4.

ON THE ACTION OF PURGATIVE MEDICINES.

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BEFORE entering upon their use, it will be well to consider the question—How do certain substances act as purgatives?

It is generally believed that most purgatives increase the number of the stools and render them more fluid in a double manner; firstly, by stimulating the intestine to increased peristaltic action, and secondly, by inducing a discharge of fluid from its mucous surface, and thus to some extent washing out its contents.[1] Some purgatives, such as aloes, are supposed to act almost entirely by stimulating the peristaltic movements, their effect on the secretion from the intestine being almost *nil;* while others, like bitartrate of potash, are supposed to induce a very free secretion from the mucous membrane, while they have so little influence upon the peristaltic movements that the fluid poured out from the intestinal wall after their use may remain in the torpid intestine so long as to be again reabsorbed.[2] Others again, like croton oil, are supposed to increase the flow of liquid into the intestine, and at the same time to stimulate the peristaltic movements.

This view of the action of purgatives is the one generally held in this country. It is supported by several French authorities, but is rejected by some of the most eminent German pharmacologists.

All are agreed in believing that the action of many purgatives is due to their power of quickening peristaltic action, but

[1] Pereira's "Materia Medica," vol. i. p. 247; Stillé's "Therapeutics and Materia Medica," vol. ii. p. 404; Ringer's "Therapeutics," 3d ed. p. 154.

[2] Garrod's "Materia Medica," 3d ed. 1868, p. 401.

several German authors are inclined to regard increased peristalsis as the only, or almost the only cause of purgation, and to deny that there is any increased flow of fluid from the intestinal walls. They consider that purgative medicines, by quickening the peristaltic action, cause the contents of the intestine to be hurried along and expelled per anum before there has been time for the absorption of their fluid constituents. Instead, therefore, of the stools being firm and consistent as in the normal condition, they are loose and watery like the fæcal matters which one usually finds in the small intestine on post-mortem examination. By making a fistulous opening in the ascending colon of a dog, Radziejewski, the distinguished pharmacologist, whose untimely death is much to be deplored, has found[1] that the intestinal contents, when poured from the small into the large intestine, almost exactly resemble the stools produced by the use of purgative medicines. He therefore, and several German authors who follow him, attribute the watery condition of the stools observed after the administration of vegetable purgatives, such as castor or croton oil, to increased peristalsis only. The objection may be raised that the stools produced by elaterium, for example, are more watery than the contents of the small intestine usually are; but this can readily be met. For it is not merely the peristaltic action of the large intestine which is quickened so that the fæces are expelled in much the same condition as they entered it. The movements of the small intestine are also accelerated, so that little absorption can take place in it, and its contents will therefore leave it in a more watery condition than usual, and being quickly hurried through the large intestine, will produce a liquid motion.

This explanation may seem satisfactory enough in regard to the action of vegetable purgatives, and of such mineral ones as calomel; but it hardly explains the effects of salines, such as bitartrate of potash or sulphate of magnesia. These are allowed by Buchheim[2] to have an additional action besides that of increasing peristalsis. They retain water with great avidity, they diffuse slowly, and by thus preventing the water which is taken with them or swallowed shortly afterwards from being

[1] Reichert u. Du Bois-Reymond's Archiv. 1870, p. 95.

[2] Buchheim's Arzneimittellehre, p. 136.

absorbed, at the same time that they quicken the intestinal movements, they wash out the whole alimentary canal from end to end, in much the same way as a simple injection washes out the rectum. A large quantity of fluid is normally poured into the intestine by the liver, pancreas, and intestinal glands, and this alone, according to Kühne,[1] is greater than the amount expelled in the most profuse diarrhœa. When, in addition to this, the quantity of fluid ingested by the mouth is taken into consideration, it seems perfectly unnecessary to believe that any increased flow of fluid takes place from the intestinal walls. Moreover, direct experiments seemed to show that purgatives did not increase the flow of fluid from the intestinal walls. Such a flow might be of two kinds: it might consist of a transudation from the blood-vessels, as supposed by Schmidt,[2] or of a secretion from the intestinal glands. In the former case it would contain a considerable quantity of albumen like the fluid in ascites or pericarditis; while in the latter, albumen might only be present to a very slight extent. A consideration of the structure of the intestine alone is sufficient to show the improbability of a direct transudation of fluid from the vessels; but Radziejewski[3] has set the matter at rest by examining the composition of fæces before and after the use of purgatives, and proving that the stools produced by them do not contain albumen to anything like the amount they ought to do if transudation fluids were present in them to any considerable extent. The most decisive experiments, however, were those which were first made by Thiry by means of the intestinal fistula which bears his name. These seemed to show in the most conclusive manner that purgatives neither increased the flow of fluid from the intestinal walls by transudation nor by secretion. In order to discover exactly what went on in the intestine, Thiry conceived the idea of isolating a portion of it and attaching one end of this piece to an opening in the abdominal walls while its nerves and vessels remained uninjured, and the whole piece was as nearly as possible in a normal condition. He therefore divided the jejunum or ileum in two places, a few inches apart from each other, sewed up one end of

[1] Kühne, "Lehrbuch der physiologischen Chemie," p. 151.

[2] C. Schmidt, "Characteristik der epidemischen Cholera," Leipzig, 1850, p. 90.

[3] Radziejewski, op. cit. p. 75.

the piece thus isolated, and attached the other end to the wound in the abdomen. The short *cul-de-sc* thus formed remained attached to the mesentery and received its vascular and nervous supply as usual. The divided ends of the intestine were then sewn together, and the continuity of the alimentary canal restored.[1] This is represented in the accompanying figure (Fig. 1), where B indicates the place where the piece C D, which originally lay between A B and B E, has been cut out, and the two ends of A B and B E sewn together so that the alimentary canal is again complete, though a few inches shorter than before. F, G, D, is the abdominal wall, and *a* and *b* are the vessels and nerves in the mesentery.

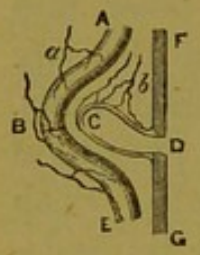

FIG. 1.

The little bag of intestine C D can be easily reached from the outside of the body, and the result of any experiment upon it readily ascertained. It apparently remains in a perfectly healthy condition, and when tickled with a feather readily secretes intestinal juice. But a purgative medicine introduced into it neither increases the secretion nor causes transudation from the vessels, although the drug produces brisk purgation if administered to the animal by the mouth. Thiry[2] in his experiments used croton oil, senna, and sulphate of magnesia. Schiff[3] repeated them with aloes, jalap, and sulphate of soda; and Radziejewski[4] with croton oil and sulphate of magnesia. All these observers obtained a like negative result. Further proof seems superfluous to show that purgatives act only by accelerating peristaltic action, and not by increasing the flow of fluid from the intestinal wall; and I have not only believed but have taught this, till the publication of some experiments of Moreau,[5] their verification by Vulpian, and the results I have myself obtained on repeating them, have led me to alter my opinions.

These experiments were made by opening the abdomen of an animal, and tying four ligatures tightly round the small intestine a few inches apart from each other, so as to isolate three por-

[1] Thiry, "Sitzungsbericht der Wiener Academie," 1864, vol. L. p. 77.

[2] Thiry, op. cit. p. 95.

[3] Schiff, "Nuove ricerche sul potere degerente," &c. H. Morgagni, July 1867, p. 5.

[4] Radziejewski, op. cit. p. 85.

[5] Moreau, "Archiv Générales de Médecine," August 1870, p. 234.

tions of intestine. A purgative medicine was then injected by means of a subcutaneous syringe into the middle part, and the intestine being then returned into the abdominal cavity, the wound in the abdominal parietes was sewn up. A few hours afterwards the animal was killed, and on examination the middle portion of intestine, into which the purgative had been injected, was found full of fluid, while the portion on each side was completely empty. All three pieces having been equally empty at the commencement of the experiment, and all three having been placed under exactly the same conditions, we cannot attribute the copious secretion into the middle loop to any other cause than the action of the purgative injected into it. Moreau's experiments have been repeated by Vulpian,[1] and I subjoin the notes of the results which I have obtained.

Exp. I.—A cat was chloroformed, and an incision about $1\frac{1}{2}$ inches long made through the abdominal walls in the middle line about the umbilicus. A coil of small intestine was drawn out, and four ligatures tied tightly round it so as to isolate three loops of intestine. One-hundredth of a drop of croton oil mixed with one drop of alcohol was then injected into the second loop by means of an extremely fine Wood's syringe. (The quantity of croton oil was obtained by thoroughly mixing 1 part of oil and 99 of alcohol.) The intestine was then replaced, the wound sewn up, and the animal allowed to recover from the chloroform. About four hours and a quarter afterwards it was instantly killed by a single blow on the head with a hammer, and the intestine examined :—

Loop 1.	Length $3\frac{4}{5}$ inches	. . .	Contained 7 minims of fluid.
,, 2.	,, $1\frac{7}{5}$,,	. . .	,, 20 ,, ,,
,, 3.	,, $3\frac{1}{5}$,,	. . .	,, 10 ,, ,,

Exp. II.—A cat was operated on in the same way as the first, and $\frac{1}{10}$ of a drop of croton oil with 10 drops of alcohol was injected into a loop of intestine which, as in the former case, lay between two others likewise isolated by ligatures. About four hours and a quarter after the operation the cat was killed in the same way as the first :—

Loop 1.	Length $2\frac{4}{5}$ inches	. . .	Completely empty.
,, 2.	,, $3\frac{2}{5}$,,	. . .	Contained 80 minims of fluid.
,, 3.	,, $3\frac{1}{5}$,,	. . .	Empty.

[1] Vulpian, "Bulletin Général de Thérapeutique," tome lxxxiv. 1873, p. 522.

Exp. III.—Made in the same way as the preceding ones. One drop of croton oil and 9 of alcohol injected into loop No. 2. Four hours and a quarter afterwards :—

Loop 1.	Length 4$\frac{5}{16}$ inches	. . .	Empty.
,, 2.	,, 5$\frac{5}{16}$,,	. . .	Contained 110 minims of fluid.
,, 3.	,, 6$\frac{1}{16}$,,	. . .	Empty.

Just about the middle of loop No. 2 the mucous membrane or about 1$\frac{1}{2}$ inch was thickened, much reddened, and inflamed.

Exp. IV.—Made in the same way as the preceding ones. Ten drops of croton oil were injected into loop of intestine No. 2. I am not quite certain that the whole of the 10 drops found their way into the intestine, as the oil passed very slowly through the fine hollow injecting needle, although considerable force was used. The syringe at one instant became detached from the needle, and a little oil escaped. I tried to guess the right amount, however, and injected it afterwards. Four hours and a quarter after injection :—

Loop 1.	Length 6$\frac{1}{16}$ inches	. . .	Contained 155 minims of fluid.
,, 2.	,, 5$\frac{1}{16}$,,	. . .	,, 180 ,, ,,
,, 3.	,, 5$\frac{3}{16}$,,	. . .	,, 75 ,, ,,

The fluid, as measured, was not quite accurate, for a tapeworm was present in the intestine, and parts of it helped to swell the apparent bulk of the fluid.

In the middle of loop No. 2 the mucous membrane was much inflamed for about two inches or rather more. This is the part with which the oil would come in contact after its injection through the intestinal wall.

The mucous membrane of all three loops, as well as that for four or five inches above the upper and below the lower loop, was much thickened, and the lumen of the intestine partially filled with a glairy fluid. Above and below these parts the intestine was firmly contracted and natural, just as when the injection was made. The mucous membrane in all the coils was somewhat pale, as also at the thickened parts outside. At the other parts where it appeared unaltered, its inner surface was of a yellow colour, probably from adherent biliary or fæcal colouring matter.

Exp. V.—A cat was experimented on as before. A small

quantity of elaterin (probably about $\frac{1}{10}$ of a grain) suspended in 30 drops of water was injected into loop No. 2. About four hours and a quarter afterwards :—

Loop 1.	Length $5\frac{7}{8}$ inches . . .	Contained 60 minims of fluid.
,, 2.	,, $6\frac{1}{16}$,, . . .	,, 110 ,, ,,
,, 3.	,, $5\frac{7}{8}$,, . . .	Empty.

In all three loops, as well as for five or six inches beyond the loops, the mucous membrane (or whole intestinal wall?) was pale and somewhat thickened.

Exp. VI.—A cat was chloroformed, an incision made in the abdominal walls, and three loops of intestine isolated by ligatures. Into the middle one (No. 2) about two grains of gamboge made into an emulsion, with about 60m. of water, were injected at 11.15. The wound was then sewn up, and the animal allowed to recover. About four hours afterwards the cat was killed by a blow on the head and the intestine examined :—

Loop 1.	Length $4\frac{1}{8}$ inches . . .	Empty. Mucous membrane yellowish on the surface.
,, 2.	,, $5\frac{6}{8}$,, . . .	Contained 185 minims of yellowish turbid fluid with numerous flocculi. The surface of the mucous membrane was slightly paler than in No. 1.
,, 3.	,, $6\frac{3}{8}$,, . . .	Empty. Colour like No. 1.

Exp. VII.—The experiment was performed on a cat in the same way as the previous one. Into the middle loop of intestine about one grain of jalapin in a small quantity of spirit (proof) and water (equal parts) was injected. The intestine was examined about four hours afterwards. The cat seemed sleepy, and the respiration appeared to be impeded by fluid in the respiratory passages :—

Loop 1.	Length $5\frac{1}{8}$ inches . . .	Quite empty. Surface of mucous membrane normal.
,, 2.	,, $6\frac{1}{2}$,, . . .	Contained 17 minims of tenacious fluid. Surface of mucous membrane moister than in No. 1.
,, 3.	,, $5\frac{1}{2}$,, . . .	Mucous membrane moist. Covered with bloody mucus.

Exp. VIII.—The experiment was made in the same way as the preceding ones. Into the middle loop, No. 2, about 7 grains of sulphate of magnesia dissolved in 105 minims of water were injected. Into each of the side loops 105 minims of water were injected. The intestine was examined about four hours afterwards :—

Loop 1.	Length 5 inches . . .	Quite empty.
,, 2.	,, 7½ ,, . . .	Contained 320 minims of fluid. This was of a pale amber colour and glairy consistence, mixed with flakes of whitish mucus. Not the slightest trace of congestion was noticeable. Mucous membrane was quite natural in No. 2.
,, 3.	,, 5½ ,, . . .	Quite empty.

Exp. IX.—The experiment was conducted like the others. Into the middle loop of the cat's intestine 85 minims of a saturated solution of sulphate of magnesia were injected. On examination four hours afterwards, the middle loop, which was 7½ inches long, contained 425 minims of fluid. The other two loops were quite empty.

Exp. X.—The experiment was conducted as before. Into the middle loop of the cat's intestine about 90 minims of a saturated solution of sulphate of magnesia was injected. The loop was about 6 inches long. After about five hours the loop was found to contain about 250 minims of fluid. The loop above it contained a little bloody mucus, the one below it was entirely empty.

These experiments show that croton oil, elaterin, gamboge, and sulphate of magnesia all cause a copious secretion from the intestine. Jalapin did not do so in the single instance in which it was tried ; but I am not quite certain that the whole of it went into the intestine, as it formed a resinous mass which I had considerable difficulty in getting to pass through the nozzle of the syringe. The fluid contained in the intestine after the use of the other purgatives appears to be a secretion, not a transudation, for it does not contain much albumen as a transudate would do. In Exp. VIII. it amounted to about 42 minims, and in Exp. IX. to about 56 minims per square inch of intestine

acted on by the purgative. The greatest secretion was caused by sulphate of magnesia; next came croton oil, elaterin, and gamboge; while jalapin stood last of all.

Such positive results as these seem to prove that purgatives do cause a flow from the intestinal wall, quite as conclusively as experiments with Thiry's fistula do the opposite; and as the conditions under which the purgatives act on the intestines more nearly approach the normal in Moreau's than in Thiry's experiment, there can be but little doubt that purgatives produce a decided secretion of fluid from the intestine, as well as accelerate peristaltic movements.

Having now come to a conclusion regarding the manner in which purgatives act, let us consider some of their effects upon the body. It is evident that the increased peristaltic action of the bowels will hurry along the food and cause its expulsion before the nutritive matters it contains have been fully absorbed.

If a purgative be taken immediately before or shortly after a meal, the result will be much the same as if less food had been taken or the meal entirely omitted. Many persons who are accustomed systematically to eat more than they require will regularly take a "dinner pill" or a course of Seidlitz or Pullna waters, although they cannot be persuaded to deprive themselves of a single opportunity of enjoying the pleasures of the table or to put the least restraint upon their appetites.

Increased peristaltic action will also remove fæcal matters as well as food from the intestine, and it will be greatly assisted in this by the increased secretion from the intestinal wall which purgatives induce.

I have already mentioned that mechanical irritation, such as tickling with a feather or rubbing with a glass rod, will cause secretion from the *cul de sac* of intestine in Thiry's fistula, and hardened fæces seem to have a similar action. Thus diarrhœa is not unfrequently caused by the presence of scybalous masses or other irritating matters in the intestine, and nothing cures this like a dose of castor-oil. At first sight it seems odd that the scybala are not washed away by the fluid which they cause to be secreted, but this secretion will probably be poured out only at or below the point where they lie, and thus it will have little effect on them, though it may wash out the lower part of the

bowel thoroughly enough. A dose of castor-oil, on the contrary, will induce secretion in the bowel above the scybala, and the fluid in its downward rush will carry the fæcal masses along with it.

Irritating substances in the intestine, besides acting locally upon the bowel in the manner just indicated, may exercise an influence upon distant organs through the medium of the nervous system. Sir Charles Bell[1] observed a case in which ulceration of the ileum was found in a man who had suffered severely from tic, but there was nothing wrong whatever with the fifth nerve, in which the pain was felt. He therefore felt convinced that although the pain was felt in the cheek, its true source was irritation in the ileum. Acting on this belief, he administered croton oil ($\frac{1}{12}$ of a drop in combination) in tic douloureux for the purpose of removing any morbid condition of the bowel, and obtained the happiest results from its employment; and Newbigging[2] has found it equally efficacious in sciatica.

It is difficult to say whether the pain felt in the cheek is simply due to the irritation of the intestinal nerves being reflected, as it is termed, along the fifth nerve, or whether the irritation induces such a change through the vaso-motor nerves in the blood-vessels of the cheek as actually to set up a new irritation in the course of the fifth nerve itself. At any rate, the vessels of the face and head are very easily affected by any irritation of the stomach or intestines, as is easily seen from the extraordinary pallor which at once overspreads the face when a state of sickness and nausea has been induced. The effect of constipation in causing a feeling of fulness in the head is well known, and Ludwig and Dogiel[3] found that when the intestines of an animal were moved by the finger the rapidity with which the blood flowed through its carotid arteries was greatly increased. The frontal headache which so frequently accompanies gastric or intestinal derangement may possibly be due to some of the intestinal contents which ought to be evacuated being absorbed and acting as poisons on the vessels of the head themselves. I

[1] Bell, "Practical Essays," p. 85.

[2] Newbigging, *Edin. Med. and Surg. Journ.*, Jan. 1, 1841.

[3] Ludwig's Arbeiten aus der physiologischen Anstalt zu Leipzig, 1867, p. 253.

am inclined to think, however, that although this may have much to do with it, yet the headache very often depends to a great extent on some alteration in the cerebral circulation caused reflexly by the condition of the abdominal organs; for I have myself had a headache, though not a frontal one, which alternated with nausea. The nausea would last for a few minutes, during which the headache would entirely disappear; then the nausea would leave me, and the headache instantly took its place. After evacuation of the stomach, both the headache and nausea disappeared, showing that in this instance at least they were due to irritation in the stomach. But in many instances no doubt, not only headache but much more serious symptoms may be due to the decomposition of food in the intestinal canal and the absorption of its products. Thus Senator[1] relates a case where a simple gastric catarrh without fever was brought on by eating something which disagreed with the patient. This was followed on the second day by great belching of gas, smelling like sulphuretted hydrogen or rotten eggs. The urine also contained sulphuretted hydrogen. As soon as this occurred the patient collapsed suddenly, and became pale and giddy, with a small, frequent, and compressible pulse. The patient remained conscious, and in a minute and a half or two minutes the collapse passed away. A similar attack came on again during the same day, but after the bowels which had been constipated were opened, the patient rapidly recovered. Senator considers that the collapse was due to poisoning by the sulphuretted hydrogen absorbed from the intestine, and it certainly seems probable that this was one cause of the attack, even if it were not the only one.

Other poisons besides sulphuretted hydrogen may be formed in the alimentary canal and absorbed into the blood, where they exert their deleterious action. Among these may be mentioned butyric acid, which has frequently been found in the stomach in considerable quantities.[2] According to O. Weber[3] it is very poisonous, exerting its action chiefly on the nerve centres. The nervous symptoms which frequently accompany gastric derange-

[1] Senator, "Berliner Klinische Wochenschrift," 1868, No. 24, p. 254.
[2] Kühne, "Physiologische Chemie," p. 58.
[3] O. Weber, "Deutsche Klinik," 1864, p. 488.

ment or disease of the intestines may therefore be frequently occasioned by poisons formed in the alimentary canal in consequence of imperfect digestion.

The administration of a brisk purgative or small doses of Epsom salts thrice a day is a most effectual remedy for frontal headache when combined with constipation; but if the bowels are regular, the morbid processes on which it depends seem to be checked and the headache removed even more effectually by nitro-hydrochloric acid or alkalies given before meals. If the headache is immediately above the eyebrows, the acid is best; but if it is a little higher up, just where the hair begins, the alkalies appear to me to be more effectual. At the same time that the headache is removed, the feelings of sleepiness and weariness which frequently lead the patients to complain that they rise up more tired than they lay down, generally disappear.

Somewhat analogous to the neuralgia of the fifth nerve in Sir Charles Bell's case, or to frontal headache, is the pain which we frequently meet with in persons having decayed teeth. The pain may be felt in the offending tooth itself, but very often it seems to give little or no uneasiness. The patients complain of neuralgic pains above the ear or along the jaw, and will often deny that they have any decayed teeth at all. It would almost seem that neither the irritation in the tooth nor irritation in the intestine alone is sufficient to produce pain, though they do so when acting conjointly; for extraction of the tooth, or stoppage of the cavity with cotton-wool steeped in melted carbolic acid, will often remove the pain although no medicine is given internally, while on the other hand a brisk purgative may also afford relief though the tooth be left untouched. It is best, however, to combine both methods of treatment, and if the tooth is not extracted or stopped, the pain is very apt to return; and it seems to me probable, though I am by no means certain of it, that this recurrence is connected with the renewal of gastric or intestinal irritation. According to Heincken,[1] otalgia may also depend on the presence of irritating matters in the intestine; and Sir Charles Bell observes that accumulations in the colon

[1] Heincken, "De Morbis Nervorum ex Abdomine," quoted by Sir Charles Bell, op. cit., p. 9

will give rise to pains in the loins, spermatic cord, or groin. Pain at the lower angle of the scapula is referred by him to disorder and distension of the duodenum. This pain is very often accompanied by flatulence, and is described by patients as a "pain in the pit of the stomach, shooting through between the blade-bones," and it is not unfrequently termed by them "windy spasms." It is relieved by rhubarb and alkalies given before meals.

Having said so much regarding the fæcal contents of the intestine and their local and remote actions, we must now consider a matter of no less importance, viz., the effect of purgatives upon the secretions which are poured into the intestinal tube by the various glands connected with it. The saliva which flows into the mouth from the submaxillary and parotid glands is swallowed and aids the digestion of starchy food in the stomach, and probably the intestine. A part of its active principle, ptyalin, is reabsorbed, and some of it is excreted in the urine;[1] but as we shall here afterwards see, it is probable that another part is excreted again by the salivary glands and thus does its work twice over. This is at present only a probability as regards ptyalin, but it is a certainty in the case of several substances which are excreted by the salivary glands, such as iodide of potassium, for example, which can be detected with great ease. When this substance is swallowed, it is absorbed from the stomach, passes in the blood to the salivary glands, and is excreted by them much more readily than by the kidneys. It again passes down with the saliva to the stomach, is reabsorbed, and again excreted. Thus it may go round and round for a long time without getting entirely out of the body. (See gastro-salivary circulation, Fig. 2.) If we wish to remove it quickly and completely, we must give a purgative so as to prevent its reabsorption from the intestinal canal by causing its speedy expulsion. The same is the case with other iodides, such as those of lead or iron. Iodine has been shown by Bernard to possess the power of making iron pass readily through the salivary glands, the iodide of iron being found in the saliva soon after it has been injected into the blood, while other salts of iron, such as lactate, never make their

[1] Cohnheim, "Virchow's Archiv," xxviii. p. 250.

appearance in it at all.[1] Several years ago iodide of potassium was proposed by MM. Guillot and Melsens as a remedy in cases of lead-poisoning. The lead, they consider, is present in the body in the form of an insoluble compound[2] which it makes with

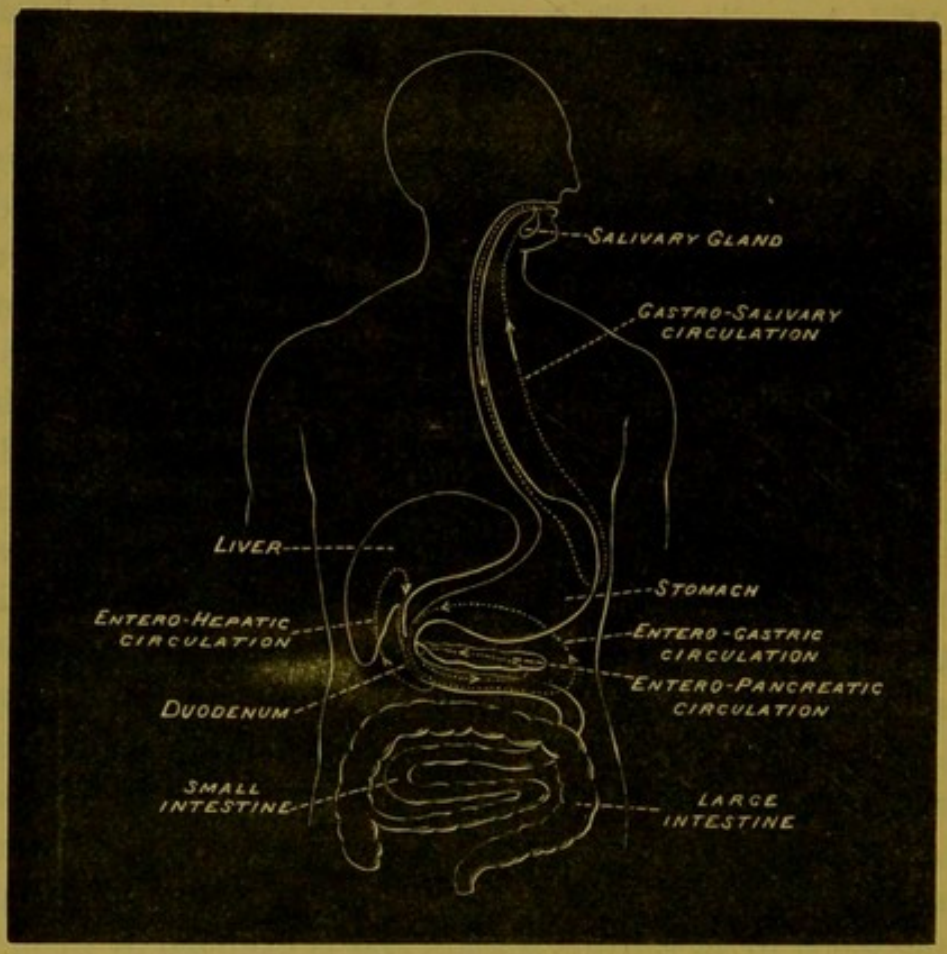

FIG. 2.—Diagram showing the manner in which substances are excreted by one organ and reabsorbed by another, so that they circulate a long while in the organism before being expelled.[3]

the tissues, but by the administration of iodide of potassium it is rendered soluble. It then finds its way into the circulation,

[1] "Bernard, "Physiologie Expérimentale," tom. ii. p. 99.

[2] Guillot and Melsens, "Archives Générales de Médecine," 4th sér. iv. p. 517; and Melsens, "Annales de Chimie," June 1849.

[3] The absorption of substances excreted by the salivary gland is indicated in the figure as taking place in the stomach, and their circulation is called gastro-salivary; but it is very probable that a considerable portion of them passes through the stomach into the intestines, and that *entero-salivary* might be a better term. Similarly, the absorption of bile has been represented as taking place in the duodenum, and that of pancreatic and gastric juices in the jejunum, but this is only to avoid confusion in the drawing, and not to indicate the part of the intestine where absorption really takes place.

and is excreted by the kidneys and other emunctories. But the iodide of lead is partly excreted by the salivary glands, for M. Malherbe, of Nantes, and Dr. Sieveking have found it in the saliva of persons suffering from lead-poisoning, and who were being treated by iodide of potassium. The lead salt being swallowed with the saliva, is again reabsorbed, and thus the cure is comparatively slow when patients are treated with iodide of potassium alone. I frequently see patients suffering from lead-poisoning brought on by working in white lead, and for some time I have been accustomed to treat them with five grains of iodide of potassium, three times a day, and a sufficient quantity of sulphate of magnesia or other purgative either thrice or once a day, to keep the bowels very freely open, and cause the expulsion of the lead from the alimentary canal as quickly as it is secreted into it. I have not made comparative experiments on the effect of this treatment and of that by iodide of potassium alone, or by purgatives alone, but from what I remember of cases treated by the late Professor Syme with castor-oil, I am fully satisfied with the treatment I now adopt. The same plan would probably prove equally useful in chronic poisoning by copper or mercury.

But the gastro-salivary circle, as we may term it, from stomach to salivary glands and from salivary glands to stomach again, is not the only one in which those metals move. Their circulation in the portal system, or entero-hepatic, as it is termed by Lussana,[1] is still more important. (See Fig. 2.) Iron is eliminated in great part by the bile: copper and manganese appear in it also, according to Albini and Moser,[2] and it seems probable that manganese, lead, and all the heavy metals pass out of the body by this channel. From the liver they pass into the intestine, are reabsorbed from it, and again pass to the liver and recommence their course. They may be present in considerable quantities in the blood of the portal system without reaching the general circulation or getting a chance of passing out in the urine. They are therefore much more closely locked up in the entero-hepatic circulation than in the gastro-salivary

[1] Lussana, "Lo Sperimentale," tom. xxix. 1872.

[2] Quevenne, Albini and Moser, quoted by Lussana, "Lo Sperimentale," tom. xix. 1872, pp. 340, 343.

one, for the salivary glands are supplied by the systemic circulation, and any blood which brings lead or any other substance to them must also carry it to the kidneys. The power of the entero-hepatic circulation to retain metals within the body being much greater than that of the gastro-salivary one, it is evident that the beneficial effects of purgatives in lead-poisoning are due to their removing the metal from the portal circulation still more than their action on the gastro-salivary one which has already been discussed. Other poisons, such as curare and probably serpent's venom, may also circulate in considerable quantity in the portal system without reaching the systemic circulation, and probably this is one of the causes, though by no means the only one, which renders these substances to a great extent innocuous when swallowed.[1]

But the circulation of iron, lead, curare, &c., in the portal system, important though it may be, is of far less interest than the circulation of the bile itself. For the sake of convenience I have merely stated that lead, mercury, &c., are excreted in the bile, and have hitherto assumed that bile circulates in a similar way in the portal system, without giving any reason for doing so.

It used to be thought by many that bile was formed in various parts of the body, and was simply excreted by the liver. This view is now given up by most physiologists, who believe that bile is formed by the liver only. But in altering their views regarding the function of this organ they went too far, and supposed that it only formed bile, which, when it had once found its way into the intestine and mixed with the intestinal contents, became decomposed and finally expelled with the fæces. A year or two ago, however, Schiff[2] found that this view of the hepatic functions was too limited, and that the liver removed bile from the blood or *excreted* it as well as formed or *secreted* it.[3] He observed that when all the bile was drawn away from the liver by means of a fistulous opening in the gall-bladder after ligature of the ductus choledochus, the quantity which flowed from the liver

[1] Lussana, op. cit.

[2] Schiff, "Pflüger's Archiv," 1870, p. 568.

[3] Although it is not correct to do so, I use the term "secreted" here as synonymous with "formed," for the sake of conveniently distinguishing between the formation of bile in the liver and its removal from the blood.

rapidly diminished after the fistula had been established, but could again be quickly increased by the simple process of putting bile into the duodenum. The bile was at once absorbed and again excreted by the liver, and it did not make much difference whether the bile just removed from the fistula in a dog was again injected into its duodenum, or whether ox bile was used instead. In the normal state of the animal the liver is always doing two things: it is *forming* new bile, and it is *excreting* old bile which it has received from the intestine by means of the portal vessels. When a biliary fistula is made and the bile is drawn away as fast as it is secreted, none gets into the intestine, and therefore no old bile reaches the liver; consequently, the quantity collected represents only the new bile formed in the liver, and is of course much less than that which would normally pass through the ductus choledochus into the intestine. If all the bile were absorbed there would be no need for the liver to go on forming it, but this is not the case, for only a part of it is reabsorbed, and the remainder is decomposed and excreted with the fæces.

So long as the liver does its duty properly, and excretes again all the bile which is absorbed by the portal blood from the intestine, very little bile can pass through the organ into the vena cava and thence into the general circulation. But whenever so much bile is taken up from the intestines that the liver cannot excrete it all, it will find its way out of the portal into the systemic circulation, and will exert an injurious action on the nervous system. The same effect will follow anything which diminishes the excreting power of the liver and renders it unable to excrete the normal amount. It is evident that if anything should cause the liver to form more bile than usual at any time, it will have extra work to do in the way of excreting it after its absorption, and there will be more bile circulating in the portal blood for some time afterwards, or at any rate until the extra quantity has been got rid of or compensation has been established by the liver forming less. Many experiments have shown that an abundant supply of food causes the liver to form more bile, and we all know that heavy dinners are apt to cause biliousness. Fasting, on the other hand, diminishes the quantity of bile secreted, and everyone knows that if he fasts for a day after taking an especially heavy dinner he may be none the worse

for it, but if he dines out every night he is almost sure to become bilious unless he takes measures to prevent it by using purgatives.

It has not yet been shown by direct experiment that the symptoms usually grouped under the head of "biliousness" are due to the presence of an excess of bile in the blood; but the rapidity with which they disappear after the removal of bile from the system, either by vomiting or purgation, renders it extremely probable. Frequently we find that the fit of vomiting which has expelled a quantity of bile is hardly over when the appetite returns, the brownish-white fur disappears from the tongue, the face loses its dingy hue, the languor disappears, the irritability of temper is replaced by equanimity, and stupidity and laziness give place to sprightliness and activity. But vomiting is a disagreeable process, and few submit willingly to it, although it would be well worth while if the same end could be gained by no other means. As most old practitioners have found, however, a mercurial pill and a saline purgative produce all the good effects of vomiting without its trouble and discomfort, and they have long been in the habit of ascribing the beneficial action of the mercury to its "cholagogue" properties. They felt convinced that biliousness was due to bile in the blood, and believed that its removal was due to the liver being stimulated by the mercury to excrete the bile more rapidly. But the careful experiments made by the Edinburgh Committee of the British Association[1] on dogs with biliary fistula showed that neither mercurials nor other purgatives increased the flow of bile from the liver, and these results seemed at first sight to contradict the views entertained by most practitioners regarding their cholagogue action. The contradiction is apparent, but not real, for in the experiments the bile was regularly removed from the body as soon as it was formed, and none of it ever reached the intestine. Consequently, any diminution in the quantity collected simply showed that the liver was forming less. Other experiments have given somewhat different results from those of the Edinburgh Committee, and Röhrig[2] has found that the administration of purgatives, as well as other measures which increase the circulation in the portal

[1] Report of the British Association, 1868, p. 214.

[2] Stricker's Medicinische Jahrbucher, 1873, p. 250.

system, augment the formation of bile. The important question in regard to the treatment of biliousness, however, is not whether the liver forms more or less new bile, but whether the bile already circulating in the blood is removed from it. The liver may be doing its best to effect this purpose, but it will not succeed if the bile it removes from the portal blood is again absorbed as quickly as it is poured into the intestine. But if the peristaltic action of the whole intestinal canal is quickened by a purgative, the bile will be hurried rapidly onwards and evacuated before there has been time for its reabsorption, and the liver being thus relieved will be able to excrete any bile still remaining in the blood. This result will not be effected by any purgative acting on the large intestine alone, for a considerable part of the bile will in all probability have been absorbed before it gets so far; but any simple purgative or mixture of purgatives which stimulates the duodenum and small intestine as well as the large one will prove most effectual. Now, the green colour which the fæces present after the administration of mercurials, and which is so distinctive that the name of "calomel stools" has been applied to them, has long been regarded as an evidence of bile and appealed to as a proof of the cholagogue action of these remedies. The opponents of this doctrine have declared that the colour was simply caused by the presence of black sulphide of mercury, just as a somewhat similar colour may be occasioned by the presence of a small quantity of sulphide of iron after the administration of mild ferruginous preparations. Their statement has been disproved by Buchheim, who has shown that the colour is really due to bile, and thus established the fact that calomel induces its expulsion from the intestine. It may therefore well be called a cholagogue, and it is evident from what has already been said that it must diminish the quantity circulating in the blood, whatever its effect may be on the amount formed by the liver.

Other substances besides bile are found in calomel stools, and among the most important of these are leucine and tyrosine. These bodies are produced by the action of pancreatic juice on albuminous substances, and their presence, which was discovered by Radziejewski, indicates that the contents of the duodenum and small intestine have been expelled before much absorption

has taken place. Now, the duodenum not only contains half-digested food and bile, but also the gastric and pancreatic juices and the ferments to which they owe their activity. It is generally taken for granted that after these ferments have once aided in digesting a meal they are destroyed or evacuated, and no importance, so far as I know, has ever been attached to their reabsorption. It appears from the experiments of Brücke, who found pepsin in the muscles,[1] that it is reabsorbed, at least in part, and is indeed excreted in the urine, as is also a diastatic ferment derived from the saliva or pancreas.[2] Pancreatic ferments also are probably absorbed, for Hüfner has found some possessing like them the properties of digesting fibrin as well as converting starch into sugar in the salivary glands and lungs.[3] If these ferments, then, are poured into the intestine and absorbed from it again in the same way as bile, it seems highly probable that they also are excreted by the same glands which formed them. (See entero-gastric and entero-pancreatic circulations, Fig. 2.) The function of the gastric follicles and pancreas would thus be a double one like that of the liver, and they would constantly excrete the ferments absorbed from the intestine and brought to them by the blood, as well as form new quantities of them to replace those which were carried off in the fæces or destroyed in the process of digestion. This view derives some probability from the observation of Schiff, that after the stomach has already digested a copious meal and become empty its power to digest albumen is almost entirely lost,[4] and the fact noticed by Bernard that when the pancreatic juice is drawn away by means of a fistula, what flows from the gland some time after the operation frequently does not possess the power of digesting albumen like the juice which has been collected immediately after the insertion of the cannula.[5] These facts have been explained in a different way by Schiff and Bernard, but it seems to me that the explanation just given supplements without excluding theirs, and clears up some points which they have not touched.

[1] Brucke, "Sitzungsbericht der Wiener Academie," 1861, xliii. pp. 622, 619.

[2] Cohnheim, "Virchow's Archiv," xxviii. p. 250.

[3] Hüfner, "Journal für practischen Chemie," vol. v. p. 372.

[4] Schiff, "Physiologie de la Digestion," tom. ii. p. 195.

[5] Bernard, "Physiologie Expérimentale," tom. ii. p. 229; compare also p. 223, where he states that the juice becomes watery towards the end of digestion.

There is this important difference between the glands just mentioned and the liver, viz., that the bile can circulate in the portal system between the liver and intestine without reaching the systemic circulation, but the gastric and pancreatic ferments absorbed from the intestine cannot reach the stomach and pancreas again without mixing with the general current and the blood, and being conveyed to other organs as well. Pepsin cannot act in an alkaline fluid like the blood, but pancreatic ferment can; and although I do not know that any experiments have been made with it, yet Binz and Siegen found that a ferment derived from the liver, and possessing like the pancreatic one a diastatic power, raised the temperature of an animal when injected into it.[1] This rise was due to its action as a ferment, and not to its mere presence in the blood as a foreign body, for it had no action whatever when it was injected after its fermentative power had been destroyed by boiling. It is therefore quite possible that the temperature of the body is normally maintained to some extent by means of the pancreatic ferments circulating in the blood, and if purgatives diminish its quantity in the way I have supposed they will tend to lower the temperature.

It must be remembered that these are only suppositions as yet, and require much further substantiation, but they help us at any rate to form some idea of the way in which purgatives prove useful when given at the commencement of a fever. They also give us some notion of the reason why persons so often take cold after the use of purgatives, and one of the dangers of their administration to old people, who produce little heat at any rate, and can only slowly form new supplies of any ferment once carried away.

It is possible that purgatives have an additional action in remittent and intermittent fevers due to malaria, and even in continued fevers due to other poisons. Lussana supposes that the malarious poison which certainly produces some of its most marked effects on the spleen and liver, circulates like other poisons in the portal circulation.[2] If this hypothesis be correct,

[1] Siegen, "Ueber die pharmacologischen Eigenschaften von Eucalyptus Globulus." Inaugural Dissertation. Bonn, 1873, pp. 32, 34.

[2] Lussana, op. cit. p. 358.

purgatives may be productive of benefit by removing part of the poison as well as by lessening the temperature.

The pancreatic and gastric ferments have a very positive and certain use in digesting food in the intestine, even should they not possess the hypothetical action in the blood to which I have just referred; and if they are usually absorbed and excreted again, a constant course of purgatives will seriously diminish their quantity. In consequence of this, the digestion of food will be carried on slowly and imperfectly, and the general health will suffer. But this will only be the case if purgatives are used which act on the whole of the bowels, for those which affect the large intestine only will interfere but slightly with the ferments, a considerable portion of which will probably have been absorbed before they get so far. We can thus perfectly understand how a constant course of blue pill[1] and black draught[2] may have most disastrous consequences, while an aloetic pill may be swallowed nightly for months together, without doing any appreciable harm.

The experiments of Moreau and Vulpian, as well as my own, show that a large quantity of fluid is drained away from the blood into the intestine by the action of purgatives, and we can thus readily understand their use in removing fluid in dropsies. The abstraction of so much fluid will tend to empty the blood-vessels, and at the same time the irritation caused by the purgative will attract a larger proportion of blood to the intestinal vessels, and thus still further lessen the blood-pressure in other parts of the body. The blood being no longer urged onward with the same force, the congestion in any inflamed part diminishes, and the painful throbbing which is felt at every pulsation when certain parts of the body are inflamed will be diminished, or may disappear, at least for a time. The diminished tension in the arteries which purgatives induce is clearly seen from the sphygmographic tracings on the opposite page, which I owe to the kindness of Mr. Mahomed.

When the kidney is the organ affected, the benefit afforded by purgatives will be twofold, for they both diminish the work it

[1] Prout, "Stomach and Renal Diseases," 5th ed., p. 52.

[2] Pancreatic ferment appears in the fæces after the use of senna. (Radziejewski, Reichert and Du Bois-Reymond's Archives, 1870, p. 72.)

has to do by eliminating water by the bowels, and at the same time lessen congestion, and thus remove an impediment to the proper performance of its function. Accordingly the administration of a purgative such as elaterium is found to lessen and sometimes to remove albumen from the urine, to render the secretion copious even when no diuretic has been given, and greatly to increase the activity of diuretics, which may have been unable to produce any action so long as the bowels were left alone.[1]

In conclusion I give a short *résumé* of the chief points in this paper. Purgatives act by stimulating the secretion of fluid

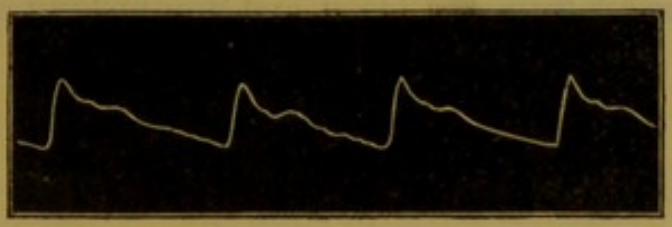

FIG. 3 is a sphygmographic tracing from the pulse of a healthy man before taking a purgative. The somewhat oblique rise, slow descent, and comparatively slight dichrotism of the pulse-wave indicate that the arterial tension is moderately high.

FIG. 4 is a tracing from the same person after the use of a purgative. The more abrupt rise and quicker fall, and decided dichrotism of the pulse-wave, as well as the greater frequency of the pulse, as indicated by the shortness of the waves, show that the tension in the arteries is much less than in Fig. 3.

from the intestines, as well as by increasing peristaltic action. They prove useful in many ways. They hurry the food out of the alimentary canal, and thus lessen the injurious effects of over-eating. By expelling irritating substances from the intestine they arrest diarrhœa, and remove headache and other pains, caused either by the abdominal irritation or by the absorption of poisonous matters produced by imperfect digestion and decompo-

[1] Geo. Johnson, *Brit. Med. Journal*, 1868, March 7, p. 215.

sition of food. They relieve biliousness by removing bile, and are most efficient aids in the treatment of chronic poisoning by lead, mercury, or other metals. It is probable that pepsin and pancreatic ferment are absorbed from the intestine and circulate in the blood, where the latter assists in the production of animal heat. They are then secreted anew by the stomach and pancreas, and do their work again. Purgatives lessen their quantity as well as that of the bile; and they thus be useful in fevers, but they injure old and feeble persons, both by diminishing their calorific power and impairing their digestion. They relieve inflammation by lowering the blood-pressure and thus diminishing congestion; and they prove beneficial in dropsies, both by abstracting water from the blood and diminishing congestion in the kidneys.

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