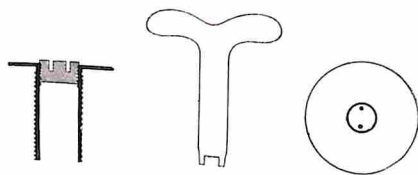


functions are decidedly increased, as measured by the oil method, while Haan<sup>1</sup> has more recently advanced similar conclusions as the result of work by another method. Gluzinski,<sup>2</sup> however, notes that alcohol diminishes the mechanical action of the stomach in moderate degree.

In considering the selection of subjects for experiment in the direction indicated, preference has been given to dogs. The series of investigations on man above referred to are already extensive, and the difficulties of obtaining definite answers to specific questions by this method of experimentation are obvious. It is rarely possible or desirable to carry out a large number of determinations on any single individual, while it is likewise practically impossible to control the physiological condition of the individual, *i. e.*, diet, etc., over prolonged periods. The animals used in this research were large dogs of 21 and 25 kilos; gastric fistulæ were made, and a German silver cannula introduced into the fundus of

the stomach. In place of a cork, metal stoppers were devised to screw into the inner cannula tube by means of a small metallic key. The arrangement is shown in the diagram. The wounds healed perfectly, and the animals remained in good health during the entire period of investigation, covering several months. Irregularities of diet were avoided by feeding definite portions of prepared dog biscuit with water; this food was eagerly eaten, and sufficed to keep the dogs in physiological equilibrium.

The determinations of the acidity of the stomach contents were carried out according to the method of Töpfer.<sup>3</sup> The gastric fluid was occasionally centrifugalized when food particles prevented pipetting off the fluid portion. Where only small quantities of fluid were available the titrations with phenolphthaliën and dimethylamidoazobenzol were combined in the same 5 c.c. of fluid according to the recommendation of Einhorn.<sup>4</sup> Comparative experiments show that this modification gives the same values as the original method. Thus in one experiment: —



<sup>1</sup> HAAN: Comptes rendus de la société de biologie, 1895, ii, p. 816.

<sup>2</sup> GLUZINSKI: *loc. cit.*

<sup>3</sup> TÖPFER: Zeitschr. f. physiol. Chemie, 1894, xix, p. 104.

<sup>4</sup> EINHORN: New York medical journal, 1896, May 9, p. 603.

	Total acidity with <i>Phenolphthalëin.</i>	Free HCl with <i>Dimethylamidoazobenzol.</i>
Töpfer method (separate titrations)	$\left\{ \begin{array}{l} 1.55 \text{ c.c. } \frac{N}{10} \text{NaOH} \\ = 0.112 \text{ per cent HCl.} \end{array} \right.$	$\left\{ \begin{array}{l} 1.0 \text{ c.c. } \frac{N}{10} \text{NaOH} \\ = 0.072 \text{ per cent HCl.} \end{array} \right.$
Einhorn-Töpfer method (combined titration)	$\left\{ \begin{array}{l} 1.55 \text{ c.c. } \frac{N}{10} \text{NaOH} \\ = 0.112 \text{ per cent HCl.} \end{array} \right.$	$\left\{ \begin{array}{l} 1.0 \text{ c.c. } \frac{N}{10} \text{NaOH} \\ = 0.072 \text{ per cent HCl.} \end{array} \right.$

Our experience with Töpfer's method (or Einhorn's modification) leads us to agree with P. Häri<sup>1</sup> that in the absence of free HCl, *i. e.*, when no reaction is obtained with the dimethylamidoazobenzol reagent, the quantitative determinations of HCl by this method cease to be accurate, and under such conditions it cannot be employed. The occurrence of such conditions, however, is not frequent in the dog; we have observed the absence of free HCl (during digestion) in one animal under circumstances resembling those of acute gastric catarrh.<sup>2</sup> The food—dog biscuit—was largely undigested many hours after the meal, the acidity was high (0.55–0.594 per cent expressed as HCl), and the gastric contents possessed an odor strongly suggesting fatty acids. Lactic acid was found present (Uffelmann's test).

In view of the increased volume of fluid found in the stomach when alcohol is introduced into that organ after ligation of the pylorus, it was of interest to learn what results follow under normal conditions of the pylorus. For this purpose 20 to 25 per cent alcohol, slightly warmed, was introduced through the gastric cannula, and at the end of 30 minutes the gastric contents were discharged into a graduated vessel. Control experiments were made with distilled water, both fluids always being introduced into the empty stomach. This condition of the organ is shown by the lack of spontaneous flow when the cannula is opened, as well as by absence of free HCl. Flocks of mucus, alkaline to litmus, are usually present. The data obtained show no marked agreement, the fluid as a rule

<sup>1</sup> HÄRI, P.: Arch. f. Verdauungskrankh., ii, pp. 182, 332; Centralbl. f. Physiologie, 1896, x, p. 731.

<sup>2</sup> Cf. V. JAKSCH: Klinische Diagnostik innerer Krankheiten, 4te Auflage, p. 200.



rapidly disappearing from the stomach. In 17 experiments with water, the *average* relative volume recovered from the stomach through the cannula at the end of the thirty minutes after introduction of quantities from 40–200 c.c. was about 30 per cent. Fourteen similar experiments with alcohol gave an average of 45 per cent. It is natural to ascribe the relatively greater volumes found in the stomach after the use of alcohol to an increased secretion of gastric juice occurring along with the rapid expulsion of fluid through the pylorus, and not to a retardation of the motor functions; for current statements assume increased motility of the stomach under the influence of alcohol,<sup>1</sup> while the experiments already reported justify the explanation given. Much emphasis cannot, however, be placed upon the averages given above, since the individual results vary widely among themselves, and no constant corresponding variations in acidity were observed, as in the experiments with ligated pylorus.

In the following series of experiments test meals were given, and the influence of alcohol and a considerable number of alcoholic beverages contrasted with that of water. Attention was directed to (1) variations in acidity and (2) time of digestion. Fifty grams of finely chopped lean meat were fed to the dog in each experiment, the stomach having been previously examined and found empty. Meat was chosen for the test meal because experience in this laboratory has shown that its composition, when it is obtained as described, does not vary much from time to time; and after a trial of mixed food, *e. g.* dog biscuit, it seemed more satisfactory to employ a simple diet in which proteid preponderated. Similar recommendation is made by v. Jaksch in considering test meals for the human subject.<sup>2</sup> Alcoholic fluids or water were introduced slightly warmed<sup>3</sup> into the stomach through the fistula, since dogs usually refuse to take the former by way of the mouth. At definite intervals of one-quarter to one-half hour, small quantities of gastric contents were permitted to flow out of the fistula. Total acidity (expressed as HCl), free and loosely combined HCl were determined by the method already described. The process of digestion in the stomach lasted, under the conditions described, about three hours, the average duration varying

<sup>1</sup> Cf. references p. 190.

<sup>3</sup> Cf. note 4, p. 176.

<sup>2</sup> v. JAKSCH: *loc. cit.*, p. 192.

somewhat with the animal.<sup>1</sup> There was no very gradual diminution of undissolved meat particles noticeable until toward the end of this period, when the stomach very soon became empty. This corresponds with the observations of Kühne on man and the dog, in experiments with duodenal fistulæ.<sup>2</sup> This investigator found only a slight disappearance of contents from the stomach until near the end of the digestion period, when the great bulk of material, excepting larger pieces of food, was discharged at once through the pylorus. Richet arrived at similar conclusions in experiments on man.<sup>3</sup> We have usually observed a complete emptying of the stomach within a period of thirty minutes; the conclusion of this process is designated in the notes as the "end of gastric digestion." Protocols of experiments follow.

ANALYSES OF ALCOHOLIC BEVERAGES USED.

	Alcohol by vol. per cent.	Dry solids. per cent.		Alcohol by vol. per cent.	Dry solids. per cent.
Gin . . . .	51.0	0.29	Stout . . .	6.2	5.4
Whiskey . .	50.0	0.32	Claret . . .	5.2	3.2
Sherry . . .	21.75	4.7	Porter . . .	5.3	4.4
White Wine .	13.32	2.5	Beer . . . .	4–5	7.0

DOG A. — Weight 25 kilos.

I. 9.25 A.M. 50 grams meat (no water).

ANALYSIS OF CONTENTS			
	Total acidity.	Loosely combined HCl.	Free HCl.
9.55	0.382	0.292	0.104
10.35	0.425	0.234	0.148
11.10	0.425	0.220	0.180
11.45	0.407	0.224	0.176
12.15	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 55 minutes.		

<sup>1</sup> In experiments on a man, with a similar meal, Jessen found the digestion time equalled 2 to 3 hours. *Zeitschr. f. Biologie*, 1883, xix, p. 149.

<sup>2</sup> KÜHNE: *Lehrbuch der physiol. Chemie*, 1868, p. 53.

<sup>3</sup> RICHT: Quoted in GAMGEE: *Physiological chemistry*, 1893, ii, p. 159.

II. 9.10 A.M. 50 grams meat + 50 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.30	0.241	0.144	0.093
10.00	0.295	0.169	0.108
10.20	0.367	0.216	0.115
10.40	0.439	0.288	0.144
11.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 20 minutes.		

III. 9.30 A.M. 50 grams meat + 100 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
10.00	0.299	0.173	0.090
10.30	0.475	0.230	0.122
11.00	0.518	0.230	0.173
11.15	0.497	0.202	0.241
11.35	0.494	0.191	0.202
11.50	0.479	0.205	0.195
12.10	0.382	0.194	0.187
12.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

IV. 2.10 P.M. 50 grams meat + 150 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
2.40	0.252	0.137	0.108
3.10	0.374	0.194	0.130
3.40	0.533	0.245	0.198
3.55	0.547	0.234	0.234
4.10	0.490	0.205	0.216
4.25	0.385	....	0.101
4.40	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 30 minutes.		

V. 9.05 A.M. 50 grams meat + 150 c.c. carbonated water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.35	0.263	0.083	0.122
10.05	0.360	0.158	0.140
10.35	0.468	0.194	0.216
10.50	0.486	0.205	0.216
11.05	0.540	0.234	0.198
11.25	0.580	0.234	0.248
11.45	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 40 minutes.		

VI. 1.00 P.M. 50 grams meat + 100 c.c. 10 per cent alcohol.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
2.45	0.497	0.209	0.230
3.10	0.464	0.220	0.173
3.30	0.436	0.180	0.202
3.50	0.400	0.162	0.202
4.10	0.263	....	0.094
4.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours and 30 minutes.		

VII. 2.30 P.M. 50 grams meat + 50 c.c. 20 per cent alcohol.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
3.00	0.313	0.118	0.090
3.30	0.374	0.187	0.176
4.00	0.439	0.194	0.151
4.30	0.515	0.205	0.184
5.00	0.407	0.144	0.248
5.30	0.264	....	0.155
5.30	Stomach nearly empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

VIII. 12.45 P.M. 50 grams meat + 50 c.c. 20 per cent alcohol.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
2.30	0.439	0.213	0.158
2.50	0.457	0.191	0.205
3.10	0.493	0.205	0.227
3.30	0.364	0.129	0.187
3.50	Stomach practically empty; end of gastric digestion.		
	Time of digestion = 3 hours and 5 minutes.		

IX. 9.15 A.M. 50 grams meat + 50 c.c. 30 per cent alcohol.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.40	0.191	0.130	0.058
10.05	0.335	0.155	0.151
10.30	0.421	0.176	0.180
10.50	0.468	0.184	0.201
11.10	0.460	0.165	0.220
11.30	0.410	0.148	0.220
11.50	0.468	0.195	0.244
12.10	0.417	0.112	0.240
12.30	0.360	0.086	0.216
1.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours and 45 minutes.		



**X.** 9.00 A.M. 50 grams meat + 150 c.c. Hochheimer.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.30	0.374	0.140	0.176
10.00	0.432	0.154	0.191
10.15	0.450	0.151	0.198
10.45	0.497	0.187	0.220
11.15	0.533	0.198	0.271
11.30	0.555	0.241	0.227
12.00	0.508	0.248	0.173
12.15	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours and 15 minutes.		

**XI.** 9.00 A.M. 50 grams meat + 50 c.c. whiskey + 50 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.30	0.252	0.101	0.119
10.00	0.392	0.176	0.176
10.30	0.403	0.151	0.191
11.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours.		

**XII.** 2.45 P.M. 50 grams meat + 50 c.c. whiskey + 50 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
3.15	0.230	0.076	0.119
3.45	0.320	0.097	0.220
4.15	0.468	0.198	0.212
4.30	0.508	0.198	0.198
4.45	0.490	0.184	0.212
5.15	0.569	0.205	0.252
5.45	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

**XIII.** 1.00 P.M. 50 grams meat + 50 c.c. gin + 25 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
2.00	0.439	0.173	0.194
2.30	0.450	0.170	0.197
2.45	0.428	0.158	0.238
3.00	0.442	0.154	0.212
3.15	0.410	0.140	0.215
3.30	0.420	0.143	0.234
3.45	0.338	0.122	0.180
4.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

**XIV.** 9.20 A.M. 50 grams meat + 50 c.c. brandy + 25 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.50	0.237	0.159	0.065
10.20	0.368	0.201	0.133
10.50	0.465	0.230	0.205
11.20	0.533	0.267	0.194
11.40	0.468	....	0.158
12.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 40 minutes.		

**XV.** 2.50 P.M. 50 grams meat + 150 c.c. lager beer.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
3.20	0.259	0.112	0.115
3.50	0.410	0.205	0.148
4.20	0.518	0.245	0.184
4.35	0.572	0.248	0.230
4.50	0.569	0.252	0.208
5.05	0.547	0.220	0.238
5.20	0.508	0.162	0.211
5.35	0.475	0.162	0.238
5.50	0.413	0.115	0.241
6.05	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours and 15 minutes.		

**XVI.** 9.40 A.M. 50 grams meat + 150 c.c. stout.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
10.10	0.364	0.140	0.187
10.40	0.446	0.166	0.180
11.10	0.555	0.220	0.295
11.40	0.616	0.212	0.302
12.10	0.580	0.266	0.247
12.40	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

**XVII a.** 9.15 A.M. 50 grams meat + 150 c.c. beer.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.45	0.248	0.151	0.082
10.15	0.367	0.201	0.123
10.45	0.457	0.238	0.137
11.20	0.526	0.266	0.209
11.40	0.511	0.213	0.223
12.15	0.465	0.216	0.176
12.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours and 15 minutes.		

XVII $\beta$ . 3.00 P.M. 50 grams meat + 150 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
3.30	0.227	0.130	0.090
4.00	0.400	0.209	0.129
4.30	0.522	0.274	0.158
5.00	0.583	0.310	0.195
5.15	0.583	0.302	0.205
5.30	0.446	0.209	0.184
5.45	0.569	0.298	0.127
6.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

XVIII $\alpha$ . 8.30 A.M. 50 grams meat + 50 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.00	0.371	0.227	0.126
9.30	0.443	0.274	0.144
10.00	0.518	0.252	0.234
10.30	0.569	0.263	0.252
11.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 30 minutes.		

XVIII $\beta$ . 2.10 P.M. 50 grams meat + 100 c.c. 30 per cent alcohol.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
2.40	0.234	0.112	0.101
3.10	0.352	0.165	0.137
3.40	0.490	0.209	0.162
4.10	0.550	0.263	0.191
4.40	0.550	0.245	0.201
5.10	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

XIX $\alpha$ . 9.00 A.M. 50 grams meat + 100 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.30	0.324	0.165	0.137
10.00	0.378	0.198	0.144
10.30	0.494	0.259	0.169
11.00	0.487	0.220	0.188
11.15	0.457	0.205	0.131
11.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 30 minutes.		

XIX $\beta$ . 2.30 P.M. 50 grams meat + 150 c.c. lager beer.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
3.00	0.260	0.119	0.137
3.30	0.378	0.201	0.137
4.00	0.465	0.191	0.188
4.30	0.533	0.223	0.248
4.45	0.562	0.233	0.306
5.10	0.465	0.223	0.176
5.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		

XX $\alpha$ . 9.15 A.M. 50 grams meat + 75 c.c. sherry + 25 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.45	0.295	0.108	0.155
10.15	0.331	0.101	0.173
10.45	0.367	0.133	0.187
11.15	0.418	0.158	0.212
11.30	0.436	0.169	0.216
11.45	0.490	0.191	0.248
12.00	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 45 minutes.		

XX $\beta$ . 2.30 P.M. 50 grams meat + 150 c.c. carbonated water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
3.00	0.238	0.043	0.126
3.30	0.360	0.130	0.176
4.00	0.432	0.187	0.169
4.30	0.533	...	0.169
4.45	Stomach empty; end of gastric digestion.		
	Time of digestion = 2 hours and 15 minutes.		

Dog B. — Weight 21 kilos.

I. 1.45 P.M. 50 grams meat (no water).

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
2.15	0.353	0.191	0.118
2.40	0.443	0.222	0.180
3.00	0.511	0.227	0.198
3.20	0.525	0.227	0.280
3.45	0.572	0.260	0.209
4.15	0.568	0.349	0.195
4.45	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours.		



II. 9.15 A.M. 50 grams meat + 50 c.c. water.

	ANALYSIS OF CONTENTS		
	Total acidity.	Loosely combined HCl.	Free HCl.
9.50	0.302	0.220	0.082
10.15	0.432	0.223	0.144
10.45	0.472	0.201	0.252
11.15	0.472	0.144	0.288
11.35	0.484	0.155	0.270
11.55	0.453	0.144	0.306
12.15	0.407	0.100	0.241
12.30	0.400	0.133	0.234
12.45	0.306	....	0.216
End of gastric digestion.			
Time of digestion = 3 hours and 30 minutes.			

III. 9.15 A.M. 50 grams meat + 50 c.c. 20 per cent alcohol + water.

	ANALYSIS OF CONTENTS		
	<i>Total acidity.</i>	<i>Loosely combined HCl.</i>	<i>Free HCl.</i>
9.50	0.136	0.086	0.036
10.15	0.285	0.108	0.144
10.45	0.479	0.173	0.244
11.15	0.472	0.177	0.252
11.35	0.518	0.237	0.252
11.55	0.486	....	0.209
12.15	0.421	....	0.213
12.30	Stomach empty; end of gastric digestion.		
	Time of digestion = 3 hours and 15 minutes.		

IV. 8.50 A.M. 50 grams meat + 100 c.c. 30 per cent alcohol.

ANALYSIS OF CONTENTS			
	<i>Total acidity.</i>	<i>Loosely combined HCl.</i>	<i>Free HCl.</i>
9.20	0.324	....	0.144
9.50	0.493	....	0.072
10.20	0.641	....	0.100
10.50	0.547	0.338	0.166
11.20	0.588	....	0.206
11.50	0.544	....	0.230
12.20	....	....	present.
12.30	End of gastric digestion.		
Time of digestion = 3 hours and 40 minutes.			

V. 2.45 P.M. 50 grams meat + 75 c.c. claret.

	ANALYSIS OF CONTENTS		
	<i>Total acidity.</i>	<i>Loosely combined HCl.</i>	<i>Free HCl.</i>
3.15	0.396	0.155	0.216
3.45	0.450	0.238	0.158
4.15	0.576	• • •	0.209
4.45	End of gastric digestion.		
	Time of digestion = 2 hours.		

VI<sub>a</sub>. 9.15 A.M. 50 grams meat + 150 c.c. beer.

ANALYSIS OF CONTENTS			
	<i>Total acidity.</i>	<i>Loosely combined HCl.</i>	<i>Free HCl.</i>
9.45	0.273	0.144	0.104
10.15	0.367	0.187	0.155
10.45	0.464	0.223	0.194
11.15	0.616	0.345	0.256
11.45	0.501	0.238	0.170
12.15	0.508	....	0.151
12.30	0.533	....	0.187
12.45	0.468	...	0.158
1.00	End of gastric digestion.		
Time of digestion = 3 hours and 45 minutes.			

VI<sub>β</sub>. 1.00 P.M. 50 grams meat + 150 c.c. water.

ANALYSIS OF CONTENTS			
	<i>Total acidity.</i>	<i>Loosely combined HCl.</i>	<i>Free HCl.</i>
2.00	0.620	0.282	0.201
2.30	0.590	0.266	0.234
3.00	0.666	0.392	0.224
3.30	0.627	...	0.206
4.00	...	...	trace.
4.15	End of gastric digestion.		
Time of digestion = 3 hours and 15 minutes.			

In the accompanying table the "time of digestion" of the experiments preceding is given in hours. The experiments marked *a* and *β* are strictly comparable, as reference to the protocols will show that they were carried out in succession on the same day.

From these results it is apparent that the time of digestion in the stomach for the proteid test meal employed is not greatly varied under the influence of alcohol. The results obtained suggest, however, a tendency toward prolongation of the period during which the meat remains in the stomach when alcoholic fluids are present. This tendency is most noticeable in the case of Dog A, and particularly in those experiments which immediately succeed each other on the same day and are therefore strictly comparable. The differences are too small, however, to have any great significance. Retardation is perhaps more marked with the malted beverages, and is apparently out of proportion to the alcohol present. With reference to the changes in the acidity of the stomach contents a large number of observations disclose no specific differences in the various digestions. The varia-

TABLE OF TIME OF DIGESTION (IN HOURS).

Dog A.					Dog B.			
No.	Water.	Alcohol.	Weak alcoholic beverages.	Strong alcoholic beverages.	No.	Water.	Alcohol.	Weak alcoholic beverages.
XVII $\alpha$	h. m.	h. m.	h. m.	h. m.	I	h. m.	h. m.	h. m.
XVII $\beta$	3	....	3 15	....	II	3 30	....	....
I	2 55	....	....	....	III	....	3 15	....
II	2 20	....	....	....	IV	....	3 40	....
VII	....	3	....	....	V	....	....	2
VI	....	3 30	....	....	VI $\alpha$	....	....	3 45
VIII	....	3 05	....	....	VI $\beta$	3 15	....	....
IX	....	3 45	....	....		....	....	....
XVIII $\alpha$	2 30	....	....	....		....	....	....
XVIII $\beta$	....	3	....	....		....	....	....
XIV	....	....	....	2 40		....	....	....
XV	....	....	3 15	....		....	....	....
XIX $\alpha$	2 30	....	....	....		....	....	....
XIX $\beta$	....	....	3	....		....	....	....
XVI	....	....	3	....		....	....	....
IV	2 30	....	....	....		....	....	....
X	....	....	3 15	....		....	....	....
III	3	....	....	....		....	....	....
XIII	....	....	....	3		....	....	....
XX $\alpha$	2 15	....	....	2 45		....	....	....
XX $\beta$	....	....	....	....		....	....	....
V	2 40	....	....	....		....	....	....
XI	....	....	....	2		....	....	....
XII	....	....	....	3		....	....	....
Average.	2 40	3 20	3 10	2 40		3 15	3 30	2 52

tions are common to all the experiments. They include a gradual rise in total acidity during approximately the first two hours of diges-

tion, followed by a gradual decrease until the stomach becomes empty; at this point free HCl is absent. The combined HCl increases with the progress of digestion, the products of proteolysis combining with relatively larger quantities of free acid.<sup>1</sup> Since the secretion of acid is continually progressing in the stomach, the percentage of free HCl increases gradually in the course of the digestion, likewise decreasing rapidly toward the end of this process. In agreement with our previous statements relative to the rather sudden discharge of the gastric contents into the intestine (p. 194), an abrupt decline in acidity toward the end of the digestion period was frequently observed. Evidence of an "after period" of secretion was not obtained.<sup>2</sup>

#### DISAPPEARANCE OF ALCOHOL FROM THE STOMACH.

It has long been known that alcohol disappears rapidly from the alimentary canal, and even so early as 1847 Bouchardat and Sandras stated that the absorption takes place from the stomach especially.<sup>3</sup> More recent and conclusive experiments in which the pylorus has been artificially closed, have demonstrated with certainty that alcohol, in distinction from water, is readily absorbed from the stomach.<sup>4</sup> Furthermore, many substances like sugar, peptone, etc., are readily absorbed from the stomach in the presence of alcohol, while their absorption from the intestine is likewise accelerated by this substance.<sup>5</sup> Thus an ordinary dose of chloral hydrate introduced in watery solution into a stomach with ligated pylorus fails to bring about narcosis;<sup>6</sup> if, however, a quantity of alcohol too small of itself to produce any pharmacological action be present, narcosis follows, just as when the open pylorus permits the intestine to participate in the absorption.

The complete disappearance of alcohol from the stomach has been observed by us in a large number of experiments in which the pylorus

<sup>1</sup> Cf. CHITTENDEN: Digestive proteolysis, 1894, pp. 53 *seq.*

<sup>2</sup> Cf. GLUZINSKI: Jahresbericht f. Thierchemie, 1886, xvi, p. 264.

<sup>3</sup> BOUCHARDAT and SANDRAS: Annales de chimie et de physique, 1847, xxi, 3 Série, p. 456.

<sup>4</sup> Cf. for example, TAPPEINER: Zeitschr. f. Biologie, 1881, xvi, p. 497; BRANDL: *ibid.*, 1892, xxix, p. 277; v. MERING: Jahresbericht f. Thierchemie, 1893, xxiii, p. 293.

<sup>5</sup> Cf. for example, J. v. SCANZONI: Zeitschr. f. Biologie, 1896, xxxiii, p. 462.

<sup>6</sup> Cf. also experiments with strychnine. MELTZER: Journ. of exper. medicine, 1896, i, p. 529.



was ligated. The following results tabulated from the experiments on secretion (pp. 179-186), demonstrate this statement: —

TABLE SHOWING ABSORPTION OF ALCOHOL FROM STOMACH.

No.	Weight of dog. Kilos.	Duration of experiment.		Volume of fluid introduced. ccm.	Content of alcohol. Per cent by vol.	Alcohol found at end of experiment. grams.
		h.	m.			
VII	23.0	3	30	200 (alcohol)	37.5	4
VIII	21.0	3	00	200 ( " )	37.5	4-5
IX	8.0	3	50	100 ( " )	5.0	0
X	7.3	3	45	110 ( " )	4.8	0
XIII	10.7	3	55	75 (sherry)	21.0	0
XIV	18.5	3	45	150 (whiskey)	16.0	0
XV	8.0	3	45	125 (wine)	13.3	0
XVI	25.0	3	00	135 ( " )	13.3	0
XVII	12.3	4	00	125 (claret)	5.15	0
XVIII	10.2	3	55	100 (beer)	4.5	0
XX	14.0	3	45	150 (porter)	3.75	0
XXI	8.5	3	55	125 (beer)	4.7	0

The rapid discharge of watery or alcoholic fluids from the stomach through the pylorus has already been referred to on p. 193. The results are in harmony with those obtained by v. Mering on dogs with duodenal fistulæ.<sup>1</sup> In his experiments, for example, 500 c.c. being administered to a large dog, 490 c.c. were expelled through the pylorus in twenty minutes. The rapidity of expulsion was found to depend on the state of repletion of the small intestine, — an observation in accord with the retarded evacuation of the stomach seen when food is given along with fluids. v. Mering further observed that when water holding CO<sub>2</sub> in solution enters the stomach, the gas is readily absorbed; <sup>2</sup> alcohol is likewise absorbed, as J. Miller has recently verified for the human stomach.<sup>3</sup> Ogáta<sup>4</sup> found that of 6.5-8.8 grams

<sup>1</sup> v. MERING: Quoted in GAMGEE: Physiological chemistry, 1893, ii, pp. 441 seq.

<sup>2</sup> Cf. also Experiment V., p. 178.

<sup>3</sup> MILLER, J.: Arch. f. Verdauungskrankh., i, p. 233. Jahresbericht f. Thierchemie, 1895, xxv, p. 293.

<sup>4</sup> OGÁTA: Jahresbericht f. Thierchemie, 1885, xv, p. 274.

of alcohol introduced into the stomach in wine or beer, 80-90 per cent disappeared within half an hour. In the presence of soluble products in the stomach, an excretion of water by that organ is said to result in proportion to the amount of substance absorbed, — an idea akin to the one suggested in explanation of the relatively larger quantities of fluid found in the unligated stomach soon after introduction of alcohol, as compared with water. The experiments which we have made verify the statements of the investigators mentioned, as the following data selected from protocols indicate: —

*Data showing disappearance of alcohol from unligated stomach.*

I. Dog, with gastric fistula.

a. 3.45 p. m. Introduced 50 c.c. 20 per cent alcohol into stomach.

4.15 " Removed gastric contents = 40 c.c. No alcohol found.

b. 3.15 " Introduced 40 c.c. 25 per cent alcohol.

3.45 " Removed gastric contents = 20 c.c. No alcohol found.

c. 2.40 " Introduced 125 c.c. 20 per cent alcohol.

3.10 " Removed a portion of gastric contents. Free HCl = 0.072 per cent. Small amount of alcohol present.

II. Dog of 18 kilos, employed in a salivary experiment. In the course of the latter the animal received at intervals 45 c.c. absolute alcohol diluted with water. Two hours after last portion was given the stomach contents (200 c.c.) were removed. They contained 1.1 grms. alcohol.

III. Dog of 18 kilos. Salivary experiment. At intervals were given 70 c.c. absolute alcohol diluted with water. One and one-third hours after last portion (40 c.c.) was given the stomach contents (350 c.c.) contained 9.4 grms. alcohol.

IV. Dog of 14 kilos. Salivary experiment. 140 c.c. absolute alcohol diluted with water were given in three portions. Three-fourths of an hour after the last portion (50 c.c.), the stomach contents (450 c.c.) contained 24.6 grms. alcohol.

V. Dog of 10 kilos. Salivary experiment. 120 c.c. whiskey, containing 50 per cent of alcohol, were given in two portions. Four and one-half hours after the last portion (60 c.c.) the stomach contents (170 c.c.) contained 2.7 grms. alcohol.

VI. Dog. Salivary experiment. 135 c.c. brandy, containing about 50 per cent of alcohol, were given in two portions. Two hours after last portion (75 c.c.), the stomach contents (240 c.c.) contained 8.8 grms. alcohol.



VII. Dog of 10 kilos. Salivary experiment. 350 c.c. wine containing 5.15 per cent alcohol were given in two portions. One and one-half hours after last portion (200 c.c.), the stomach contents (190 c.c.) contained 5.5 grms. alcohol.

It is of interest to note that the large volumes of fluid (170-450 c.c.) found in the stomach in Experiments II.-VII. correspond with the data already presented with reference to the increased secretion of gastric juice due to alcohol and alcoholic beverages.

#### SUMMARY.

Some of the more important conclusions to be drawn from the results of the experiments reported in the preceding pages may be advantageously summarized here.

Upon the secretion of saliva, the presence of strong alcohol or an alcoholic beverage in the mouth has a direct stimulating effect leading to a sudden increase in the flow of saliva. This acceleration of secretion, however, is of brief duration. The stimulating effect is manifested not only by an increase in the volume of the secretion, but also by an increase in both organic and inorganic constituents. The effect produced is in no sense peculiar to alcohol, but is common to many so-called stimulants, such as dilute acid (vinegar), ether-vapor, etc. Indeed, the effect is precisely analogous to that induced by an increase in intensity of stimulation, when the salivary glands are electrically excited through their nerves.

As to the possibility of alcoholic fluids absorbed from the stomach giving rise to an indirect stimulation of salivary secretion, or exercising any appreciable influence upon the composition of the secretion, our results give a negative answer. Thus, alcoholic fluids introduced directly into the stomach (of dogs) by injection through the stomach wall, thus doing away with any local action in the mouth, produce no appreciable effect upon the rate of secretion, as induced by a constant external stimulus, of either submaxillary or sublingual saliva. Even doses of alcohol sufficient to produce prolonged narcosis when introduced in this way fail to check the flow of saliva. There is likewise no specific influence exerted on the composition of the secretion. Hence, so far as our results go, alcohol and alcoholic fluids are without any specific effect upon the secretion of saliva, except to produce a transitory stimulation of secretion while in the mouth cavity.

Upon gastric secretion, alcohol and alcoholic fluids have a marked effect, increasing very greatly both the flow of gastric juice and also

its content of acid and total solids. Further, this action is exerted not only by the presence of alcoholic fluids in the stomach, but also indirectly through the influence of alcohol absorbed from the intestine. Thus, ordinary ethyl alcohol introduced into the empty stomachs of dogs, with the duodenum ligated, shows a marked stimulating action upon gastric secretion — as compared with the action of water under like conditions — increasing not only the volume of gastric juice very greatly, but also its acidity, content of solid matter, etc. Moreover, alcohol absorbed from the intestine, the latter being entirely shut off from the stomach, may likewise cause stimulation of the gastric glands, with a marked increase in the rate of secretion, etc. Whiskey, brandy, sherry, claret, beer, and porter all agree in producing stimulation of gastric secretion. Further, as already stated, the gastric juice secreted under alcoholic stimulation is more acid, contains more solid matter and more combined hydrochloric acid than the ordinary secretion. It is likewise strongly proteolytic.

If these results are considered in connection with our previous observations upon the influence of alcohol and alcoholic drinks upon the purely chemical processes of gastric digestion, it is seen that side by side with the greater or lesser retardation of digestive proteolysis caused by alcoholic beverages there occurs an increased flow of gastric juice rich in acid and of unquestionable digestive power. The two effects may thus normally counterbalance each other, though it is evident that modifying conditions may readily retard or stimulate the processes in the stomach according to circumstances. Foremost among the latter is the rapid disappearance of alcohol from the alimentary canal.

Since any influence exerted by alcohol or alcoholic beverages upon the solvent or digestive power of the gastric juice in the stomach must depend upon the presence of alcohol in the stomach contents, it follows that the tendency toward rapid removal of the alcohol from the alimentary tract by absorption must necessarily diminish correspondingly the extent of the retardation of gastric digestion which the presence of alcohol in the stomach may occasion. Since, however, the stimulation of gastric secretion induced by alcohol is brought about not only by the direct action of alcohol in the stomach, but also by the indirect action of alcohol absorbed from the intestine, it follows that possible inhibition of the digestive action of the gastric juice would probably be of shorter duration than the stimulation of secretion, and that consequently in the body alcoholic fluids would



hardly lead to any retardation of gastric digestion. This point has been very carefully and thoroughly tested by numerous experiments on healthy dogs with gastric fistulæ, using proteid test meals, with the result that certainly in the stomach of dogs digestion is not retarded in any pronounced degree under the influence of alcohol or alcoholic fluids. Of hastened digestion, the results obtained give little or no suggestion, and we must therefore conclude that the two diverse factors above referred to more or less counterbalance each other so that gastric digestion in the broadest sense of the term is not markedly varied under the influence of alcohol or alcoholic fluids. This conclusion, it may be mentioned, stands in perfect harmony with the results of the investigations of Zuntz and Magnus-Levy regarding the influence of alcohol (beer) on the digestibility and utilization of food in the body. These investigators found by a series of metabolic experiments on men with diets largely made up of milk and bread, and on individuals accustomed and unaccustomed to the use of alcoholic beverages, that the latter did not in any way diminish the utilization of the food by the body.<sup>1</sup>

Especially worthy of note is the rapid disappearance of alcohol from the stomach and alimentary tract when alcoholic fluids are taken. As our results show, the introduction of even 200 c.c. of 37 per cent alcohol into the stomach of a dog with the duodenum ligated at the pylorus may be followed by the nearly complete disappearance of the alcohol in 3-3½ hours by absorption through the stomach walls into the blood. With the outlet from the stomach into the intestine open, the rate of absorption of alcohol is greatly increased. We may well believe, as stated by Ogáta, that when 6-8 grams of alcohol are taken into the stomach in the form of wine or beer that 80-90 per cent of the alcohol will disappear from the alimentary tract inside of half an hour. Indeed, our own experiments on dogs with gastric fistulæ lead to this conclusion. Thus, in one experiment 50 c.c. of 20 per cent alcohol were introduced into the stomach, and on withdrawing the stomach-contents half an hour later no alcohol whatever was found in the 40 c.c. of fluid obtained. In view of this rapid disappearance of alcohol from the alimentary tract it is plain that alcoholic fluids cannot have much, if any, direct influence upon the secretion of either pancreatic or intestinal juice.

<sup>1</sup> ZUNTZ and MAGNUS-LEVY: *Archiv f. d. ges. Physiol.*, 1891, xlix, p. 438; MAGNUS-LEVY: *ibid.*, 1893, liii, p. 544.

