of adrenoxidase in the blood,* the respirations are reduced, the pulse becomes weak, and reflex activity is markedly diminished. The reduction of the blood circulating in the cutaneous capillaries, supplemented by the deficient oxygenizing power of the blood, not only gives rise to partial anæsthesia of the surface, but also to a great reduction of the peripheral temperature. The awakening after such a dose is often attended with marked evidence of general disturbance; *i.e.*, mental torpor, confusion, headache and sometimes nausea and vomiting.

General vasodilation is a well-known feature of the action of chloral. Demarquay[45] long ago observed that it caused in animals, not only vasodilation, but also engorgement of all vessels. Kobert[46] was led experimentally to conclude that it caused paralysis of the vascular walls. As Labbée and other investigators noted that the rabbit's ear grew pale after its use, the general vasodilation had evidently caused recession of the blood into the great central trunks, thus tending to deplete the brain and the peripheral capillaries. This accounts, with the lowered oxygenizing power of the blood, for the fact, mentioned by Cushny,[47] that "the motor areas are rendered less irritable by chloral, and eventually fail to react to the strongest electrical stimulation." It also explains the mental torpor and the partial anæsthesi Even relatively small doses will cause relaxation of the arteries as observed by Labbée. Rajewsky, moreover, observed that small, as well as large, doses reduced the blood-pressure.

In some instances, a therapeutic dose causes flushing of the face, hyperæsthesia, restlessness, excitement and even delirium with hallucinations. This effect is due to the relaxation of the arterioles.* A greater quantity of arterial blood being admitted into the cutaneous and cerebral capillaries than usual,* a period of morbid activity follows.

Arloing found not only that the small vessels were dilated but that the supply of blood in the peripheral tissues was increased. This condition doubtless prevails in the deeper organs, including the cord, for Rajewsky[48] observed reflex irritability in frogs and that at this time the spinal ganglia were overexcitable. Moreover, Levinstein[49] observed a rise of temperature followed by marked fall. Some investigators, having noted sphygmographically an increase in size of the limb immersed, concluded that chloral increased the arterial pressure. But a similar effect is produced when the peripheral capillaries are dilated passively by unusual dilation of their arterioles. Cerna, working in Wood's laboratory, found it impossible to raise the blood-pressure in curarized dogs, with any dose of chloral. Even with the sphygmograph, Preisendörfer[50] found that the supposed period of preliminary rise was

* *Author's conclusion.*
[45] Demarquay: Bull. gén. de thérap., méd. et chir., T. lxxvii, p. 307, 1869.
[46] Kobert: Therap. Gaz., Jan. 15, Feb. 15, June 15, 1887.
[47] Cushny: *Loc. cit.*, p. 187, fourth edition, 1906.
[48] Rajewsky: Centralbl. f. med. Wissen., Bd. viii, S. 261, 1870.
[49] Levinstein: Lancet, Feb. 21, 1874.
[50] Preisendörfer: Deut. Archiv f. klin. Med., Bd. xxv, S. 48, 1880.

followed by a steady decline of blood-pressure, while Andrews and DaCosta[51] ascertained that very large doses "decidedly lessen arterial pressure."[52]

A toxic dose tends to paralyze the adrenal center and to arrest therefore the functions of the adrenals, and the formation of *adrenoxidase.** It tends to kill, therefore, by paralyzing the respiratory function.* The patient sinks into a profound sleep from which it is practically impossible to awaken him, the skin, owing to the morbid condition of the blood, being absolutely insensible. The pupils are widely dilated and the muscles are completely relaxed. The heart having lost the sustaining aid of the adrenal secretion and being nourished with blood deprived of its main constituent,* becomes steadily weaker and more irregular, the pulse presenting the same character. The temperature steadily declines and the respirations become gradually slower and irregular until they cease, death occurring from asphyxia. The heart continues to beat a short time, stopping in diastole. Occasionally, however, respiration and cardiac action cease together.

The diminution of adrenal secretion, *i.e.*, adrenoxidase, being the cardinal factor of the morbid process, it becomes a question whether chloral actually reduces its production. B. Ward Richardson[53] found that this drug reduced the coagulability of the blood—a morbid phenomen due, we have seen, to diminution of fibrin ferment. As previously shown, this body is adrenoxidase.* Now Model[54] observed that chloral predisposed to hæmorrhage—a phenomena due to reduced coagulability of the blood—while, on the other hand, Duncanson[55] and Lange[56] found that adrenal extract (which becomes adrenoxidase in the blood) controlled the hæmorrhages of hæmophilia, a condition due to deficiency of fibrin-ferment.

Again, we have seen, that removal of the adrenals or ligation of their efferent vessels causes a rapid reduction of the blood-pressure and of the temperature, ending in death, the characteristic phenomena of chloral poisoning. This is surely due to the fact that the blood is deprived of the adrenal secretion, for Strehl and Weiss,[57] after removing one adrenal, found that they could control the temperature and the blood-pressure at will by pinching and releasing the efferent vessels of the remaining adrenal. Now, when chloral has brought an animal to the verge of death, adrenal extract immediately counteracts the lethal condition. Gottlieb[58] "chloralized rabbits until the heart beats became irregular and excessively slow. An injection of suprarenal extract at once restored the regularity and volume of the pulse. He tried the same

* *Author's conclusion.*
[51] DaCosta: Amer. Jour. Med. Sci., Apr., 1870.
[52] Cited by Wood: *Loc. cit.*, p. 148, thirteenth edition, 1906.
[53] B. Ward Richardson: *Loc. cit.*
[54] Model: Münch. med. Wochen., Bd. xlvii, S. 1739, 1900.
[55] Duncanson: Brit. Med. Jour., Feb. 21, 1903.
[56] Lange: Münch. med. Woch., Bd. l, S. 62, 1903.
[57] Strehl and Weiss: Arch. f. d. ges. Physiol., Bd. lxxxvi, S. 107, 1901.
[58] Gottlieb: Arch. f. exp. Path. u. Pharm., Bd. xxxviii, S. 99, 1896.

experiment when the pulse was no longer registrable by the manometer; a similar result was obtained, and the heart almost immediately resumed its normal action." Here the adrenal secretion became converted into adrenoxidase and thus supplied the blood for a short time with its *pabulum vitæ*—in lieu of the animal's own adrenals, inhibited through paralysis of its center by the poison.

Chronic Poisoning.—The prolonged use of chloral hydrate provokes phenomena due to continued depression of the adrenal center, lowered metabolism, and the resulting general vasodilation.*

Respiratory disorders are frequently observed. The most prominent symptom is dyspnœa due to the diminution of adrenoxidase in the blood.* This may be severe and even alarming when the general vasodilation becomes sufficient to slow the circulation, and when the right heart, owing to the inadequate supply of adrenal secretion and adrenoxidase,* becomes feeble. The dilated capillaries allowing the blood fluids to traverse their walls with unusual facility, œdema may occur into the mucous membranes, skin, or deeper organs. *Mental disorders* are also witnessed in some cases in the form of intellectual torpor, loss of memory, or impulsive illusions and hallucinations due to fluctuations in the caliber of the vessels and the quantity of blood supplied to the brain. If the use of the drug be stopped suddenly, the vasomotor nerves soon resume the ascendency over the vessels, and the brain, receiving an influx of blood containing a greater supply of adrenoxidase, becomes overactive. Manifestations resembling delirium tremens may appear under such conditions. *Cutaneous disorders* are frequently observed. These are mainly due to the accumulation of wastes in the blood, owing to its reduced catabolic activity, and to the reduced propulsive vigor of the blood-stream which the vasodilation involves. They may assume the form of erythema, ecchymoses, petechiæ, or of ephemeral red patches, either in the skin or mucous membranes. The lesions sometimes cause considerable trouble, however, ulceration, fever and pyæmic toxæmia.

H. W. Mitchell[59] reported an interesting case which, as he says, "illustrates the resemblance between alcohol and chloral delirium." The mental disorder became so marked that the patient had to be placed in an asylum. Withdrawal of the drug, stimulation, forced feeding, hydrotherapeutic measures, with a hypnotic the first three nights, were followed by complete recovery. The author refers to Elliott,[60] who states that "there was no appreciable difference in delirium tremens resulting from the use of alcohol or chloral."

* *Author's conclusion.*
[59] W. H. Mitchell: *Loc. cit.*

The *treatment of chloral poisoning* is described in a special section at the end of this volume.

Therapeutics.—Chloral is mainly used in *insomnia,* especially when associated with nervous irritability. Its great value in this connection is due to the fact that by lowering metabolic activity it depresses the functions of all cellular elements including those of the nervous system, in which, we have seen, adrenoxidase likewise circulates.* The slight fall of blood-pressure which the lowered metabolism in the muscularis of the vessels causes when therapeutic doses are given, promotes ischæmia of the cerebro-spinal system and facilitates the soporific effects.* Its influence on pain (which is due to hyperæmia of the sensory terminals*) is slight, however, because the dilation of the arterioles caused by the remedy allows an excess of blood to penetrate the capillaries, thus offsetting what analgesic effect the lowered metabolism in the cellular elements might otherwise procure.* The recognized value of chloral in *chorea, paralysis agitans* and *uræmic convulsions* as a palliative is also due to its depressing influence on the vital and vascular mechanism,* which in these conditions are both overactive.* This applies as well to *puerperal eclampsia, epilepsy, hydrophobia* and *infantile convulsions,* in all of which chloral is frequently used; but it should be remembered that it is by no means a curative remedy* and that it tends, like all depressants, to promote the formation of the toxic wastes which act as spasmogenic agents.*

DRUGS WHICH RESEMBLE CHLORAL IN THEIR PHYSIOLOGICAL ACTION.

Paraldehyde acts much as does chloral. It primarily lowers the functional activity of the adrenal center, and by thus indirectly reducing the proportion of adrenoxidase in the blood, correspondingly inhibits metabolism in all tissues. As a result the muscular layer of the vessels is relaxed and general vasodilation, though not so marked as in the case of chloral, follows.

* *Author's conclusion.*
[60] Elliott: Lancet, May 24, 1873.

The sleep produced by therapeutic doses usually comes on within five minutes. It is not attended by anæsthesia, but resembles that caused by chloral, being calm and restful, and usually lasts five or six hours. It is likewise due to diminished metabolic activity in the cerebral nervous elements, and its effects are more marked in normal than febrile subjects. Occasionally, especially in the latter, it provokes unpleasant dreams and nightmares, and flushing, owing to a slight dilation of the arterioles and the admission in the cerebral and peripheral capillaries of a slight excess of arterial blood over that compatible with normal sleep. As a rule, the awakening is not followed by untoward symptoms; at times, however, depression, mental torpor, and lack of energy are complained of.

A *toxic dose* produces general muscular relaxation and unconsciousness and, sometimes, cyanosis. The cardiac contractions and the pulse become gradually weaker and intermittent. The respirations, at first rapid, soon become shallow and irregular, and death occurs from asphyxia. The symptoms that appear in paraldehyde habitués are similar to those observed in the chronic form of chloral poisoning, and likewise include emaciation, great muscular and cardiac weakness, and mental disorders. These are sufficiently severe in some cases, that it becomes necessary to place the patient under restraint.

Sulphonal.—Besides lowering the functional activity of the adrenal center,* sulphonal tends to decompose the hæmoglobin, as shown by the many cases in which hæmatoporphyrin, *i.e.*, iron-free hæmatin, is found in the urine. Any drug capable of such an action cannot but undermine the health. Preference should be given, therefore, to chloral or paraldehyde.

In therapeutic doses sulphonal produces apparently normal sleep of several hours' duration, from which he may awaken in his usual condition. Not infrequently, however, he experiences mental torpor, some lassitude, and perhaps vertigo. If the use of the drug is prolonged, it may give rise to general weakness, principally of the lower extremities, and sometimes to faintness, nausea, vomiting and serous diarrhœa. When large doses are used, the foregoing symptoms may more or less suddenly be accompanied by more serious ones. Respiratory phenomena, the salient features in acute cases, then appear: the face and

body become cold and livid, the lips and nails cyanosed, the respirations reduced in number and shallow, and the heart's action feeble and intermittent.

In *acute poisoning* met with in subjects addicted to the drug or others to whom it has been administered some time, premonitory symptoms, such as colic about the epigastrium, vomiting, diarrhœa, or obstinate constipation, a papular eruption and marked weakness, may appear; but such is seldom the case in neurasthenics. In these, which constitute the majority of cases, the acute symptoms usually appear suddenly and terminate fatally.

Trional.—Trional, which is very similar to sulphonal chemically, resembles it also in its physiological effects. Its depressing action upon the adrenal center is more marked,* however, while its dissociating effect upon the hæmoglobin is probably less active. It is, therefore, somewhat more powerful as an hypnotic, and when acute symptoms of poisoning occur, the chances of recovery are greater, and are not as likely to appear after one or two doses. The majority of cases of poisoning occur in persons who have taken the drug some time.

The symptoms due to *toxic doses* are often initiated by colic, persistent nausea and vomiting, and diarrhœa, owing to a sudden relaxation of the vessels and outpouring of blood-fluids into the alimentary canal. This is usually followed by obstinate constipation due to paresis of the intestinal muscles—a paresis witnessed in various parts of the body, particularly the extremities. The heart's action and the pulse now become very weak and rapid, and dilation murmurs are sometimes discernible over the mitral and aortic valve-signs—signs of impending heart-failure. Respiratory disturbances occur concomitantly; the lips and nails may become cyanosed and the patient lapses into coma. Death occurs most frequently in cases in which hæmatoporphyrin is found in the urine. But large quantities of urobilin and bilirubin are still worse as prognostic signs, since they indicate that the disintegration of hæmoglobin has reached its most advanced stage.

* *Author's conclusion.*

ALCOHOL.

Physiological Action.—The effects of alcohol upon the alimentary canal vary with the proportion contained in the ingesta. When the latter contain less than five per cent. of absolute alcohol, the secretory activity of the salivary gastric glands is increased reflexly and the digestive process is either stimulated and facilitated, or unimpaired. When, on the other hand, this proportion is exceeded, the digestion is not facilitated and may be delayed. A beverage containing ten per cent. of absolute alcohol and above, interferes with the digestive process in proportion as the percentage is high, by inhibiting the diastatic and proteolytic activity of the gastric juice.

The experiments of Buchner,[61] Chittenden and Mendel,[62] Storck[63] and others, have shown that when there is not more than five per cent. of absolute alcohol in the beverages ingested, the salivary digestion is enhanced, but that a higher proportion of alcohol tends to delay the process, especially when it exceeds 10 per cent. Chittenden, Mendel and Jackson[64] ascribe the increased flow of saliva to reflex action, provoked by the irritation of the alcohol on the oral nerve endings.

Gastric digestion is correspondingly influenced. The stimulating action of small quantites of alcohol is emphasized by the observation of Nothnagel and Rossbach[65] that a single drop injected into the stomach of a dog, through a gastric fistula, suffices to provoke a flow of gastric juice through the cannula. Chittenden, Mendel and Jackson, Radzikowski[66] and others also found that alcohol in moderate doses markedly increased the secretion of gastric juice, its proteolytic activity and the proportion of hydrochloric acid. Richet[67] likewise observed that it increased the acidity of the gastric juice. Similar effects are obtained, as shown by Froum, Moulinier, and Spiro,[68] when alcohol is administered by enema and when, as observed by Grénet,[69] it is injected into the blood. Elliston[70] found, moreover, that after the ingestion of small doses the increased secretion of gastric juice continued much longer than when none had been administered.

The pernicious influence of a large percentage of alcohol in the ingesta is no less evident. Claude Bernard has shown that strong doses of alcohol coagulate the gastric secretion and its ferments. Gluzinski[71] found that they impaired the digestion of albumins, the digestion being retarded. Two ounces of brandy taken before or during a meal, inhibit the digestion of starches. Taken after meals this quantity inhibits digestion. Lauren[72] found that it reduces the activity of pepsin on

[61] Buchner: Deut. Archiv f. klin. Med., Bd. xxix, S. 537, 1881.
[62] Chittenden and Mendel: Amer. Jour. Med. Sci., Jan., Feb., Mar., Apr., 1896.
[63] Storck: N. O. Med. Jour., Dec., 1901.
[64] Chittenden, Mendel and Jackson: Amer. Jour. of Phys., Mar., 1898.
[65] Nothnagel and Rossbach: "Mat. Med. et Therap.," Fr. edition, 1889.
[66] Radzikowski: Arch. f. d. ges. Physiol., Bd. lxxxiv, S. 513, 1901.
[67] Richet: Cited by Manquat: *Loc. cit.*, vol. ii, p. 652.
[68] Spiro: Münch. med., Woch., Bd. xlviii, S. 1871, 1901.
[69] Grénet: C. r. de la Soc. de biol., vol. lv, p. 376, 1903.
[70] Elliston: Med. Press and Circular, Sept. 16, 1891.
[71] Gluzinski: Cited by Manquat: *Loc. cit.*, vol. ii, p. 653.
[72] Lauren: Chem. Zeit. Rep., p. 313, 1893.

albumins. Thibault[73] noted that when the alcoholic strength exceeded 12.5 per cent. the proteolytic activity of the gastric juice was at once reduced. Chittenden and Mendel,[74] who also obtained stimulating effects from weak solutions, found that when the ingested mixture contains from 5 to 10 per cent. of absolute alcohol, retardation of the digestive process becomes noticeable, and that a 15 to 18 per cent. beverage retards it from 25 to 35 per cent.

Alcohol having a marked affinity for oxygen, the harmlessness or beneficial effects of weak solutions, such as beer, is due to the fact that a small quantity of alcohol is promptly oxidized by the adrenoxidase of the oral, gastric and intestinal secretions.* The glandular elements, to compensate for the deficiency of adrenoxidase thus created, reflexly increase their functional activity.*

When sufficient alcohol is taken to exceed the oxidizing powers of the secretions of the alimentary canal, the excess is absorbed into the general circulation and is oxidized therein by the adrenoxidase of the plasma and red corpuscles,* a very small quantity (about two per cent.) being excreted in its natural state.

Liebig many year ago advanced the view that the greater part of the alcohol absorbed from the alimentary canal becomes oxidized in the body, and that but a very small quantity is eliminated by the lungs and kidneys. His opinion was opposed on the plea that it was practically all eliminated unchanged, but the experimental work upon which this view was based was shown by Baudot[75] to have been faulty, and the weight of evidence contributed since has fully sustained Liebig's co lusion. Anstie,[76] Thudicum and Dupré[77] in experiments upon a large number of subjects found that the quantity of alcohol eliminated with the urine was trifling, *i.e.*, from 0.25 to 0.82 per cent. Schulinus,[78] Buchheim[79] and Lieben[80] not only confirmed this fact, but found that while the elimination with the excretions was inappreciable during the two or three hours following its ingestion, 25 per cent. of the drug had disappeared from the blood and tissues. This in turn was sustained by a second series of investigations by Anstie,[81] who not only again found that although the aggregate of alcohol eliminated in the urine, fæces, sweat and breath of a dog to which large quantities had been administered was trifling, the body of the animal contained none. Binz and Heubach[82] and Bodländer[83] and others also ascertained experimentally that alcohol was eliminated in trifling quantities. Precision

* *Author's conclusion.*
[73] Thibault: Jour. de pharm. et de chem., Feb. 15, 1902.
[74] Chittenden and Mendel: *Loc. cit.*
[75] Baudot: L'union méd., vol. xix-xx, pp. 273, 357, 374, 390, 1863.
[76] Anstie: "Stimulants and Narcotics," Phila., 1868.
[77] Thudicum and Dupré: Tenth Rep., of Med. officer of Privy Council, London, 1868.
[78] Schulinus: Archiv. f. Heilkunde, Bd. vii, S. 97, 1866.
[79] Buchheim, Nothnagel and Rossbach: "Therap.," p. 350, 1889.
[80] Lieben: Ann. d. Chem. u. Pharm., Bd. vii Supp., S. 236, 1870.
[81] Anstie: Practitioner, July, 1874.
[82] Binz and Heubach, Nothnagel and Rossbach: "Therap.," p. 350, 1889.
[83] Bodländer: Pflüger's Arch., Bd. xxxii, S. 398, 1883.

was recently given to this question by the comprehensive researches of Atwater and Benedict,[84] which showed that in the adult man only 1.9 per cent. of the alcohol contained in six ounces of whiskey is eliminated. Abelous, Bardier and Ribaut[85] found that even when three c.c. per kilo of (warm-blooded) animal was given, 87 to 90 per cent. of the total ingested was destroyed within eight hours. Cushny[86] emphasizes the fact that the 5 to 10 per cent. generally thought to be eliminated "is too high a valuation for the alcohol excreted and that only 2 to 3 per cent. of that ingested escapes oxidation."

The loss of oxygen which alcohol imposes upon the tissues by undergoing oxidation in the blood-stream, interferes with general nutrition and, therefore, lowers the activity of the vital process. Any quantity of alcohol absorbed into the circulation thus acts as a depressant.

The utilization of the blood's oxygen for the oxidation of alcohol entails a corresponding loss for the tissues, the result being a reduction of the activity of all vital processes. That such is actually the case is illustrated by the fact that although Binz,[87] Jaquet[88] and Wilmanns found that respiratory activity is augmented, the quantity of carbonic dioxide eliminated is on the whole reduced, as observed by N. S. Davis, Hammond,[89] Boeck and Bauer,[90] Rumpf[91] and many other investigators. The labor of breathing is thus augmented, but intracellular metabolism is impaired, owing to the paucity of oxygen. Indeed, Bouchardat and Sandras[92] observed in a rooster intoxicated with alcohol that the comb became cyanotic. This is apparently contradicted by the observations of Demarquay, Duméril, Perrin and others that small doses either do not modify the temperature, or, as noted by Wood,[93] raise it slightly, *i.e.*, about 1° F. (0.4° C.); but as is shown below this is the result of passive peripheral vasodilation. As these and many other investigators have found, larger doses, *i.e.*, doses capable in this connection of seriously deoxidizing the blood, lower the temperature in proportion as the quantity is large. In dogs, Rosenfeld[94] observed a reduction of nearly 10° F. (6° C.). Bouvier found that the fever of pyæmia could be reduced to normal by administering sufficiently large doses. Dumouly[95] found that 20 gms. (5 drachms) of absolute alcohol in solution acted as an antipyretic. Inhibition of tissue metabolism is further suggested by the experimental work of Ridge, Lauder Brunton, Parkes and Wollowicz, B. W. Richardson, Hammond, Vierordt, Schmiedeberg and others, which showed that even moderate doses of alcohol have a narcotic depressing effect.

Over twenty years ago French investigators held that alcohol robs the blood of oxygen which should subserve the nutritional process. Dujardin-Beaumetz,[96] for example, contended that alcohol, whose affinity for oxygen is so marked, could not enter the blood without undergoing

[84] Atwater and Benedict: S. E. Dept. of Agricul. Exp. Station Bull. No. 69.
[85] Abelous, Bardier and Ribaut: C. r. de la Soc. de biol., vol. lv, p. 420, 1903.
[86] Cushny: *Loc. cit.*, p. 139, fourth edition, 1906.
[87] Binz: Centralbl. f. klin. Med., S. 407, 1895.
[88] Jaquet: Archives de pharmacodynamie, vol. ii, 1895.
[89] Hammond: Physiol. Memoirs, p. 43, Phila., 1863.
[90] Boeck and Bauer: Zeit. f. Biol., Bd. x, S. 336, 1874.
[91] Rumpf: Arch. f. d. ges. Physiol., Bd. xxxiii, S. 538, 1884.
[92] Bouchardat and Sandras: Manquat: *Loc. cit.*, vol. ii, p. 657.
[93] Wood: *Loc. cit.*, p. 294, thirteenth edition, 1906.
[94] Rosenfeld: "Der Einfl. d. Alk. a. d. Organismus," Wiesbaden, 1901.
[95] Dumouly: Thèse de Paris, 1880.
[96] Dujardin-Beaumetz: C. r. de l'Acad. de méd., Apr. 1, 1884.

oxidation, especially in view of the loose hold oxyhæmoglobin has on oxygen. Bouchard[97] refers to alcohol as "that substance which, to so high a degree, slows the nutritional processes."

Alcohol is not a food; it does not replace proteids, fats or carbohydrates. The heat energy it liberates when oxidized is not utilized by tissue-cells, *i.e.*, in tissue metabolism, and is therefore wasted.* The tissues being deprived of the oxygen thus consumed by alcohol, catabolism is correspondingly delayed; and this in turn, proportionally retards the assimilation of materials by the tissues. The only effect of alcohol absorbed from the alimentary canal, therefore, especially in view of the fact that it supplies the organism with no tissue-building material, is to interfere with the nutritional process. In other words, it only spares the proteids, fats and carbohydrates as do asphyxiating agents, *i.e.*, by hindering tissue respiration.*

Alcohol is believed by some investigators to replace proteids, and by the majority of them to replace fats and carbohydrates. H. F. Hewes[98] aptly remarks in this connection: "The property of sparing tissue is possessed by several narcotic substances, as morphia. It would be as reasonable to class this substance among the foods as alcohol, if this property were taken as the distinctive quality of a food." Indeed, the greatest authority on thermochemistry, the late Prof. Berthelot,[99] held that alcohol is not a food.

Atwater and Benedict, in the exhaustive study referred to, conclude that the potential energy of alcohol is converted in the organism into working energy as thoroughly as is that of ordinary food. This cannot be accepted in the sense that alcohol can replace food, since the energy liberated is merely heat energy. As emphasized by F. S. Benedict,[100] alcohol does not build muscular or adipose tissue, thus failing in the essential rôle of true foods; it only furnishes a supply of heat while being oxidized. Indeed, were the working energy thus liberated, alcohol would exceed considerably in value that of ordinary aliments, since, as calculated by Dupré,[101] alcohol liberates during its oxidation nearly five times the heat units that an equal quantity of lean beef would produce. Kassowitz[102] has also laid stress recently on the fact that alcohol only acts as a stimulus, and that the substitution of a given proportion of non-nitrogenous food by a quantity of alcohol of equal caloric value, is associated with diminished working capacity and a dissipation of vital resources.

All this is further emphasized by the fact that concurrently with increased heat production, alcohol causes decreased nitrogen excretion. Thus, Bevan Lewis[103] ascertained calorimetrically that, while, as a rule, the heat production was at first lessened in rabbits by small doses, this

* *Author's conclusion.*
[97] Bouchard: "Mal. par ralent. de la nutrition," second edition, p. 184, 1885.
[98] H. F. Hewes: Boston Med. and Surg. Jour., Sept. 6, 1900.
[99] Berthelot: Brit. Med. Jour., Mar. 14, 1903.
[100] F. S. Benedict: Boston Med. and Surg. Jour., July 10, 1902.
[101] Dupré: Practitioner, July, 1872.
[102] Kassowitz: Pflüger's Arch. f. Physiol., Bd. xc, S. 421, 1902.
[103] Bevan Lewis: Jour. Ment. Sci., Apr., 1880.

was replaced by a considerable increase in heat production, especially after large doses. This was confirmed by E. T. Reichert and H. C. Wood[104] in dogs. The greater relative heat-value of large doses is obvious in these experiments, and yet, Norris and Smith[105] found that 1.9 c.c. to the kilo of animal increased the excretion of nitrogen two per cent., but that 2.3 c.c. per kilo *decreased* it two per cent. This reached nearly nine per cent. when 2.7 c.c. per kilo were used.

That the waste of heat energy simply inhibits tissue metabolism is shown by the diminution of catabolic products. Hammond[106] found that alcohol decreased the excretion of urea, chlorine and phosphoric acid. Riess[107] observed that it lessened the excretion of chlorides, phosphates and sulphates, and to a marked degree that of urea. Rosenfeld[108] and other investigators, after producing nitrogenous equilibrium in man, found the nitrogen elimination distinctly decreased, *i.e.*, lower than the intake. Alcohol was undoubtedly the active factor in this morbid process, for while A. Ott[109] observed an extremely low excretion of nitrogen the first day alcohol was used, H. Keller,[110] on the other hand, found that as soon as the use of alcohol ceased, the excretion of nitrogen rose rapidly until it was one gm. above normal—this excess persisting three days. Indeed, Miura[111] was led to conclude, by a series of comprehensive experiments also showing a marked decrease of nitrogen, that the effects of alcohol in this particular were similar to those of a reduced diet.

This is equally true of carbohydrates. Miura found that when sugar was replaced by isodynamic quantities of alcohol, a low nitrogen excretion occurred in subjects placed in a condition of nitrogenous equilibrium, but that on restoring the sugar the nitrogenous equilibrium was resumed. It is evident, therefore, that alcohol is not a substitute for carbohydrates. This accounts for the fact recorded by explorers in the Arctic regions, that the use of alcohol greatly reduced their resistance to cold. Again, Chittenden[112] found that alcohol reduced oxidation in the liver. This he characterizes a pernicious influence of which carbohydrates and fats are free. While the latter bodies are simply oxidized into carbonic acid and water and converted into glycogen and fat, alcohol is not. He concludes, therefore, that this establishes a distinct line of demarcation between alcohol on the one hand and carbohydrates and fats on the other. And this applies to the rest of the organism as well. Briefly, in the words of Woodbury and Egbert,[113] the physiological action of alcohol on the human body is destructive, but never constructive.

Untoward Effects.—The first stage of alcohol poisoning, that known as drunkenness, may be provoked by varying doses, small quantities sufficing, in persons unaccustomed to its use, to produce phenomena which only occur after the ingestion of large quantities in habitual drinkers.

When a so-called "stimulating" dose of alcohol is ingested,

[104] E. T. Reichert and H. C. Wood: Cited by Wood: *Loc. cit.*, p. 295, thirteenth edition, 1906.
[105] Norris and Smith: Jour. of Physiol., vol. xii, p. 220, 1891.
[106] Hammond: *Loc. cit.*
[107] Riess: Zeit. f. klin. Med., Bd. ii, S. 1, 1881.
[108] Rosenfeld: Die Therapie der Gegenwart, Bd. vii, 1900.
[109] A. Ott: Arch. f. exp. Path. u. Pharm., Bd. xlvii, S. 267, 1902.
[110] H. Keller: Zeit. f. physiol. Chemie, Bd. xiii, S. 128, 1889.
[111] Miura: Zeit. f. klin. Med., Bd. xx, S. 1371, 1892.
[112] Chittenden: Med. News, Apr. 22, 1905.
[113] Woodbury and Egbert: Jour. Amer. Med. Assoc., Mar. 31, 1900.

it liberates heat-energy while being oxidized by the adrenoxidase in the blood, and the quantity of energy thus liberated is in excess of that produced normally by the interaction of the adrenoxidase and nucleo-proteid.* An artificial exacerbation of metabolism being thus provoked in all tissues, the contractile power of the cardiac and vascular muscles is correspondingly increased.* As a result, the heart-beats and pulse become stronger and more frequent, and the blood-pressure is raised, the blood being projected forcibly into all capillaries. The latter being passively dilated and congested, the well-known flushed face and eye, the warm skin, the strong and rapid pulse, the cerebral excitement which prompts to garrulousness, boisterousness, outbursts of anger, etc., and the temporary augmentation of physical strength, are produced.

When a depressing dose is taken, this stage is soon antagonized in two ways: (1) The alcohol and adrenoxidase being free in the blood, while nucleo-proteid is secreted in the latter by leucocytes only as needed,* the reducing action of the alcohol deprives the adrenoxidase of oxygen which it should supply to the tissues.* Metabolism being impaired in proportion, and the nerve centers, general and subsidiary (including the vasomotor centers), and the muscularis of all vessels receiving partially reduced blood,* general vasodilation (including relaxation of the cutaneous arterioles) follows, and the capillaries of all organs, including the skin and brain, are the seat of a passive hyperæmia. The pulse is still full at this stage, but easily compressed.

The exacerbation of muscular power coincides, as is well known, with the period of cerebral excitement and with the characteristic congestion of the face, eyes, etc. Cushny[114] writes: "The flushing of the skin, which occurs in alcoholic intoxication, would seem to point to some vascular action, but it is impossible to say at present what the nature of this action is. It indicates dilation of the skin vessels, but whether this is of central or peripheral origin, whether due to stimulation or dilator centers or paresis of vasoconstrictors, it is impossible to say." As Claude Bernard pointed out that marked hyperæmia of the brain was also present, the cause of this phenomenon may be said to be as obscure as that of the facial hyperæmia; and this applies as well to the muscular erethism.

Castillo,[115] Binz,[116] Eagleton,[117] Kochmann[118] and others have wit-

* *Author's conclusion.*
[114] Cushny: *Loc. cit.*, p. 137, fourth edition, 1906.
[115] Castillo: Phila. Med. Times, Oct. 23, 1880.
[116] Binz: *Loc. cit.*
[117] Eagleton: Univ. Med. Mag., Sept., 1890.
[118] Kochmann: Deut. med. Woch., Bd. xxxi, S. 942, 1905.

nessed the preliminary rise of the blood-pressure referred to. Abel,[119] Rosenfeld,[120] Cabot[121] and others did not observe it; while the third phase, vasodilation, was noted by Zimmerberg,[122] Gutnikow,[123] Pässler,[124] Schule[125] and Rosenfeld. The fact that all three phases may occur, as shown above, accounts for the contradictory results recorded by various investigators.

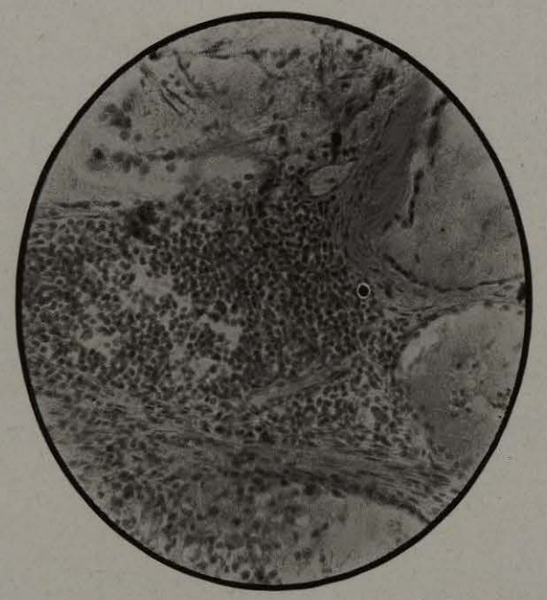
That the vasoconstriction is due to augmentation of the metabolic processes in the vascular walls by the direct action of the alcoholized blood is also indicated by the fact that these investigators, Wood and Hoyt,[126] noted that alcohol "elevates the blood-pressure after vasomotor paralysis from section of the cervical cord." Their experiments tended to show, moreover, that the cerebral excitement and increased activity were due "to the enormously increased flow of blood running riot through the cerebrum." Hemmeter[127] likewise observed a marked increase in the rapidity of the blood-flow, and a still greater one when more alcohol was administered; in some of Wood and Hoyt's experiments the speed of the current increased 33 per cent. The red face and the still redder nose and eyes of the common drunkard attest to the fact that after the prolonged use of alcohol the arterioles may remain dilated. Finkelnburg[128] found, by introducing a trocar between the vertebræ, that the cerebro-spinal pressure was considerably increased.

As to the influence of the general vasoconstriction upon the capillaries, Kochmann[129] found experimentally that "in moderate doses alcohol increases the vascular tension; when the rise is at its maximum, the peripheral vessels are dilated." He noted, moreover, that the latter effect was produced "even when the doses are too weak to cause an increase of vascular tension."

The influence of large doses is shown by the experimental observation of Wood and Hoyt[130] that "sometimes no effect was produced until the alcohol had been given in sufficient amounts to reduce the pressure." Vasodilation may also occur under the influence of small doses. Thus, Kellogg[131] states that "the full bounding pulse usually produced by the administration of an ounce or two of brandy properly diluted, gives the impression of an increased vigor of heart action, but it is only necessary to determine the blood-pressure by means of a Riva-Rocci instrument, or Gaertner's tonometer, to discover that the blood-pressure is lowered instead of raised. This lowering may amount to twenty or thirty millimeters, or even more."

While the varying effects produced by alcohol indicate that it has no direct action on the vasomotor center (which would always be influenced in the same way) they suggest, on the other hand, that it is due to an intravascular chemical process. Cabot[132] found that alcohol did not influence the temperature in febrile cases, as shown by 1105 measurements taken by him before, during and after its administration—an observation confirmed in animals by Wood and Hoyt. This

[119] Abel: "Physiol. Aspect of the Liquor Problem," vol. ii, 1903.
[120] Rosenfeld: *Loc. cit.*
[121] Cabot: Trans. Assoc. of Amer. Phys., vol. xviii, p. 402, 1903.
[122] Zimmerberg: Dissert. Dorpat, 1869, cited by Cabot: *Loc. cit.*
[123] Gutnikow: Zeit. f. klin. Med., Bd. xxi, S. 152, 1892.
[124] Pässler: Verh. Congr. f. inn. Med., Bd. xvi, S. 438, 1898.
[125] Schule: Berl. klin. Woch., Aug. 13, 1900.
[126] Wood and Hoyt: Memoirs of the National Acad. of Sciences, vol. x, Third Mem., 1905.
[127] Hemmeter: Med. Rec., Sept. 12, 1891.
[128] Finkelnburg: Deut. Arch. f. klin. Med., Bd. lxxx, S. 130, 1904.
[129] Kochmann: Arch. inter. de pharmacodyn. et de thérap., T. xv, p. 443, 1905.
[130] Wood and Hoyt: Univ. of Penna. Med. Bull., May, 1905.
[131] Kellogg: Modern Medicine, Nov., 1905.
[132] Cabot: *Loc. cit.*



FIBROSIS OF ANTERIOR PITUITARY DUE TO ALCOHOLISM. *[Sajous.]*