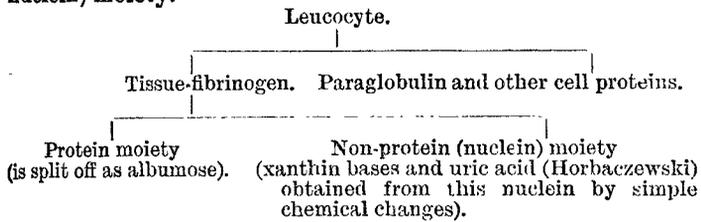


contains a protein (or albuminous) and a non-protein (or nuclein) moiety.



PHYSIOLOGICAL EFFECTS OF THE ADDITION OF TISSUE-FIBRINOGEN TO THE BLOOD.

1. *Immediate increase of coagulability* (Wooldridge's "positive phase of coagulability"). (a) Observed by Groth and Krüger after injections of leucocytes (intra-vascular coagulations produced). (b) Observed by Wooldridge after injection of solutions of tissue-fibrinogen (intra-vascular coagulations in portal area in the dog). (c) Observed by the author after injection of tissue-fibrinogen (intra-vascular coagulation in any vascular district where blood has been rendered adequately venous). (d) Probably comes under observation clinically in the increase of coagulability in the venous system in the resorption stage of pneumonia.

2. *Subsequent diminished coagulability* (Wooldridge's "negative phase of coagulability").—(a) Observed by Groth and Krüger after the injection of leucocytes; (b) observed by Wooldridge after tissue-fibrinogen injections, especially in the blood of the extra-portal vascular areas; (c) shown by author probably to depend upon the setting free of albumose or peptone by the disintegration of the tissue-fibrinogen in the blood; (d) no clinical record of occurrence.

3. *Excretion of albumoses or peptone in the urine* (referable to the protein constituent).—(a) Observed by the author after injection of tissue-fibrinogen solutions both in the dog and in the rabbit. (b) Observed clinically in connexion with the disintegration of leucocytes in pneumonia, pus-absorption, pyæmia, and proliferating tumours of bone marrow, &c.

4. *Increased excretion of uric acid* (referable to the nuclein constituent).—(a) Observed by Horbaczewski (in man and animals) after administration of nuclein prepared from the leucocytes of the spleen. (b) Shown by Horbaczewski to go hand in hand with every increase of leucocytes in the blood. (c) Comes under observation clinically in connexion with the increase of leucocytes in pneumonia (croupous) and leucocythæmia, burns, and scalds.

5. *Later occurring increased leucocytosis* (referable to the nuclein constituent).—(a) Observed by Groth two or three days after the injection of leucocytes; (b) observed by author after injections of tissue-fibrinogen; (c) observed by Horbaczewski after the administration of nuclein prepared from the leucocytes of the spleen; (d) possible connexion with immunity from anthrax obtained by tissue-fibrinogen; experiments with nuclein in progress.

I have not time here to go into the important issues which Horbaczewski's work opens up. I would merely point out that to the triad of symptoms which has been referred to in the body of this lecture we are now able to add two additional symptoms—namely, those that are enumerated on the table under headings 4 and 5. I would also point out that we find all the symptoms, 1, 2, 3, and 4, making their appearance in every ordinary case of croupous pneumonia, so that we may regard this disease as affording an almost classical instance of the effects of tissue-fibrinogen on the blood. The association of an increased uric acid excretion with peptonuria and with a more coagulable condition of the blood is not, however, limited to croupous pneumonia. It occurs also in connexion with, for instance, certain "rheumatic" or "gouty" conditions, and in connexion with burns and scalds. In the case of these last, we find thromboses in the portal area (leading to gastric and duodenal ulcers) associated with peptonuria and an increased uric acid excretion.

And now, in conclusion, I would desire to be allowed to express my very sincere thanks to the Councils of the Royal Colleges of Surgeons and Physicians, and more especially to the Laboratories Committee of the Conjoint Colleges, not only for their kindness in permitting me to work in their laboratories, but also for the very liberal manner in which I have been supplied with every appliance which was necessary for my work. Lastly, I feel that I have a debt of very special gratitude to discharge to Dr. Sims Woodhead for much unselfishly afforded assistance,

and, above all, for his continual gift of sympathetic interest in the work upon which I have been engaged. I believe that I am only expressing what is felt equally by every other worker in these laboratories when I say for myself that the help and sympathetic interest of such a director of studies as Dr. Woodhead have come to me as an especial and superadded stimulus to endeavour that the researches which emanate from these Laboratories may be such as to justify the labour and care and expense which have been involved in their establishment and maintenance.

THE THERAPEUTICS OF CERTAIN AILMENTS.

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CHLOROSIS.

THE leading symptoms of this affection, so often seen in young females at the age of puberty and from that period up to the eighteenth year, betoken an enfeebled circulation, which is dependent upon a marked deficiency of hæmoglobin, and to rectify this all authorities recommend the use of iron in large doses. But, as a rule, text-books do not descend to details as to the mode of administration. This is the important point, and to illustrate this I now give my experience of eighty cases, which during the last five years have come under my observation. I explain to the patient the object of the treatment by saying that her blood is thin, and that iron will alone do good, and that she must take it in a systematic manner. Her assent is gained by stating that if she acts as directed in less than a week there will be visible improvement of her health. This prognosis proves effectual, and she is told to take of pil. ferri or Blaud's pill three daily, and to go on increasing by one each day until fifteen at least are taken daily, and then to diminish the number by one daily. The time of taking them does not matter much, but it is better to swallow them at 9 A.M., 2 P.M., and 7 P.M. The tasteless character of the pills is mentioned, their non-aperient character explained, and in no case except one have I heard about any difficulty in swallowing them. Health is always restored in four weeks. The menses, if deficient or irregular, come on at the normal periods; but the patient should be told that the poverty of blood may return in the course of four or six months, and that it will be necessary, if this be so, to resume the treatment, beginning with the gradual increase mentioned, and going up to nine daily, and decrease by one daily. This number proves sufficient in the majority of cases, and, as a rule, there is no further relapse.

SEA-SICKNESS.

Some persons, unfortunately few in number, stand the sea well, and to them a voyage is from beginning to end a source of unmixed pleasure. Others stand it so badly that the prospect of a voyage is entertained with feelings of actual dread, or as a thing that must be endured. They expect to be sick, and this expectation is generally fulfilled. If we take a professional view of *mal de mer* we may say, more especially in relation to the treatment to be adopted, that there are two stages: first, pallor, nausea, vomiting, which is succeeded by a second stage, of exhaustion, retching, depression, and in many cases sleeplessness, or sleep not refreshing in its nature and attended by dreams of a painful character. The approach and duration of the first stage varies, but when begun it continues until the stomach is empty, and is succeeded by the second stage, which may be prolonged for a more or less indefinite period, in many cases extending even over the whole voyage. Various remedies have been advocated to avert the first stage—such as cocaine, antipyrin, nitrite of amyl, morphine, bismuth,—but at the present time it is generally conceded that no drug, or combination of drugs, cuts short an attack begun, or prevents its occurrence in those who are predisposed to it. Indeed, many believe that vomiting should be encouraged, by drinking warm water, so that the stomach may be sooner freed from its contents. In the second stage the remedies most relied upon are preparations of opium or morphine, hydrate of chloral, and bromide of potassium. Opium or

morphine, if retained, will cause sleep, but at the expense of awakening with severe headache and a lack of appetite. Hydrate of chloral is dangerous if it be given in a hypnotic dose of thirty grains, for in such a dose it markedly weakens the action of the heart and leads to great depression. Bromide of potassium is safe, and its utility is recognised. Dr. Lauder Brunton says that "in sea-sickness it is perhaps more useful than any other remedy." The great objection, however, to its use is its saline pungent taste, which renders it very objectionable when the stomach is irritated and weak, and leads to its almost immediate rejection. Besides, unless it be given in large doses, it exercises little influence on the system as a hypnotic. Yet undoubtedly the bromide contains properties which cannot be minimised, and the question is how can these properties be rendered more valuable? The answer will now be given: By bringing to its aid another drug—chloralamide—which within the last three years has become a favourite remedy in treating cases of insomnia, because it is a safe and reliable hypnotic. It is prepared by combining chloral with foramide, and is a colourless crystalline body, soluble in nine parts of water and one and a half parts of alcohol. It differs from hydrate of chloral in its less solubility and its non-toxic action. Chloral depresses the action of the heart; chloralamide does not, for in a dose of thirty grains it will cause sleep without any change in the circulatory or respiratory system. In a word, it possesses all the advantages and none of the disadvantages of chloral. It is prepared by E. Schering of Berlin, which firm has a world-wide reputation as the makers of pure and reliable chemical compounds. The combination, therefore, of these drugs—chloralamide and bromide of potassium—was much to be desired. It is, however, no easy matter to do this, at least in a palatable and presentable form, and requires the services of a skilled pharmacist. At my suggestion and after many trials, Messrs. Burgoyne, Barbidges, and Co., London, have succeeded in making a solution palatable and stable. It will suit the most fastidious taste, and the therapeutic influence of the two chief constituents is markedly aided by the addition of other adjuvants. Their preparation is known as "chlorobrom," an ounce of which contains thirty grains of chloralamide and thirty grains of bromide of potassium. In this dose, when given in cases of insomnia dependent upon nervous excitement or mental strain, sleep ensues in the course of half an hour, and lasts from six to eight hours. This sleep is most refreshing, and the awakening from it is attended by no headache, no thirst, and no depression. The patient rises as if from natural sleep, perfectly fitted to undertake the duties of daily life, and, so far as I have seen, the habit of taking it is not engendered. There is no desire for its further use except when the same condition of sleeplessness occurs. The physiological action of chlorobrom being thus potent and beneficial when administered to persons on land, it occurred to me that I would try it in cases of sea-sickness when opportunity offered. This I did in my autumn holiday, first to Norway, and then to the United States. I knew it would do good if it was retained by the stomach, and the question of giving it was narrowed down to this crucial point. It was with great satisfaction that I noted, in ten cases where I gave it after the first stage of active vomiting had ceased, that in each it was not rejected. To make assurance doubly sure, I gave samples of the solution to ship surgeons for trial, and requested them to give me their unbiased opinion as to its action. Their verdict is altogether confirmatory, as the reports which follow show. Given at the time mentioned, for this is the *sine quâ non* of its administration, it has been invariably successful. It has always been retained, and it has always done good. A lady to whom I gave it writes a graphic and telling description of her sensations when sick, and the manifest improvement which followed upon its use. "I was very restless and sleepless, indeed was unconscious of having slept any for two nights. After taking a tablespoonful I quickly fell asleep, slept the whole night, and awoke as refreshed as when sleep is natural. I took it a second time with the same result. My good health and appetite for the remainder of the voyage I attributed to those two nights' sound sleep. I had no return of *mal de mer*, nor even any of its sensations. During the homeward voyage I longed very much for a dose; had I got it after the first sickness had passed off I am quite sure I would have got all right. After sea-sickness one feels so worn out and restless; now the hypnotic, besides producing sleep, soothed one so

much that these feelings quite passed away. I certainly would not care to go another voyage without having it with me." I carefully watched its action in the case of a gentleman who, in a voyage from America in the autumn, shared a state cabin with me. On the morning of the first day after leaving port he became very sick, and continued so all day. In the evening he was very restless, and the retching was extreme. I gave him an ounce of the solution. He fell sound asleep in fifteen minutes, his breathing being easy and his pulse-rate normal. He awoke refreshed after eight hours' sleep, and continued well during the remainder of the voyage. Four ship surgeons, who have tried it, report as follows. Full reports of each case treated by these surgeons are in my possession, but their publication here would occupy too much space. Dr. Nevin, s.s. *Furnessia*, Atlantic Ocean, Sept. 13th, 1891, after giving it in three cases, says: "Its effect is instantaneous." Dr. Belcher, s.s. *Circassia*, after giving it in four cases, writes: "I have grave doubts if this solution would in any way check *mal de mer* in its first stage, but I feel confident it would assist and relieve, if not cut short, subsequent suffering if wisely used, more especially in those who have either debility or other troubles to battle with." Dr. Arthur Scott, Tilbury Docks, London, Dec. 18th, 1891, surgeon to s.s. *Clan Mackintosh*, on his return voyage from Calcutta, after giving it in ten cases, writes: "It appears to me to possess the inestimable advantage of being retained by the stomach, of ensuring sleep, and of leaving the patient free from headache." Dr. Andrew Wylie, s.s. *Hispania*, Port Said, Dec. 31st, 1891, after giving it in two cases reports: "Before the solution was taken everything was vomited, but the solution was not vomited, and small quantities of food taken afterwards were retained. It secured a sleep of eight hours, and the patients on awakening had good appetites, and declared they had never felt better in their lives." From my own observations, and from the conclusions of ship surgeons which have been given, I feel justified in saying that chlorobrom has the crowning advantage of being absolutely safe. It succeeds when other remedies fail; it secures by sleep the gastric and mental repose which nature craves for; it takes away all distress, all depression, and all the indescribable but terrible sensations of *mal de mer* in its second stage.

Dose.—In the case of females the dose is one tablespoonful; in males, one tablespoonful and a half. This solution has as yet only been tested in the second stage of sickness which is observed in a sea voyage lasting longer than twenty hours, but from its action I feel inclined to suggest its adoption as a prophylactic in short voyages—as across the Channel from Harwich to Rotterdam, or from Holyhead to Ireland. If so, these two rules should be followed out: 1. The passenger should prepare for the voyage by taking for two successive nights an antibilious pill which contains mercury and podophyllin. This stimulates the biliary secretion and its evacuation by the alimentary canal. 2. When on board, and if the passage be made by the night service, the passenger should avoid taking any food, but retire to the cabin, undress, lie down, and take an ounce dose of the solution. In all probability there would be a sleep so sound as to prevent any nausea or sickness, and on awakening land would be in sight.

INFLUENZA.

In my experience of this epidemic I have most faith in prescribing salicylate of sodium (pure) in twenty-grain doses every four hours for twenty-four hours. Copious perspiration follows, and the distressing features of the affection disappear, if there be no complications; but if these be present the salicylate should be abandoned, and therapeutic measures adopted according to the extent and gravity of the case. In ordinary cases, after discontinuing the salicylate, I prescribe for a week four grains of quinine in half a glass of sherry at 11 A.M., and the same quantity of quinine in a whole glass of sherry at 4 P.M. The patient should not go out of his bedroom until the expiration of at least ten days. In cases where the nervous depression is marked even after recovery, it is advisable to order the patient to go for a change to a bracing health resort or to take a short sea voyage.

PHTHISIS.

Repeated testimony has been borne by almost every observer to the undoubted efficacy of cod-liver oil and the hypophosphite of lime in the early stage of phthisis. The

former gives nourishment to the body, and the latter exercises an alterative influence upon the process of tubercular change. Yet cod-liver oil should not be given by routine, but with definite rules as to its administration. To secure proper assimilation it should be prescribed in a teaspoonful dose at bedtime for three successive nights, then a dessert-spoonful at the same time. On the sixth and seventh days it should be taken in a dessert-spoonful dose after dinner and at bedtime, and afterwards in a table-spoonful dose after each meal. If so prescribed it does not cause eructation or nausea, and the doses may be increased in accordance with the wishes of the patient until the end of the fifth week, when it should be stopped for a week, and resumed. With each dose of the oil five grains of hypophosphite of lime dissolved in a little hot water should be taken. Thus administered, these medicines notably increase the strength of the patient, and returning health is evidenced by increased weight. If circumstances permit, and if the patient be young, a sea voyage is of inestimable advantage in maintaining the progress made to recovery, and if the voyage be to New Zealand and back in many cases the patient's health is established. I firmly believe that the hypophosphite of lime is the only form of hypophosphite of any value in tubercular disease. This opinion was expressed by me in communications to THE LANCET in 1876, when this salt was first introduced to the profession as an efficient therapeutic agent. All my subsequent experience confirms this view, and I do not consider its influence is increased by its combination with the sodium and iron salts.

CHRONIC CONSTIPATION.

Most purgative medicines, if used for any length of time, require their doses to be increased, and the habit of employing them is engendered. Cascara sagrada, on the other hand, can be prescribed with advantage in diminishing doses, and in time can be omitted altogether. Thus, a teaspoonful of the liquid extract, if given at bedtime, will cause action of the bowels after breakfast, which is accompanied by no griping and no intestinal uneasiness. The next night the dose should be fifty minims, the next forty, the next thirty, the next twenty, and afterwards a ten-minim dose should be taken for eight successive nights. As a rule it may then be discontinued, as the action of the bowels comes on in a natural manner at the same hour of the day.

ANGINA PECTORIS.

In this affection there is little doubt of the benefit of the inhalation of the nitrite of amyl or of the taking of nitro-glycerine—the latter being preferable for continued treatment. As illustrating this I shall give a short account of a case which came under my observation three years ago. I was called to see a man aged forty-five, whose condition was very pitiable. He was lying propped-up in bed, and complained of difficulty of breathing and intense cardiac pain. I prescribed a hydragogue cathartic, consisting of three grains of calomel and a quarter of a grain of podophyllin, and told him after the medicine had acted to take a tablet of nitro-glycerine twice daily. In the course of two days I saw him again, and found him much better. He has continued under my observation more or less since I saw him first, and can attend to his daily duties as a time-keeper in a large public work. The difficulty he experienced in walking with any ease has diminished by adopting a certain procedure in taking the tablets. His own words are: "There is a remarkable improvement in my health with regard to walking, and all through the tablets. By putting one in my mouth previously to starting to my work in the morning, I am able to walk at my ease to the gate-house without halting. Previously to doing this I had to halt, until the pain ceased, from three to five times, and such has been the case for over two years; I can now walk the distance in less than five minutes, and I have known it to take me twenty. I can now walk from my house to the tram-car without a halt, when it usually took me from five to seven stops." Glasgow.

MUNIFICENT GIFT.—Mr. E. A. Pearn of Compton Leigh, near Plymouth, has given a mansion and twenty-four acres of land for the benefit of the Royal Albert Hospital, Devonport, and the South Devon and East Cornwall Hospital, Plymouth. On the land he purposes to erect a convalescent home, and will endow it for the joint use of the two institutions named. The gift has been gratefully accepted.

DISEASE OF THE TEMPORAL BONE.¹

By A. J. PEPPER, F.R.C.S. ENG.,
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IF I were asked to mention the surgical diseases in which preventable deaths are most common I should cite strangulated hernia, perforation of the vermiform appendix, and suppuration in the mastoid cells. No doubt the majority of cases of inflammation of the middle ear and the surrounding bone tend to spontaneous cure, or at least to such amelioration as to place the sufferers apparently out of danger. I say apparently, because so long as a perforation of the tympanic membrane remains with discharge, however slight, whether continuous or intermittent, there is an abiding cause of a possible fatal issue. How often do we meet with instances of ear disease in which, perhaps, years have intervened between the initial attack and the subsequent accession of acute symptoms—a renewal of the storm with its attendant threatenings. But there is another reason for the delay or neglect, as the case may be, in resorting to early operative interference. I refer to the regional anatomy of the parts affected. The close juxtaposition of the brain, the lateral sinus, and the carotid artery to the area of primary mischief has undoubtedly led the practitioner too often to defer or abandon the only treatment likely to be of the least avail. I cannot too strongly insist that such a reason implied or expressed is wholly untenable, that, in short, patients ought not to be left to a chance recovery when they can almost to a certainty be placed in security so far as life is concerned. The beneficial results offered by operation are not confined to cases where the disease is limited to the middle ear and mastoid cells, for on several occasions consecutive abscess in the brain has been successfully treated.

As regards the causes of inflammation of the petro-mastoid bone, it may be said that with few exceptions the affection is secondary to disease of the middle ear. Primary tubercular caries is comparatively rare, whilst syphilitic caries is much more so. Otitis media is usually the result of (1) some exanthematous fever, notably, scarlatina and measles; (2) disease of the naso-pharynx, such as ulceration and adenoid growths (here the morbid change is due either to the inflammation spreading in the continuity of the mucous membrane of the Eustachian tube, or to obstruction to the escape of secretion from the tympanum); (3) exposure to cold. I will not weary the reader with detailing the sequence of events, which ends in the petro-mastoid bone being involved, but at once proceed to discuss the latter condition, its features, phases, consequences, and appropriate treatment. According to Gruber the various parts of the temporal bone are attacked in the following order of frequency:—1. The mastoid cells. 2. The roof of the tympanic cavity. Here the principal danger to be feared is extension of the disease to the middle fossa of the skull, with meningitis and abscess of the temporo-sphenoidal lobe of the brain as natural consequences. 3. The posterior wall of the meatus. In this case an abscess may form between the bone and the external ear simulating true mastoid abscess. 4. The plate of bone separating the mastoid cells from the lateral sinus, in which thrombosis of the sinus and cerebellar abscess are events to be feared. 5. The floor of the tympanum and posterior wall of the carotid canal. Coagulation in the vein and hæmorrhage from the artery are possible sequelæ. 6. The petrous portion proper involving destruction of the labyrinth.

The above division is rather of pathological interest than clinical significance, for the disease is but seldom limited to the area first involved. I think it may be fairly said that few patients the subjects of chronic mastoid suppuration would lose their lives if the treatment were carried out on rational surgical lines, for even in the worst cases—providing of course that intra-cranial mischief and pyæmia have not commenced—a wide opening and free excavation of the bone by relieving tension and affording a ready escape for discharge are rapidly and surely followed by marked relief from symptoms which disquiet the surgeon and distress the patient. As regards acute cases, where dangerous and too often fatal symptoms supervene closely on abscess formation in the middle ear, there is less time in which to act, for

¹ A paper read at the Harveian Society, Feb. 18th, 1892.