Genesis of Gall-stones

SIR.—Lord Moynihan, in a letter in your issue of May 27th, has taken Mr. Patey to task for failing to mention, in his admirable article on "The Mechanism of Gall-stone Formation," the work of Dr. Shiskin, and also for his statement "that attempts to correlate the amount of cholesterol in the blood with gall-stones have failed." Lord Moynihan restates his own views on cholesterol metabolism in this connexion, but we scarcely think that these are in accord with present-day views of workers in this field.

Hypercholesterolaemia is not easily defined without a knowledge of normal limits. Lord Moynihan quotes MacAdam and Shiskin's work, in which twelve normal cases were examined, the detailed figures not being presented in their original paper. They found upper and lower limits of plasma cholesterol of 0.191 per cent. and 0.133 per cent., with an average of 0.161 per cent. He has quite unjustifiably divided the lower half of this region as normal and the upper half as high normal. He then quotes figures of analyses made in abdominal conditions such as gastric ulcer, in which hypercholesterolaemia is not known to occur, and finds 23 per cent. of the cases show hypercholesterolaemia, 50 per cent. as normal, and 27 per cent. show hypocholesterolaemia. Surely, then, it is obvious that he has started with inadequately defined normal limits, as is indeed the case, since the data derived from perfectly normal people by many workers show far wider variations than his arbitrarily chosen limits. It is, in fact, practically impossible to state that a moderate degree of hypercholesterolaemia is present in an individual case from single observations unless the individual's normal plasma cholesterol content has been previously well studied. That he finds somewhat high figures for the plasma cholesterol content in cholelithiasis is not surprising, since both Campbell and ourselves have shown that such hypercholesterolaemia occurs whenever biliary obstruction is present, but *not* in uncomplicated cholelithiasis. But why does Lord Moynihan ignore the more complicated changes which occur in the blood in these cases of biliary stasis, such as have been demonstrated not only by ourselves but also by Adler and Lemmel, Thannhauser and Schaber, Stern and Suchantke, and Burger and Habs? In biliary obstruction we have shown that two types of change occur: the first, a reversal of the free to ester ratio, is caused apparently by the effect of the absence of bile from the intestine (however deviated therefrom) on fat and sterol absorption; the second, a hypercholesterolaemia with a reversal of the usual proportion of free and ester forms, is produced when biliary obstruction and retention persist for some time. The further study of these phenomena is complicated by the capacity of the intestine of excreting bihydrocholesterol.

In Lord Moynihan's paper (*Journal*, 1925, i, 393, and not as quoted) Dr. Shiskin's results are presented only as one graph of changes in pregnancy and one during menstruation, drawn with exaggerated ordinates, but which can hardly be compared with serious studies in which all details are published and available for examination. Surely Mr. Patey can hardly be blamed for not quoting results which admittedly had never been published. That some degree of hypercholesterolaemia sometimes occurs in pregnancy we have shown, but the real point of interest again is the remarkable and constant cyclical change that occurs in the free to ester ratio.

Mr. Patey's statement as to the correlation between gall-stones and cholesterolaemia is quite correct if we exclude the effect of biliary obstruction. There is no unequivocal evidence that either high fat feeding, or hypercholesterolaemia, or pregnancy with its inconstant

hypercholesterolaemia, can cause any increase in the cholesterol content of the bile. Further, gross hypercholesterolaemia such as occurs for long periods in sub-acute forms of nephritis leads to no increase in the incidence of gall-stones. On the other hand, the evidence in Fowweather and Collinson's paper that hypercholesterolaemia is produced in gall-bladder disease by a "flood of cholesterol" (quoting Lord Moynihan's words) reabsorbed by the gall-bladder from the bile, is unconvincing.

Lastly, we would suggest that no comprehensive theory of gall-stone formation can be adequate if it ignores the close chemical relation between cholesterol and the bile acids, and more particularly the properties and distribution of the various bile acids which are so important in maintaining the different sterols of bile in solution. At present we have no satisfactory method of estimating even the total quantity of bile acids present in bile, much less of determining their relative proportions.—We are, etc.,

J. A. GARDNER.

H. GAINSBOROUGH.

London, W., May 29th.

Return to Principles

SIR.—When I read in the *Journal* of May 20th, in Lord Horder's address (p. 859) on "New Treatments for Old" and in your leading article (p. 881), of "deviations from the physiological that constitute disease," and of "the disharmony we call disease," I was reminded of one of my medical teachers of more than forty years ago, who introduced each description of all the "labels" he had selected for his course of lectures by the words "a morbid process"; and I feel now, as I felt long ago, that knowledge is not advanced much, if at all, by such phrases, and that we are no further on. Indeed, is a "morbid process" not the better term, since it connotes the something further which causes the "deviation from the physiological," an invasion of something new which somehow determines "physiological disharmony"?

To identify a disharmony of physiology (disease) you say "the medical man has at his disposal a well-tryed method upon which he can rely . . . diagnosis." This stops far short of what is required. We can all diagnose pneumonia, influenza, erysipelas, osteoarthritis, and the rest; but these are not the disharmonies, they are the full-blown effects of an antecedent disharmony. What is the nature of that disharmony, that departure from physiology, which produces what we diagnose and call disease? Would anyone say, in a case of pneumonia, that the real disharmony is the consolidation? Yet some knowledge of the underlying processes has been stated, is gaining ground, and may yet answer the questions as to the real principles which govern health and disease.

But, leaving this out and departing at once from Harvey's exordium, which he quotes, Lord Horder suggests an interregnum—the cessation of laboratory work and of the seniors' activities in the hospitals—and a conference "to try to see where we are." Well, to me the answer, on the old lines, is "Nowhere," and will, on these lines, for long be the answer, despite the enormous masses of accumulated useful knowledge. Nor are we better off in therapeutics, unless light is also dawning slowly. We assuredly do produce the results we want, and help to cure, or alleviate, our patients, but, as Lord Horder says, "we know so little about the way in which drugs act." We know the effects many drugs can be trusted to produce, but how they do it, and what happens in the process that leads to the result we wish, we seldom know. "It is always Nature that cures, not we"; and we can only help. But by what process does Nature cure? Not yet can that be answered with full and complete knowledge.

Thus we have reached a stage where we call disease a physiological disharmony, the primary nature of which we do not know; where we say Nature cures, not we, but how she does it we do not know (we only know some of the steps she takes); where we know little or nothing of just how our drugs produce their action, though, fortunately we can so often predict and depend on it. We are told to use remedies which will help to "restore physiological equilibrium," though we do not know the primary essential of that equilibrium, nor what has caused and constitutes the primary upset of it. The position is not too satisfactory.

Yet there are movements in a better direction, but I fear some of these come under Lord Horder's ban. I do not, for a moment, advocate the indiscriminate trial of all the nostrums we are bombarded with, nor the foolish administration and advocacy of any of them—especially the best and good ones (and these are *not* nostrums)—as recounted by Lord Horder in his "Good Samaritan" story. But I do say the general practitioner is the man to "try them out" with all the care and discrimination he can bring to bear. Many practitioners must see thousands of cases—simple, early, uncomplicated—which consultants never see, in which the best of the newer remedies are useful. And in cautiously accepting the stated method of action, and using these remedies, under whatever class of therapeutic activity they fall, we do no more and no worse, and may do much better, than those who decry them and decline to use them, preferring the older remedies, though avowedly with little or no knowledge of how the older remedies act in producing the results expected.

None but the most foolish would expect of any drug an action so miraculous as to do away with all necessary care (for example, the three-day cure of influenza) or fail to employ concurrently every adjunct to the whole welfare of the patient.—I am, etc.,

Glasgow, May 23rd.

R. O. ADAMSON.

Meningitis from Bowel Toxaemia

SIR,—In the *Journal* of April 8th there is a report of two cases of tuberculous meningitis resembling cerebro-spinal fever in which the main points were: (a) brothers, aged 6 and 3 years; (b) duration five and three days respectively; (c) both died within twelve hours of admission; (d) cerebro-spinal fluid showed trace of albumin and numerous small lymphocytes.

I venture to suggest for consideration a diagnosis of meningitis due to bowel toxaemia, probably of Flexner group origin. It is a not uncommon condition in South India, and Flexner group infections are not unknown in Britain. There may or not be a previous bowel history; there is usually constipation, but when the stool is obtained it is loose, often contains mucus and cellular exudate, is strongly acid, and Flexner group organisms are cultivated. The cerebro-spinal fluid is under pressure clear, globulin is increased, and lymphocytes are numerous; there is no sugar.

The meningitis is either fulminating and fatal, or acute, with good prognosis under intensive treatment with subcutaneous salines (for an adult 8 pints in twenty-four hours), liquid protein diet (swallowing power quickly returns after the salines), and alkalis. A curious feature is that, except in to-be-fatal cases, the coma is only apparent; the patient looks comatose, but there is an awareness and alertness of mind without the power of expression. I have known a patient signify disapproval of a relative's inaccuracy of statement by moving one finger, and during the early stages of recovery the clear-mindedness is very marked. A further point is that Flexner group infections cause attacks of influenza-like

fever. Was the mother's attack a week before the source of infection for the two boys?—I am, etc.,

Medical School, Vellore, South India,
April 28th.

FLORA R. INNES.

Rupture of Lung without External Signs of Trauma

SIR,—The remarkable case recorded in your issue of May 27th (p. 938) by Dr. F. W. Martin recalls to my memory a case which I reported in the year 1882 of a young man who had been knocked down by a cart and pushed along under its wheel without being actually run over. Admitted to the Great Northern Hospital (then in the Caledonian Road), he lay for more than two months with puzzling symptoms, indicating severe damage to thoracic and abdominal organs, without any external signs of injury. Post-mortem examination showed that the right lung had been torn and that a portion of it had passed through the diaphragm—presumably ruptured at the same time—and a large piece of collapsed lung was found in the pelvis. Hernia of lung into the abdomen is an almost unknown occurrence, and the case is therefore doubly interesting. The whole case, with comments, will be found in the *Lancet*, 1882, i, 139.—I am, etc.,

London, S.W.3, May 27th.

E. CLIFFORD BEALE.

Crypto-empyema

SIR,—I was interested in the article by Professor A. Rendle Short in the *Journal* of May 20th (p. 870), in which he refers to three cases of empyema where the diagnosis was difficult, where repeated needling failed to reveal the presence of pus, but where pus was found at operation. Professor Rendle Short states: "A skiagram is useful; it will show some opacity, but it cannot be relied on to tell us exactly where the abscess is." I cannot entirely agree with this statement. Radiology is extremely useful in a large number of cases in determining where the pus is, and particularly in those cases of encysted empyemas to which Professor Rendle Short refers. Radiograms taken in the direct lateral position are extremely useful in the localization, for example, of (a) an interlobar empyema, and (b) an empyema encysted between the base of the lung and the diaphragm. These illustrate two types of cases to which Professor Rendle Short refers. In cases of difficulty of this sort, routine postero-anterior and direct lateral radiograms should be taken, where possible. The latter will often show the exact localization of the pus.

I think that needling should not be used too freely, as there is a considerable element of danger of infecting the general pleural cavity when one may be dealing with encysted effusions.—I am, etc.,

W. PATON PHILIP, M.B., D.M.R.E., D.P.H.

Consulting Physician, Papworth Village Settlement;
May 24th. Tuberculosis Officer, Cambridge County.

The G.P. and Midwifery

SIR,—I may be wrong in my conclusion, but I feel that Professor J. M. Munro Kerr, in all that he writes, does so with a bias against the capacity of the general practitioner of medicine to carry out his duties in reference to midwifery in accordance with the highest standards of modern practice. In my, I suppose, bucolic outlook and insight, he writes with his head in the clouds; full of expert knowledge; full of the wise saws of official reports, and the brotherhood of the F.C.O.G.; full of all the conveniences, and, in his becoated, bemasked, and waited-upon existence, the advantages of the clinic and the