There are persons admitting to late middle age and called by their friends old who, though they have heard much about the sun myth and have been chastened by Sir J. G. Frazer, yet like a fairy story for its own sake; to such we may commend *The Disobedient Kids*,[10] a copy of which reached us only a day or two before Christmas. It is an unusual production, having been turned into English, illustrated, and printed in Prague; it contains ten stories chosen from among those written over half a century ago by a Czecho-Slovakian lady, Bozena Němcová. The translation is by Dr. Tolman, at whose request the book has been sent to us. In the circumstances we cannot be sure how far the stories are indigenous; we find a Tom Thumb story, and a repetition story of the style of the House that Jack Built, and others which may be either parallels or reminiscences. The volume is illustrated with much skill and humour by Artus Scheiner, whose drawings in colour and in black and white have been most excellently reproduced under the direction of the publisher. The English is good and clear, but some of the turns of expression have a transatlantic character. It is termed "literary," but we do not take the antithesis; is it colloquial or commercial?

Earlier numbers of the *Practical Handbook of British Birds*,[11] which is being issued in serial form under the editorship of Mr. H. F. WITHERBY, have been noticed in this column. During the past year two more parts, the tenth and eleventh, have appeared: these include pages 81 to 256 and Plates 2 to 5 of Vol. ii. Part X is devoted to birds of prey—owls, falcons, eagles, hawks, harriers, kites, kestrels, and their brethren; Part XI covers storks, herons, ibises and spoonbills, and a number of swans and geese. The standard of the letterpress and illustrations is well maintained. One of the six contributors to this excellent handbook—and the writer of all the notes on migration of birds—is Mr. N. F. Ticehurst, F.R.C.S., of St. Leonards, who is a representative of medicine in the select company of scientific British ornithologists which includes (to name but two others) Dr. A. F. R. Wollaston and Dr. Philip Gosse.

The first part of Professor HERING'S book on pathological physiology[12] deals with the functional disorders of the heart, the vessels, and the blood, each described under two headings; the causes (or coefficients) giving rise to the disorder are first explained, and then the results to which these causes give rise. The book is clearly written, but gives no details of the experimental work or the literature upon which it is based. It is intended primarily for the use of medical students and their teachers, but also for medical men.

The *Handbuch der Cystoskopie*,[13] by Professor Dr. LEOPOLD CASPER, is one of the most complete works on the theory and practice of cystoscopy that we have come across. The earlier chapters deal with the history and the construction of the modern cystoscope. The optics and mathematics of the subject are fully dealt with and provide somewhat stiff reading for those not especially interested in this somewhat technical side of cystoscopy. After describing the anatomy and appearance of the normal bladder the author considers the commoner pathological conditions encountered by the cystoscopist. These are illustrated both by means of black and white and of coloured plates, which are collected into an atlas at the end of the book. Some of these illustrations are unconvincing, and few of them can be considered first class. The work concludes with a chapter on radiography, pyelography, photography of the bladder, and operative cystoscopy. The work is one that will appeal to experts rather than to medical practitioners in general.

We have received an interleaved copy of the *Pharmacopoeia of St. Bartholomew's Hospital*,[14] in which the doses are given in both imperial and metric measures, as in the *British Pharmacopoeia* of 1914. A few pages are devoted to the treatment of cases of poisoning, and a posological table is included. The book is of convenient size, and contains much additional information of service to those for whose use it is designed.

[10] The agents in London are Philip Allan and Co., and the price 6s. In America the agents are Harper Bros., New York, and the price 1 dollar. There seems to be a preference against this country, which is not explained.

[11] London: Witherby and Co. 1921. 4s. 6d. net per part.

[12] *Pathologische Physiologie.* I. Abteilung: *Die Funktionsstörungen des Herzens, des Gefässe und des Blutes.* By Dr. H. E. Hering. Leipzig: G. Thieme. 1921. (Med 8vo, pp. viii+120. M.39.)

[13] *Handbuch der Cystoskopie.* Von Dr L. Casper 4 Auflage. Leipzig: G. Thieme. 1921. (Imp. roy. 8vo, pp. 396; 161 figures, 12 plates. Bound, M.264.)

[14] *Pharmacopoeia of St. Bartholomew's Hospital.* Edited by J. Langford Moore, F.C.S., Pharmacist to the Hospital. London: Spottiswoode, Ballantyne and Co., Ltd. 1921. (3¼ × 5¼, pp. 100.)

MEDICINAL AND DIETETIC PREPARATIONS.

Inoculation Tests for Protein Therapy.

BLACKLEY may be regarded as the discoverer of specific skin reactions in diseases due to hypersensitiveness to proteins, for in 1873 he showed that pollen rubbed into the scarified skin produced large urticarial wheals in patients suffering from hay fever. The observations of Pirquet and Schick upon the local reactions in serum disease, and the work of Arthus upon the local reactions in anaphylaxis, showed that in hypersensitive individuals and animals the injection of the specific protein to which they were hypersensitive produced a strong local reaction.

Auer and Lewis in 1910 pointed out that spasm of the bronchial muscles was characteristic of the anaphylactic reaction in guinea-pigs, and this drew attention to the probability that asthma in man was due to hypersensitiveness to specific proteins. The fact that asthma is very frequently due to hypersensitiveness to proteins has since been established by numerous workers. Asthma may be caused by a very large number of different proteins of animal or vegetable origin, and the only way to ascertain the protein responsible is to test the sensitiveness of the patient's skin with a variety of pure proteins. The technique of determining, by means of skin reactions, the protein responsible for producing asthma was worked out by Walker and Wodehouse in 1916 and 1917. The method is now coming into general use and the technique is very simple; a light scratch, insufficient to draw blood, is made in the skin, and a dilute solution of protein is applied; if the patient is not sensitive there is no reaction, but if the patient is hypersensitive to the particular protein applied an urticarial wheal appears in from fifteen to thirty minutes. The severity of the reaction varies, a mild reaction consists in a wheal about one-quarter of an inch in diameter; in a severe reaction the wheal may be an inch in diameter and surrounded by an erythematous ring. The only hindrance in applying the test is the difficulty of obtaining a supply of purified sterile proteins.

Messrs. Duncan, Flockhart, and Co. of Edinburgh (104, Holyrood Road), have prepared pure protein solutions in a very convenient form; the solutions are in glass capillary tubes; they supply thirty-two different kinds of proteins, which are obtained from all the commonest animal and vegetable foods, and from substances, such as horse dandruff and pollen, which may be inhaled as dust. This outfit makes the testing of specific hypersensitiveness a very simple matter, for a dozen different proteins can easily be tested in less than an hour. Selections of dried proteins for these reactions have been available for some time, but the supply of the proteins in a soluble form ready for immediate use is obviously a great convenience, as it saves the trouble of preparing a large number of solutions. The exact clinical value of these tests is not yet fully known. About 50 per cent. of asthmatics show definite dermal hypersensitiveness to proteins, but unfortunately a large number of cases show dermal hypersensitiveness to several proteins. In these cases of multiple dermal hypersensitiveness the asthma usually is due only to one particular protein. A considerable number of normal persons, moreover, show dermal hypersensitiveness. A positive reaction with a particular protein in a case suffering from symptoms resembling asthma, therefore, does not prove conclusively either that the patient is an asthmatic, or that, even if he has asthma, the disease is due to the protein to which he has reacted. If due regard is paid to the clinical history, the tests are, however, of great value in determining the cause of asthma. The advantage of knowing the cause of asthma is obvious, for it enables the patient to avoid the exciting cause, and also in many cases the patient can be desensitized by vaccine treatment.

Digifoline.

"Digifoline" is claimed to be a standard, constant, and permanent liquid preparation of digitalis suitable for internal, hypodermic, and intravenous use. It is a clear, light-coloured fluid, which does not produce any marked local reaction when injected hypodermically, and which, when tested on the frog, we find to have an activity equal to that of standardized tincture of digitalis. The manufacturers claim that digifolin (this spelling is, we think, to be preferred) is free from the irritant saponins which occur in the tincture of digitalis, and that it contains all the active glucosides of digitalis. The difficulties attending the administration of tincture of digitalis in full doses are well known; gastric irritation is very liable to be produced by oral

administration, and no preparation of digitalis has hitherto been prepared which is satisfactory for hypodermic or intravenous administration. Satisfactory therapeutic results have been reported to follow oral and hypodermic administration of digifolin, and the preparation appears to represent a distinct advance in digitalis preparations. Its exact value can only be known after more prolonged therapeutic trials have been made, but it seems to deserve a full trial. Digifolin is supplied in tablet and fluid form for oral administration, and in ampoules for hypodermic injection, by the Clayton Aniline Company, 68½, Upper Thames Street, London, E.C.4.

THE VITAMIN THEORY IN RICKETS.

THE Report of the Medical Research Committee on Accessory Food Factors (Vitamins),[1] published in 1919, included a section dealing with rickets, which definitely placed it among the deficiency diseases. This conclusion was largely based upon the experimental work of E. Mellanby upon puppies, and stated that the cause of rickets in dogs was the lack in their food of an antirachitic factor, which had "in many respects a similar distribution to the fat-soluble A factor, and is possibly identical with that substance."

Dr. Mellanby himself in several later articles further expounded this new and interesting doctrine of rickets. It soon aroused wide interest, drew upon itself active discussion and criticism, and stimulated experimental study of the subject along these new lines he had laid down. Meanwhile he has been actively prosecuting his experiments, and he now sums up the results of five years' research in an interim report on "Experimental Rickets," just published.[2]

The broad statement may be fairly made that Dr. Mellanby takes now a larger view of the etiology of rickets than he did in the first account of his research. He does not put rickets in the same category of deficiency diseases as scurvy and beri-beri, where the withdrawal of one single element in diet, and that a factor unconnected with the provision of energy, is the decisive cause of the disease. He now admits the co-operation in rickets of other prejudicial factors—a disturbed balance of the main constituents of the diet, an unwholesome environment, lack of exercise. Beri-beri and scurvy are "nutritional diseases very limited in their etiology, but this does not hold in rickets" (p. 6).

Dr. Mellanby's Results.

Throughout the investigation the important criterion of rickets in the young dog was disturbed calcification in the growing bones, these changes being established by radiograms, by chemical analysis, and by histological evidence. The histological examination was the decisive one, and the crucial test was the presence of osteoid tissue.

It is clear that the diagnosis of rickets in these experiments has been made with scrupulous and strict accuracy; and the report is enriched by a beautiful series of radiograms and microscopic photographs of the bones. The conditions which produce the bony changes characteristic of rickets are given in the following order: "A deficiency of calcium and phosphorus in diet; a deficiency of fat containing the antirachitic vitamin in diet; excess of bread, other cereals and carbohydrates; absence of meat; excess of the protein moiety of caseinogen free from calcium; confinement." He goes on to say: "Because of the interdependence of all these dietetic factors, it is impossible to say what is the absolute amount of each necessary to produce the optimum result." But he adds: "Probably the most common cause of rickets in children is a combination of relatively deficient antirachitic vitamin and excessive bread" (p. 75). It will be readily seen that these conclusions are much more cautious and ambiguous than the original statement in the report concerning accessory food factors, "there is good evidence that rickets is a deficiency disease . . . " (p. 91).

Dr. Mellanby found that the diet most favourable to the rapid production of rickets in a young puppy was one containing an adequate amount of protein (separated milk), an excess of carbohydrate (bread), a sufficiency of water-soluble B and C vitamins and of salt, but very defective in fat. By adding measured amounts of various animal and vegetable fats and by observing the degree of rickets produced, he was able to estimate the antirachitic power of each variety of fat. The broad result was that animal fats were powerfully antirachitic; the vegetable oils were either feebly so, or destitute of this power. Now experiments on young rats showed that the animal and vegetable fats fell into the same groups in respect of their power to promote growth, or according to the vitamin hypothesis in their content of fat-soluble A. There are discrepancies in this general statement; but on the whole it is true, and it led Mellanby to the conclusion that the disease in each species, lack of growth in the rat, and rickets in the puppy, is probably due to the same vitamin fat-soluble A. He finds other points in favour of this identity, in the fact that in each animal the disease took several weeks to develop, and also that beyond a certain age in the young rat and in the puppy, the respective diseased condition became very difficult to produce. These were the points in favour of rickets as a vitamin-deficiency disease, and of the identity of that vitamin with fat-soluble A shown to be essential for growth in rats.

But there are difficulties and objections to this interpretation. (1) In the first place, the puppies with rickets did not cease to grow; on the contrary, the worst degrees of rickets were found in those with most rapid growth, while if growth ceased, the rickety changes in bone were not produced. That is to say, we are asked to believe that this same vitamin stops growth in the young rat, while in the puppy it causes rickets but allows growth to proceed. (2) Then lean meat, a food poor in fat-soluble A for rats, was shown to possess definite antirachitic power in puppies. Several explanations of this difficulty are suggested, but they are conjectural and unsupported by evidence, and the discrepancy remains. (3) Green leaves are substances specially rich in fat-soluble A as shown by experiments on rats. In puppies a few experiments were made with cabbage and extracts of cabbage, and these failed to prevent rickets and set up diarrhoea. Further experiments in this direction are promised, and the importance of their success or failure is admitted.

Each of these difficulties is by itself not of small account: together they create a formidable obstacle to the acceptance of fat-soluble A as an antirachitic vitamin.

The report contains also interesting observations on other factors of diet and environment that favour the production of rickets. An excess of carbohydrate has an important effect in doing so; so has confinement; so also a defect of the caseinogen moiety of milk containing calcium. But these conditions only act when the diet is also defective in fatty substances rich in fat-soluble A. These observations are interesting both scientifically and clinically, but they need not be discussed in connexion with the present question of the vitamin theory in rickets. By increasing the complexity and number of agencies that produce rickets they certainly do not strengthen the vitamin theory, but, on the other hand, they do not seem to directly oppose it.

Other Investigations.

Now let us examine the results of other investigations carried out to test the doctrine of rickets as a deficiency disease produced by a defect of a vitamin similar to or identical with fat-soluble A. Noël Paton, Findlay, and Watson[3] are strongly opposed to the vitamin theory in rickets. Taking pups from the same litter they produced rickets in some of these, confined in the laboratory but on a liberal diet of porridge and full-cream milk; while in others, at liberty in the country but fed on skimmed milk and porridge, no rickets developed. And in their last series of experiments by paying strict attention to cleanliness they have reared pups free from rickets on a series of diets with a low fat intake (even as low as 0.5 gram of milk fat per kilo of body weight), always provided that the total energy value of the diet was sufficient. They thus claim to have produced rickets in pups on a diet rich in fat-soluble A (an abundant supply of full-cream milk); and to have reared pups free from rickets on a diet very poor in fat-soluble A (separated milk and bread). From experimental and clinical evidence they propound the view that the primary factor in rickets is not dietetic but is the result of overcrowding and insanitary conditions, and that some kind of non-specific bacterial infection may be an important factor.

While in Britain most of the recent experimental work on rickets has been carried out on the dog, in America the rat has been chiefly used. In the last few months Hess, McCann and Pappenheimer, and Shipley, McCollum and co-workers have published interesting experimental work on rickets in the rat. This work is the more important in that the rat is the animal on which the work upon fat-soluble A has been done, and from which our knowledge of this accessory food factor has been derived. Hess's research[4] dealt with a large series of young rats fed on a diet which was complete except