Experimenting with rubber it is not difficult to record rough agreement with theory, but precisely regular results are difficult to obtain. This is due to several disturbing agents, such as departure from Hooke's law, and the fact that in stretched rubber, as in many other materials, the tension diminishes with time, and at a rate which bears no simple relation to other conditions.

Application to Physiology.

The complex problems presented by the dynamics of curved muscular sheets will not be attempted here; it is intended to leave unobscured certain physical principles which must be included, explicitly or implicitly, in any exact consideration of the subject. A few notes only are added further to clear the ground.

It is frequently assumed that all solids follow Hooke's law sufficiently nearly for any practical purpose. I have made a long series of experiments on animal tissues and have found that they all deviate sensibly from Hooke's law, and that many deviate widely. Nor would a definition of "solids" which excluded animal tissues set the matter right. Hooke's law can only be assumed in physiology as a means to a first approximation.

The heart is the most interesting field for the application of these principles, but the bladder is more suitable. The left ventricle is usually said to contain about 100 c.cm. of blood at the beginning of systole, and to discharge about 60 c.cm. during its contraction; if it were spherical its internal radius would be roughly 2.9 cm. at the beginning of systole, and 2.1 cm. at the end. The radius of the bladder is subject to immensely greater variations. The bladder is also thin-walled, nearly spherical, and its pressure is more easily determined than that of the heart.

Everyday experience provides data of considerable interest. Other things being equal, the trajectory of a stream of liquid projected into free air varies with the velocity of outflow, and the velocity is proportional to the square root of the pressure at the opening of the reservoir. After the beginning of micturition, and independently of the abdominal musculature, the trajectory remains nearly constant for some time, and then shortens towards the end, showing that for the first half or so of micturition the pressure in the bladder is nearly constant. Tension and radius must decrease together, although the muscular wall is thickening as the bladder contracts, and it might therefore be expected to exert greater pressure.

Summary.

1. The pressure exerted by any structure comparable to a stretched membrane is dependent on its curvature.
2. The pressure within a cylindrical and a spherical membrane is $\frac{t}{r}$ and $\frac{2t}{r}$ respectively, where r is the radius of curvature and t is the tension.
3. With rubber-like materials, as a curved membrane is progressively distended, the pressure rises rapidly at first, then more and more slowly as it approaches a limiting value.
4. Such materials are only a rough guide to the behaviour of membranes made of muscle and other animal materials.
5. In any exact consideration of the mechanics of vessels and of hollow viscera the curvature of the wall must be taken into account.
6. When such allowance is made, purely physiological effects will be more clearly visible.

Note.—Since the above was written Dr. J. R. Gillespie of Belfast has pointed out the application of these principles in the study of the capillary circulation (BRITISH MEDICAL JOURNAL, 1921, vol. i, p. 873).

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FOCAL INFECTION IN RELATION TO THE ETIOLOGY OF SKIN DISEASES.*

BY

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THE term "focal infection" may be understood in three senses: First, it may imply that living and virulent bacteria are carried by the blood stream to near or remote organs, there to set up active infection; secondly, that foci such as the tonsils or dental alveoli may act as carriers of bacteria which, harmless to the person who carries them, may by contact affect other persons; thirdly, we may understand by focal infection a collection of bacteria in a crypt, pocket, tube, or fold of tissue, which, while not actively growing or multiplying, may infect the body by their cell substance which is liberated by the action of ferments or enzymes, either by self-digestion (autolysis) or by the enzymes of the cells of the invaded tissue (heterolysis).

With the first two of these aspects of focal infection I am not at present concerned. The third aspect may be conveniently designated by the term introduced by Adams—namely, *subinfection*. Now, since the chief ingredient in the bacterial cell substance is some protein body, we might more accurately name the subject of this present discussion protein poisoning in relation to cutaneous diseases.

It will help to throw some light on this obscure subject if we start with the statement of a fundamental biological fact—namely, that terrestrial vertebrates and bacteria have entered into a symbiosis, in which for the return of food maintenance the enzymes of the bacteria are thrown into line with the enzymes of the body in the scheme of defence against foreign proteins. Our food consists of foreign proteins, carbohydrates, and fats, and it is essential for the welfare of the body that these should not be allowed to pass through the wall of the intestines into the interior without first being deprived of their toxicity. There exists in the body an organized system of defence against foreign proteins. The first line is taken by the cells of the mucosa of the stomach and the higher intestines, the second line by the bacteria of the colon, and the third line by the free moving cells of the lymphoid tissues. As regards the distribution of bacteria throughout the body we find the major portion of them in lymphoid tissue in parts to which food has access. But they are not wholly confined to the surfaces of the body, for it has been demonstrated that no organ is absolutely sterile, but only potentially so.

The flora of the mouth and tonsils is restricted; it consists chiefly of the haemolytic and non-haemolytic streptococci and the staphylococci. The pneumococcus, which is closely related to *Streptococcus viridans*, is a fairly constant inhabitant of the mouth and tonsils. Occasionally more virulent organisms are found, such as the *Streptococcus mucosa* and the meningococcus. Special pathogenic organisms such as the diphtheria bacillus do not form a part of the normal colonies of the mouth and tonsils. Nor does the colon bacillus, for this bacterium is not adapted to growth in the tonsils or mouth; if implanted experimentally in the tonsil it apparently dies out. In addition to the bacterial flora the endamoeba appears to be a constant denizen of the tonsils and alveoli. All human tonsils from a few hours after birth to the end of life are infected with these bacteria; they are not distributed through the lymphoid tissue, but are confined to the crypts and follicles.

The benign physiological action of the tonsillar and alveolar bacteria is digestive and, probably, in no way essentially differs from bacterial digestion in the colon. This will become more apparent if we study the normal relation of the tonsils. After partaking of food, some undigested food particles, often in a state of fine division owing to the soft nature of the modern human diet, find access to the dental troughs and the tonsillar crypts. Milk, cheese, vegetable debris mingled with saliva, salivary corpuscles and mucus collect in the follicles, forming the so-called "cheesy" matter familiar to all laryngologists. In this way tubercle bacilli are introduced; indeed milk may be considered the customary vehicle for this organism. These are attacked by the oral and tonsillar bacteria, and their complex proteins are reduced by

* Paper read at the first meeting of the British Association of Dermatology and Syphilology.

ACCORDING to the *Castilla Médica* a State regulation is now in force in Spain by which vaccination against typhoid fever is compulsory, when typhoid or paratyphoid fever are prevailing in epidemic form, for all persons attending cases or in relation with the sick, directly or indirectly.

enzyme action to smaller molecular groups, one being poisonous and the others non-poisonous. In short, the follicles of the tonsil may be regarded as accessory organs to the colon by which food-remains are digested and disintegrated. The net result of this is the liberation of the protein contents of the cells, both of the food and of the bacteria. But in this digestive process the lymph cells play a major part; they are attracted to the follicles in search of food and thereby their enzymes split up the proteins both of the bacteria and the food cells.

If we examine microscopically the tonsils which the laryngologist usually terms "septic" we find that they do not show the clinical or microscopical picture associated with active infection. The crypts are distended with the so-called cheesy material, and in some cases "pus," or what is commonly called pus, is seen to exude on pressure. But these signs are not accompanied by any subjective or inflammatory symptoms. The patient is quite unaware that anything is wrong with his tonsils.

Microscopical sections of "septic tonsils," taken from a case of chronic alopecia areata, were submitted. In the section of the one tonsil the familiar appearance of the crypts lined by stratified epithelium and surrounded by the lymphoid tissue was to be observed. In the crypt itself was a collection of lymph cells, which could be seen as if passing from the lymph nodes through the epithelium into the crypt. Between the cells were diplococoid bacteria, but nothing resembling the chain form of the streptococci. The diplococoid form has been shown by Adami and others to be a resting form of the colon bacillus and of the streptococci. From this actual tonsil streptococci were cultured. In a section taken from the opposite tonsil of the same case the very remarkable fact was to be noted that the stratified epithelium lining the crypts had been replaced by columnar epithelium.

What is the meaning of this appearance? We are all familiar with epithelial metaplasia, as, for example, when the normal ciliated epithelium of the trachea is replaced by stratified epithelium in the position of the cartilage rings, but I am unaware of any record of squamous epithelium being converted into this columnar form. The structure of this particular tonsil, as represented in this section, is identical in all essential points with the structure of the vermiform appendix. In the latter organ, starting from the cavity, we have the columnar epithelium, the mucosa with the lymphoid follicles, the submucosa, the two muscular coats, longitudinal and transverse, and the fibrous capsule outside. The muscular tissue is absent from the tonsil, but its place is taken by the muscles of deglutition, which compress the tonsils in the act of swallowing. As in the tonsil, lymph cells pass from the lymph nodes through the epithelium into the cavity of the appendix.

Another point of similarity between the tonsils and the caecal appendix is found in their rich vascular and lymphatic supply, apparently out of all proportion to the size of the organ. This rich vascular supply may be taken as evidence of the high rate of metabolism in the tonsils and appendix and of the free interchange of material between the blood plasma and the lymph cells. Regarded in this light the appendix may be said to be the tonsil of the great bowel; nor is there anything far-fetched in this comparison. Kelly of Baltimore, in his classical treatise on the vermiform appendix, expresses the belief that there is a near relation between the tonsils and appendix as regards function, and his view is supported by other observers.

The first section shows the existence of fibrosis, and I specially desire to draw your attention to this pathological change as evidence of protein poisoning. Fibrosis as a result of subinfection has been demonstrated by Adami and Opie in gin-drinkers' liver, or chronic hepatic cirrhosis. The cirrhosis is not the result of the action of the alcohol on the liver cells, but depends on the presence in the hepatic tissues of the colon bacillus. As in the tonsil, there is no evidence of active inflammation or of active growth and multiplication of bacteria. The process of fibrosis, both in the liver and in the tonsil, is a local reaction to protein poisoning in which the physiologically active cells are slowly replaced by fibrous tissue. I would submit to the consideration of laryngologists that fibrosis in the tonsil is a more reliable indication for tonsillectomy than the presence of cheesy matter in the crypt. I have placed under the microscope a section of the appendix taken from a case suffering from erythema nodosum. It will be seen to show all the signs of chronic subinfection with advanced fibrosis. The lumen of the appendix is almost entirely obliterated by the growth of

fibrous tissue and fat cells, while the mucosa has almost entirely disappeared. The tonsils in this case showed marked signs of stasis, with cheesy material in the crypts. They were regarded by Mr. Guthrie, who examined them, as probable sources of focal poisoning, and their enucleation was advised. The general clinical symptoms of the case pointed to chronic protein poisoning, but owing to the long history of appendix trouble it was thought desirable that the appendix should be first removed.

Clinical evidence shows that in the great majority of persons bacterial digestion in the tonsils and mouth promotes only local reactions, and is not accompanied by general and remote consequences, but in not a few individuals symptoms arise which we must attribute to protein poisoning. The experimental parenteral introduction of foreign proteins into animals has shown that the complete protein molecule is a violent poison. Its first introduction into a perfectly normal animal may be followed, if the dose be sublethal, by no very remarkable symptoms, but the second injection of the same protein after an interval of some eight days provokes violent symptoms which may end fatally in a few minutes.

It is not necessary that we should follow the biochemists in their efforts to explain the chemical reactions which follow the entrance of the complete protein molecule into the blood stream and tissues. It will suffice to state the general underlying principle as given by Vaughan, that the foreign protein in the blood evokes the development of an unusual digestive ferment in the cells of the body, and when the mechanism of this heterotopic digestion is once formed, the cell henceforth is sensitized to the particular foreign protein which evoked the proteolytic function. All foreign proteins, whether they be animal, plant, or bacterial, are sensitizers. Bacterial vaccines are protein sensitizers.

To this state of protein sensitization Richet gave the name of Anaphylaxis; von Pirquet proposed the name "Allergy," which etymologically means "altered reactivity." Pathological symptoms accompany this sensitization; the blood-forming organs are specially affected, and anaemia, leucopenia, and eosinophilia appear. The non-striped involuntary muscles are highly sensitive to the protein infection; this is indicated by spasm of the venules and vaso-dilatation, accompanied by the clinical picture of urticaria, flushing of the face, oedema, and erythrodermia. In other cases the sensitization may affect the fibrous tissues, the aponeuroses, the synovial membrane of the joints, producing various forms of arthropathy. When the skin cells are sensitized in cases of chronic allergy various symptoms arise—loss of hair, either diffuse or in area, forms one of the commonest; also increased pigmentation and increased fat formation; in short, we have evident signs of stasis in the cutaneous tissues. Other clinical forms of disease are lupus erythematosus, lichen planus, and prurigo. These we may regard as different clinical pictures, varying according to the particular group of cells which are sensitized. All these cutaneous diseases have been shown by Barber, Whitfield, and Leslie-Roberts to disappear spontaneously after tonsillectomy. A very remarkable case, which has only recently come under my observation, is that of a married woman, aged 34, with a pale, sallow complexion, who had suffered from lichen of the planus type for five months; the eruption was scattered over the wrist, the forearm, and the abdomen in the region of the waist. I found the alveoli in a state of advanced pyorrhoea, and sent her to a leading dental surgeon, who advised the extraction of all her teeth. This was done, and twenty days after the operation the eruption had entirely disappeared, with the exception of a minute trace on the right wrist. No external treatment had been used, except a soothing lotion, and no vaccines had been given.

In respect of the erythematous group of reactions I think there can be no doubt that erythema multiforme and erythema nodosum are connected with protein sensitization, but the fleeting character of these reactions, as contrasted with the chronic persistent character of the four dermatoses mentioned above, points to some difference in the mechanism.

With regard to diseases belonging to the dermatitis herpetiformis group I think they can be, provisionally at least, included under the head of protein poisoning. I can recall the case of a lady I saw in consultation with a doctor, suffering from severe dermatitis herpetiformis, who recovered under the use of autogenous streptococcal vaccines.

Attempts are being made to include the eczematous reactions under the head of protein sensitization. There are some eczematoid vesicular reactions which I believe are

connected with the state of allergy, but what we may describe as the normal eczematous reactions are essentially related to physical conditions in the external environment. These cases—and they make up the vast majority of eczematous patients—are sensitized to friction owing to a defect in the physical conditions of the rete and cuticle with inherited or acquired increased permeability of the capillary walls. Such cases can be cured by simply raising the pressure of the rete and cuticle over the capillaries.

Exact knowledge is needed, and when this comes we shall be better placed for classifying the protein sensitization diseases. I am not yet prepared to say what value is to be attached to local signs of cell irritability provoked by the intra-epidermic applications of various proteins. There are many conditions which affect cell irritability besides protein sensitization, and for myself I prefer to wait for further evidence.

BILE SALT AS A VEHICLE FOR A PEDICULICIDE.

BY

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For several years we have been experimenting with various substances for the destruction of head lice, but nothing was found which prevented the hatching out of the nits. It was considered that as bile salts are stated to assist the passage of emulsions of fats through the mucous membranes by their property of reducing surface tension, they might have the same effect in assisting oily emulsions to penetrate the shell of the louse's egg. Experiments were made with various strengths of sodium taurocholate in watery solution with eucalyptus and sassafras oils. The best compound was found to be

Sodium taurocholate	...	...	10 grams.
Ol. eucalypti	...	...	50 c.cm.
Water	...	...	to 1,000 c.cm.

Dissolve the bile salt completely in water, add the eucalyptus oil, and shake well.

A higher concentration of bile salt rendered the hair very sticky, whilst a lower did not form so good an emulsion. More than 5 per cent. eucalyptus rapidly separated out. The formula yields an emulsion like milk in appearance, and but little of the oil separates out after several days.

Most lice, if immersed in the liquid, cease movements in a few seconds, but a few individuals did not die for three minutes. In no case did any of those tested recover when dried on blotting paper and incubated. Larger insects, such as wasps, house-flies, and fleas, when dropped in the emulsion became wetted all over immediately, and died in less than a minute.

During the past eighteen months the emulsion has been tried on over 500 patients on whose heads living lice were seen. It is well rubbed into the head until all the hair is wetted. The head is then wrapped in a bathing cap or towel and the application left on all night. The head is washed with soap and water next morning, and a fine-toothed comb used daily for a fortnight, notes being kept of any lice found. In 23 per cent. of the cases no lice were found after one application. In the remainder a few recently hatched very small forms were discovered, in no case before four days after the first application, in most cases not until after a week, and in a few not until the tenth day. A second application on this reappearance sterilized 63 per cent., while 14 per cent. required a third application.

It appeared that the embryos on the point of emergence were killed, whilst the most recently deposited eggs were more resistant.

Some of the worst infested heads, in which the towel swathing the head was nearly black with dead lice on the morning after the first application, were sterilized with one application, while some of the lightly infected required three applications, so that it would seem that there must be different powers of resistance in certain strains of lice.

This preparation is not toxic, is not irritating to the skin, is not inflammable, and is elegant to use as it is easily washed out of the hair. The cost of the ingredients works out at 6½d. a pint.

Possibly the property of bile salt solutions to wet the lice and their eggs can be combined with some substance more poisonous than eucalyptus oil to the louse's egg, so that one application would always be sufficient.

The Hettzsonian Lectures

ON

AMOEBIc LIVER ABSCESS.*

DELIVERED BEFORE THE MEDICAL SOCIETY OF LONDON

BY

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[Abstract.]

LECTURE II.—VARIETIES AND TREATMENT.

THE lecturer continued his remarks on pathology by referring to suppurative cholangitis, a rare disease in which he had been greatly interested ever since he met with three cases at St. Mary's Hospital in his third year studentship. Fourteen years later he recorded a case which he had diagnosed and operated on at Calcutta European General Hospital, in which a mass of gall stones was removed from the hepatic ducts. Unfortunately, this case was taken in hand too late, and the suppuration tracked out and opened into a bronchus, with a fatal result. The rarity of this complication in India was explained by the fact that, although gall stones were nearly as common in India as in Europe, in the eastern country most of them were of the soft pigmented variety, and the hard, disease-producing cholesterol form was comparatively infrequent, at least in Calcutta. Suppurative cholangitis would, therefore, seldom give rise to difficulties in differentiation from liver abscess in the tropics. He also spoke of diffuse suppurative hepatitis produced by *B. coli communis*. He had seen this condition in a Calcutta hospital, the patient having leucocytosis with over 90 per cent. of polynuclear leucocytes. He showed a colour drawing to illustrate the condition found *post mortem*, indicating a large diffuse suppuration throughout that half of the liver which was supplied by the right branch of the portal vein, in which an extensive clotting was present, while the remaining half of the organ was healthy.

Frequency of Large Single Abscess.

In his previous lecture he had shown that multiple small amoebic abscesses were nearly always overshadowed by the acute sloughing dysentery to which they were secondary, so that they could not easily be recognized during life, still less easily treated surgically. This variety might therefore be put on one side, and they could turn with more hopefulness to the comparatively chronic, large, fibrous-walled form, and see what lessons the *post-mortem* room and the laboratory could teach them in dealing with this formerly very common and very fatal tropical liver disease.

He gave some statistics which appeared to indicate—it was not a matter for precision—that in about 70 per cent. of cases of large liver abscess the abscess was single. Among 38 cases in which there was found to be more than one abscess there were two abscesses in 44.7 per cent., three in 26.3 per cent., four in 18.4 per cent., and over four in 10.6 per cent. In this connexion he drew attention to the practical importance of the fibrous limiting wall in large amoebic abscess which he had described on the previous occasion. In friendly discussions with surgical colleagues he had often been told that the high mortality of the open operation was due to the amount of destruction of the liver tissue. This he was convinced was not the case. He showed a coloured drawing of a liver with three medium-sized amoebic abscesses side by side, with only about one-third of an inch separating one from another, and said that it might be a matter for wonder that in such a delicate organ as the liver they did not coalesce into one; but on cutting sections it was found that each abscess was limited by a dense fibrous wall, and that the liver tissue in between was perfectly healthy. Once the fibrous wall was formed there was no further destruction of liver tissue, at least as long as the cavity remained free from bacterial infection. He had twice seen six pints of pus aspirated from the liver at a single drainage, and yet a complete recovery took place. If such amounts of pus did not destroy enough liver tissue, to cause death he would like to know what basis the surgeons had for attributing the mortality in open operation to destruction of tissue.

Secondary Bacterial Infection after Open Operation.

The lecturer went on to speak of the importance of secondary bacterial infection after open operation on large

* An abstract of the first lecture appeared in the BRITISH MEDICAL JOURNAL of February 11th, 1922, at p. 224.