in this case with an example of "true" intestinal sand as distinguished from the "false" sand which owes its origin to undigested vegetable particles, occasionally coated with earthy salts. Pears, figs, and bananas are apparently specially liable to produce this "false" variety, which was, I believe, first described in England by Professor Delépine at a meeting of the Pathological Society of London in 1890. One of the most recent, as well as one of the best, papers on the subject is one by Sir Dyce Duckworth and Dr. A. E. Garrod, published in the *Medico-Chirurgical Transactions*, 1901, to which is appended a bibliography.

The case now recorded agrees with M. Dieulafoy's series in having occurred in a gouty middle-aged woman (about two-thirds of the cases are women of about 35 years of age) and as regards the history of concurrent muco-colitis. The absence of painful paroxysms, vomiting, and flatulence is interesting, as in most recorded cases these symptoms have been marked. The albuminuria (with granular casts and uric acid) was also apparently a gouty manifestation in this case.

In the discussion which followed Duckworth and Garrod's paper, Dr. A. Crombie, late of Calcutta, expressed the opinion that the affection must be commoner in India than in England, and he mentioned the fact that in ten years' experience at the Presidency General Hospital, Calcutta, he had met with three cases all accompanied by severe colic, which varied directly with the quantity of sand passed. It is to be regretted that there is nothing to show that these cases were examples of "true" intestinal sand, or "enteric lithiasis" as the condition has been termed; for in the "false" cases colicky pain, varying directly with the amount of sand passed, is also a prominent symptom, and there is no mention of any other circumstance which would guide us to a knowledge of the true nature of Dr. Crombie's cases, as there apparently was no chemico-microscopical examination made in any of them.

The Cause of True Intestinal Sand.

The large amount of lime salts present is especially noteworthy. Bunge has pointed out that the proportion of lime present in milk even exceeds that to be found in an equal bulk of lime water. Hence in cases which have been for long on an almost exclusively milk diet, the source of the large proportion of lime salts present in true intestinal sand is to some extent explained. The intestine is, moreover, now known to be one of the main channels for the excretion of calcium salts from the system. And the so-called "chalk-stone" deposits present in gout contain in addition to their principal constituent (sodium urate) varying proportions of the phosphates and urate of calcium. As true intestinal sand appears to be closely associated with gout, and has not apparently been observed in non-gouty patients who have been placed for long periods on a milk diet, one is inclined to regard the condition as allied in some manner to the "tophaceous" deposits in other parts. But how are we to explain the absence from the sand of uric acid and its compounds which so characterize these gouty deposits in other parts of the body? It is easy to conjecture that the inorganic constituents of the sand are derivable from the milk diet and by excretion into the bowel from the system; and that, on the other hand, uric acid and its compounds are excreted by the kidneys, and to a small extent by the skin, and separate out in those tissues in which the blood supply would appear to have a greater opportunity of depositing them than would be the case in the intestine. Sluggish action of the bowels is alleged as a cause of intestinal concretions, but this can only be a predisposing circumstance. For the milk diet and the sluggish state of the bowels do not alone appear to be able to bring about the condition of true intestinal sand. All, then, that we can at present say is that the condition would appear to be closely related to gout and to be favoured by a milk diet.

THE TECHNICAL EDUCATION OF PLUMBERS.—A class will be held at the King's College, London, during August and September, 1903, for teachers of plumbing and for training advanced students as teachers. The subjects of the course will be chemistry, physics, sanitation, and advanced plumbing work. Classes on theoretical and practical plumbing will be carried on at nine centres in Lancashire under the auspices of the County Councils and the Worshipful Company of Plumbers.

The Croonian Lectures

ON THE

NATURAL HISTORY AND PATHOLOGY OF PNEUMONIA.

By THE LATE J. W. WASHBOURN, C.M.G., M.D., F.R.C.P.,
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Delivered at the Royal College of Physicians, London, by
W. HALE WHITE, M.D., F.R.C.P., and edited by
J. W. H. EYRE, M.D., etc.

LECTURE IV.—[ABSTRACT.]

[AFTER directing attention to the chief points in the anatomy of the respiratory tract, the lecturer continued:]

INHALATION OF FINE PARTICLES.

In ordinary respiration about 450 c.cm. of air are taken in and given out at each respiration: after a normal expiration succeeding a normal inspiration, 2,500 c.cm. stationary air remain in the lungs. Consequently only a small proportion of the total air in the lungs passes in from the atmosphere at each inspiration, and it is concluded that the tidal air does not reach the alveoli, fresh oxygen reaching the alveoli chiefly by diffusion. Some of the tidal air goes direct into the alveoli, for Zuntz and Loewy have shown that the capacity of the upper air spaces and the bronchial tree to the infundibula is only 140 c.cm., that is, about a third of the amount of the tidal air. During abnormal inspiration, as in coughing, still more of the tidal air passes directly into the alveoli.

The air we breathe contains many fine particles, both living, such as bacteria, and dead, such as soot particles, the majority of which are entangled in the mucus of the respiratory tract and are conveyed upwards by the ciliated epithelium. In the experiments conducted by Dr. Pembrey and myself we always found numerous particles entangled in the mucus from the nose right down to the smaller bronchi, chiefly, however, in the upper part of the respiratory tract. When the period of inhalation was very short, the mucous membrane of the turbinates appeared to act as a most effective filter. This filtering of the inspired air was noted by Tindall, who found that the latter part of the expired air was optically pure.

Haldane¹ found that the air in a room contained fewer bacteria after it had been occupied by a number of individuals than before, the bacteria having been filtered off during the process of respiration. Straus² counted the number of bacteria in inspired and expired air, and found that in one experiment the inspired air contained 20,700 bacteria in the cubic metre, while the expired air only contained 40. Some particles, however, from time to time reach the alveoli, and we shall have to consider what happens to them there, for this has an important bearing upon the question of infection through the lungs.

ABSORPTION OF FLUIDS.

Fluids when injected into the trachea are rapidly absorbed. Peiper³ found that 20 to 25 c.cm. of distilled water could be injected into the trachea of a rabbit without even causing dyspnoea. A dog received 250 c.cm. of water in one hour, in doses of 30 to 50 c.cm., without noticeable effect, while strychnine when injected into the trachea produced tetanic symptoms within 80 seconds. Sehrwald⁴ found that sticky fluids only reach as far as the bronchi and were more slowly absorbed.

ABSORPTION OF PARTICLES SUSPENDED IN FLUIDS.

Still more remarkable were the experiments of Nothnagel,⁵ who killed animals by cutting through the trachea and large vessels and allowed the blood to pass into the trachea. On examining the lungs he found that the alveoli were filled with blood which had also passed through the alveoli into the lymphatics in the interalveolar and interlobular connective tissue, even in the three and a-half to five minutes that elapsed between the operation and the immersion of the lungs in alcohol.

Fléiner⁶ repeated and confirmed these experiments, and stated that absorption took place entirely through the alveoli,

none occurring through the mucous membrane of the trachea or bronchi.

According to these experiments, it is the easiest matter for particles which reach the alveoli of the lung to pass into its parenchyma, and thence to pass into the bronchial glands, there being no defence against the invasion of the lungs when the particles have once reached the alveoli. Pembrey and I repeated these experiments in the following way, using rabbits in both sets of experiments. For the blood inhalation the trachea and large vessels were cut at the same time, and by a little manipulation the blood as it flowed from the vessels was aspirated by the inspiratory movements into the trachea and lungs. For the Indian ink inhalations the rabbit was anaesthetised, and a cannula placed in the trachea. The carotids were cut, care being taken that no blood should get into the trachea. At the same time an emulsion of Indian ink was passed into the trachea. The loss of blood in each case caused deep inspiratory efforts, and the animal died in a minute or two. The lungs and bronchial glands were immediately removed, hardened in alcohol, and sections made.

In the case of blood inhalation we found that portions of the lung were solid, and of a bright red colour from the aspirated blood, contrasting with the pallor of the rest of the lung. The solid portions depended upon the position of the animal during the experiment; when the animal was in the supine position the posterior border was chiefly affected; when in the prone position the lungs were affected in patches, the posterior borders not being especially affected; and when in a vertical position with the feet down the bases of the lungs were especially affected.

Microscopical examination showed that the alveoli were filled with blood, but it was difficult to say whether the blood had penetrated the alveolar walls for two reasons. First, it is not easy to say whether blood in the walls of the alveoli is in the pulmonary capillaries or outside them. Secondly, in many cases the walls of the alveoli were so compressed by the blood in the alveoli as to render them very narrow. However, we believe that blood had penetrated into the walls. Sometimes we found blood in the periarterial lymphatics, but these were never so distended as to render the matter very obvious.

On examining the bronchial glands there was clearly blood in the lymph spaces, but on examining the bronchial glands of normal rabbits we found a similar condition, and we concluded that the bronchial glands of rabbits are mixed lymph and haemolymph glands, such as have been described by Leydig, Gibber, Robertson, Clarkson, Vincent, Harrison, and Warthin,* and we consequently believe that Nothnagel's experiments are not of the importance which they at first appeared to be.

In the Indian ink experiments it was seen microscopically that the particles had penetrated the walls of the alveoli, where they were found lying in the lymph spaces. Some were enclosed in large cells similar to the "dust cells" but the majority were free. There was no evidence of absorption through the bronchi. An interesting point in our experiments is the taking up of the particles by the cells in the few minutes which elapsed after the injection.*

In the bronchial glands the Indian ink had penetrated, as was apparent on opening the chest. However, we found that the lining membrane of the pulmonary veins and the left auricle was stained with the dye, showing that a rupture of the vessels had occurred during the convulsions, which observation was also confirmed by a microscopical examination of the lung.

We will next consider what happens to the particles which have been inhaled.

INHALATION OF FINE PARTICLES.

A large number of experiments have been made as to the fate of fine particles suspended in the inhaled air, Arnold⁹ perhaps being the investigator who has made the most extensive experiments. As a result of these experiments it has been definitely established that after prolonged inhalation of air heavily laden with fine particles the latter are found in the peribronchial and perivascular lymphatics, in

the adenoid tissue of the lung in connexion with these lymphatics, and in the bronchial glands.

The point most in dispute is the exact mode by which the particles enter. Another question of even more importance from the point of view of pathology is how far the mechanism of the lung facilitates or hinders the entrance of particles from the alveoli or tubes into the lung. The bulk of evidence is strongly in favour of the view that no absorption of particles takes place through the mucous membrane of the trachea or bronchi. On examining the mucous membrane very carefully Arnold found no particles in its walls except in cases of very prolonged inhalation, and they were then found, especially in parts where lymphoid tissue existed, and it is probable that the particles were being excreted into the bronchus and not in process of absorption.

Aufrecht opposes this view, pointing out that in all the experiments the size of the particles which are found in the tissue of the lung has not been noticed in explaining how these particles have gained entrance, and states that sometimes particles of dust are found in the tissue of the lung larger than the size of the alveoli. In an experiment of injecting Thoma's *Phosphatmehl* into the trachea of a rabbit the animal was killed four days after; large particles were found in the bronchial wall and in the peribronchial tissue. He considered that the particles had passed through the wall of the bronchi, because he found splitting of the muscular tissue.

All observers agree that the particles found in the lung after inhalation, whether in the lumen of the alveoli or in the lymph spaces and lymph vessels, are partly free and partly enclosed in cells, and there is a general agreement that at an early stage of inhalation the majority of the particles, whether in the lumen of the alveoli or in the lymphatic spaces and vessels, are free, while at a later period many of the particles are enclosed in cells—the so-called "dust cells." We shall now have to consider the origin of these cells and their functions. In the lumen of the alveoli after inhalation most observers agree that two kinds of cells containing particles are found. The one is a small round cell with a round nucleus, which is sometimes tattered or in process of being "cut off," fragmented and with a small amount of granular protoplasm, and the other is a large cell with an oval vesicular nucleus and a finely granular protoplasm.

The walls of the alveoli are lined, as we have already stated, with two kinds of cells, the one being a large flattened cell, and the other a small cell with granular protoplasm. At first sight it would appear that these two kinds of "dust cells" represent shed alveolar cells, and this, indeed, is the view that has been taken by some. Others hold that the small cells are leucocytes, while Tchistovitch considers that both are derived from wandering cells, the smaller being microphages and the larger macrophages.

Slaviansky,⁸ by injecting different coloured particles into the trachea and veins, found both in the cells in the lumen of the alveoli. Tchistovitch, by injecting carmine into the veins, found twenty-four hours later leucocytes and large epithelioid cells containing carmine in the alveoli. Aufrecht states that the "dust cells" are always derived from alveolar epithelium, and that in no case has he seen particles of dust in white blood corpuscles.

Whatever be the source of these cells, one of their functions is to pick up fine particles from the alveoli and to carry them along the bronchi and trachea, to be expelled with the sputum. All observers have noted the presence of cells containing particles in the mucus of the trachea and bronchi after inhalation.

The cells also take up particles after they have penetrated into the tissue of the lung. In the peribronchial and perivascular lymphatics, according to Arnold, the particles are chiefly free, while in the peribronchial and perivascular lymphoid nodules they are all enclosed in cells.

Tchistovitch¹⁰ has developed the theory of phagocytes to the absorption of particles by the cells. In his experiments he used newly-born guinea-pigs, to avoid confusion with soot particles which may have been derived from soot accidentally inhaled previous to the experiment. He exposed the animals to inhalation of soot for a couple of hours, and killed them either immediately afterwards or at varying periods later. He states that the soot was first found lining

* A joint paper by Washbourn and Pembrey upon the results of these experiments is in course of preparation.

the walls of the alveoli, but that there was never any evidence of absorption by the alveolar walls. Indeed, he states that the alveolar cells in the newly-born guinea-pig are non-nucleated, and that the nuclei which are visible on the alveolar wall belong to the endothelium of blood vessels and to the cells of the connective tissue. He says that the small nucleated cells in the alveolar walls are practically absent. The particles, however, are taken up after a few hours, both in the alveoli and in the lymph spaces, by phagocytes. In opposition to Arnold, he states that the first cells to take up particles are lymphocytes, small macrophages, and polynuclear cells, and that at a later period come the epithelioid macrophages, which resemble alveolar epithelium, but which are derived from the endothelium of the blood vessels and lymphatics. He says that in the blood vessels there were also a large number of similar polynuclear leucocytes, lymphocytes, and macrophages.

PASSAGE FROM LUNG TO PLEURA.

The older observers noted from time to time the presence of inhaled particles in the parietal pleura. Von Knauff, for instance, refers to the presence of particles in the adenoid tissue of the pleura mediastinalis. The lymphatics of the pulmonary pleura, too, are filled with particles after prolonged inhalation, these particles being derived from the superficial alveoli. Grawitz, by blowing fine particles of dust, etc., into the trachea of rabbits, found isolated particles in the costal pleura after twenty-four hours. Aufrecht repeated this experiment, using an emulsion of cinnabar. Fleiner injected Indian ink into the pleural cavity, and found (after an interval of from five to forty-five minutes), that the corpuscles were taken up by the pleura costalis and the pleura mediastinalis, but not by the pleura pulmonalis. The absorption is dependent upon the normal respiratory movements, for by producing a pneumothorax absorption is prevented. The particles then pass partly into the lymph glands at the back of the chest (intercostal glands), and partly into the glands along the internal mammary artery, behind the manubrium sterni, and in front of the trachea. The supraclavicular glands are also found filled with Indian ink.

In the pleura there appears to be a natural passage of lymph from the cavity to the parietal pleura, and any particles which should pass through the pulmonary pleura into the cavity are absorbed by the parietal pleura and taken to the glands. There would also appear to be a passage, though not an easy one, from the superficial alveoli of the lung to the pleural cavity through the lymphatics of the pulmonary pleura.

Pembrey and I have made a number of experiments in this connexion, using soot, cinnabar, and emery powder, and experimenting upon 14 rabbits. The experimental animal was placed in an airtight chamber, to which was connected a special arrangement for the delivery of soot particles. By a slight modification of the apparatus we were able to use heavy particles, such as cinnabar and emery. The inhalation lasted three-quarters of an hour, and the animal was killed at varying periods. Some were killed by a blow at the back of the head immediately after the experiment, others twelve hours later, and others at the end of a week. The trachea was immediately ligatured, the thorax opened, a cannula was passed into the pulmonary artery, the blood washed out with a saline solution at a temperature of 37° to 38°, and a picro-sublimate solution was then injected. The object of this procedure was to fix the alveoli in a condition of distension without disturbing their contents. The lungs and heart were then placed in picro-sublimate solution and hardened in the usual way.

In all cases the air which was breathed by the animals was heavily laden with particles, and the animals on removal from the chamber were completely black, red, or brown, according to the nature of the inhalation, and in all the animals which were killed at an early period the respiratory tract from the nose downwards was lined with particles.

With regard to the soot inhalations, we found by making control observations that great care had to be exercised in drawing conclusions, inasmuch as the ordinary laboratory rabbits frequently had a large number of cells filled with soot in their lungs. In the conclusions which we have drawn we have made every allowance for this fact. We have, more-

over, made control experiments upon newly-born guinea-pigs.

The two chief lines of defence against the entrance of particles into the lungs are the nose and larynx; the mucus over the turbinate bones retains an enormous amount of dust; animals upon which tracheotomy has been performed are therefore in an unfavourable condition, and exact conclusions cannot be drawn from experiments made upon them. Violent respiratory movements facilitate the entrance of particles into the lungs, and easily lead to rupture of minute blood vessels in the lungs. Small areas of collapse are frequently seen in the lungs of animals which have inhaled soot or dust. Particles getting into the alveoli are then got rid of in the following manner:

Some pass through into the lymphatics, and either reach the bronchial glands, where they are retained, or are retained in the adenoid tissues (peribronchial and perivascular), and thence may be excreted to the bronchi by means of cells; whilst some are taken up by cells and thus passed into the bronchi, and are ultimately extruded through the upper air passages.

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MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

THE TREATMENT OF AGUE BY INTRAMUSCULAR INJECTION OF QUININE.

PRACTITIONERS who have had experience of the treatment of malaria by both intramuscular and hypodermic injections of quinine solution will scarcely endorse Colonel Smyth's condemnation of the intramuscular method and his preference for the hypodermic. The latter injections are often very painful, and may give rise to tender swellings (notwithstanding gentle friction) which are persistent and which may break down and form abscesses. Hypodermic injection into the forearm may cause a paralysis of one or more fingers, which does not pass off for some time.

On the other hand, intragluteal injections are practically painless and the swellings soon disappear, while their effect on the fever is fully as favourable and rapid as in the case of the hypodermic method. In one patient I injected 5 gr. to 10 gr. of quinine twice a day for six weeks into the gluteal muscles without a bad effect of any kind, and with most satisfactory results on his fever. In the practice of a tropical hospital under my direction, in which cases of pernicious malaria were numerous, we abandoned the hypodermic method for the intragluteal with the happiest results.

Of course, the strictest antiseptic precautions must be used, or abscess will follow. A sterilizable serum syringe should be used, which should be sterilized after each injection. The skin should be cleansed with turpentine and spirit, and 5 gr. to 10 gr. of the acid quinine hydrochlorate dissolved in a drachm or less of water, and boiled. The syringe, which before use is washed out with hot water, takes the solution up while hot, and injects it deeply into the gluteal muscles. Finally, the puncture is sealed with collodion, and friction is employed to diffuse the solution. Although this method is invaluable in severe cases, most people during an ordinary attack of fever would prefer to take their quinine by the mouth.

Bexhill.

A. G. WELSFORD, M.D., F.R.C.S.

In the BRITISH MEDICAL JOURNAL of November 15th Lieutenant-Colonel John Smyth, A.M.S., remarks on the above treatment of ague that a recent writer "seems under the impression that he is more or less the inventor of the method, and is not sure whether it should not go by his name."

In the *Medical Times and Gazette* of July 10th, 1876, will be