Discussion to the papers by F. T. de Dombal, G. Watkinson and J. C. Goligher

CHAIRMAN: PROFESSOR J. C. GOLIGHER

HADLEY. I was delighted to hear Mr de Dombal's definition, and two points occurred to me as he went on. The first is the use of the term 'granular proctitis' which is still in curiously wide usage. To me, granular proctitis means, simply enough, if you like, colitis of a relatively inactive degree and confined to the rectum. In some circles it seems to be used as a separate disease, which I think is a pity. If we could agree here this morning that my definition is right, we might perhaps persuade people to abandon its use. I think it is a pity it should continue to be used as an indication of a specific disease, which it is not.

The second definition, I may perhaps have missed, and that is I would very much like to hear Mr de Dombal's definition of what constitutes a severe attack of colitis. This is really very much more important. I think that perhaps the greatest danger that a patient with a severe attack faces is that the severity of the attack is underestimated, and therefore intensive medical treatment is persisted with a little bit too long and surgery delayed until perhaps it is too late.

CHAIRMAN. Thank you Dr Hadley. Would you like to deal with those two points?

DE DOMBAL. On the first point I couldn't agree with you more. I think granular proctitis is a variant of proctocolitis and I think it would be better if we were to call this disease which we have discussed all morning not 'ulcerative colitis' but 'idiopathic proctocolitis'. I think then that this difficulty of regarding granular proctitis as a different disease, instead of merely a variant of this overall clinical entity, would not arise. I think it is a mistake to call this a different disease, 30 or 40% of our patients with proctitis, some of them showing the granular mucosa, subsequently developed total, or near total, ulcerative colitis and I think that this demonstrates very well that this is merely a variant, merely one presentation or variation of this overall disease complex.

On the second point, we have defined a severe attack by the criteria laid down by Truelove & Witts in 1955 as a patient who is having five or six bowel actions a day with macroscopic blood in the stools, fever of 100°F or so, tachycardia of 90 or 100 to the minute, anaemia—haemoglobin less than 70%, and a high ESR of over 30 mm/hr. Now, I think there are two points about that. First of all, I would agree with you that the danger is in severe attacks that we underestimate the problem. I think as a general medical principle of treating severe attacks, which cannot be stressed often enough, is that they are medical emergencies and I think if we were all of us to accept this fact then we should lose less patients in severe attacks. Certainly in the 52-63 age group whom I was describing before there were one or two patients who, it must be admitted, drifted on in the hope that they would get better; eventually they didn't and when they came to surgery, as the Professor has said, they came to surgery virtually in a moribund condition. The patient should have

3 or 4 days of intensive management and if at the end of that time they are not better, a decision can be taken about surgery. I think what is dangerous is to keep on giving them one drug, or possibly something, a bit of something else and so on and so forth, until at the end of this you wake up to the fact that after 3 weeks time, you have got a very ill patient on your hands who is not getting better and then the patient's life is in danger.

CHAIRMAN. On this point of granular proctitis I feel compelled to say that I think Brian Brooke did a disservice here. He has done so many good things in connection with colitis, I may be allowed to comment on this one bad thing he did. He wrote an article in the *Lancet** and he separated off proctosigmoiditis from ordinary ulcerative colitis. Well, I would say that we disagree with this conception entirely, as Mr de Dombal has made out. These are just different degrees of the same condition, different extents of involvement. And on the question of the Truelove-Witts definition of severe attack, we almost need a definition of a super-severe attack I think, for analysing our very ill patients and how they should be treated.

SWALLOW. I'd like to put a further question about proctitis. In eighteen of the fifty cases of proctitis who later developed total involvement, I've been wondering whether you have taken proctitis as disease limited to the lower rectum with normal mucosal bowel above or whether these were patients who had involvement of the rectum as far as one could see with a sigmoidoscope and, therefore, quite possibly had sigmoid involvement as well. I am quoting from memory but I think that Lennard-Jones made some observations about percentages of patients with proctitis who developed more extensive involvement. I didn't think it was such a high figure as 36% within such a limited time. I am wondering if all those eighteen cases had an extensive proctitis or just limited disease.

CHAIRMAN. One could not say that one had got above the disease on sigmoidoscopy in all cases but in a very considerable number one was able to get above the disease. I can think of very many patients whom I have seen with involvement of the rectum up to about 8-10 cm on sigmoidoscopy with normal mucosa above who have subsequently come back, in the fulness of time with more extensive disease and subsequently come to operation. So there is no doubt about it, this does happen, but I would not like to say that all these patients referred to in this group had such clear-definition sigmoidoscopy—am I right in saying that?

DE DOMBAL. There were in fact five of this group who did have limited disease on sigmoidoscopy, but funnily enough these five didn't seem to progress very much. So there is a point here, I think, a very valid one, these may just be patients who are not showing radiological

*BROOKE, B.N. (1953) What is ulcerative colitis? *Lancet*, i, 1220.

evidence and subsequently do show radiological evidence. I think possibly they extend far more commonly than we have hitherto realized and we should be on our guard for cases in the future.

CHAIRMAN. In this connection could I make one point in connection with diagnosis. Colitis is an easy disease to diagnose but in the course of the years I have seen a number of patients who have not been accurately diagnosed and I would say that the commonest reason why these have not been diagnosed is that the patient has not been sigmoidoscoped. It seems absolutely incredible that in this day and age clinicians could be seeing these patients with suspected colitis and not sigmoidoscoping them. But I must tell you that quite a number of physicians do not like the sigmoidoscope and when they see a patient with diarrhoea and they cannot find anything on physical examination, what happens next? It's out with the fountain pen, the X-ray form, barium enema please, and the patient goes off and has his barium enema, comes back negative. The sigmoidoscopy is *never* done then. So if you don't do it at that stage before you have your barium enema it will be missed—until the patient goes to another consultant, which he can't do quickly enough.

COMMENT. I should like to suggest that in the severe forms of colitis one should take into consideration the level of the serum albumin. I think where you have significant deficiency of the serum albumin, it is of prognostic importance.

CHAIRMAN. A further point of definition: I wonder whether you have any objective criteria for the definition of toxic megacolon, whether you take the transverse 6 cm, or more or what?

DE DOMBAL. No, we haven't got a definition of toxic megacolon, usually it can go to about 3 ft wide, but I agree that we do need a definition. The serum albumin in severe attacks falls. There is a regular sequence of what happens to the proteins; as the serum albumin falls the two globulins rise, and they do so before the attack becomes clinically apparent, there is a sort of iceberg phenomenon, the two globulins start to rise and then the attack becomes clinically apparent. During the attack one of two things happen. Either the γ -globulin goes up or it goes down, if it goes up he gets better, if it goes down he gets worse. This is our experience with about fifty-three patients in severe attacks of colitis and in about fifteen patients with Crohn's disease. It may be possible, ultimately, in a patient whom you are wondering whether to bring to surgery or not, to have a look at the serum proteins and say whether he is going to get better or worse. I think that this is something which requires further examination.

HANCOCK. Steroids are contra-indicated in toxic dilation as suggested by Dr Watkinson. Is this the general view? Is it right in such cases to give them steroids say for 24 or 48 hr? Secondly, chloramphenicol parenterally for ulcerative colitis: I hesitate to push this drug, but I am interested in it because I have done some work on drug complications and obliterations of the immune responses by toxic drugs and irradiation. Chloramphenicol is an immunosuppressant and it suppresses protein synthesis and it probably is a strong anti-inflammatory agent without the toxic effects of

steroids, and finally, its systemic use as far as I can see, is not followed by marrow-aplasia. Established examples are indeed few and far between. Chloramphenicol, I consider would be far better if you are going to look for immunosuppressants.

Thirdly, ileorectal anastomosis in a child, is there a place for this? particularly in the anxious mother and the poor or unintelligent patient. Fourthly, your method of sigmoidoscopy—do you do it in the left lateral or do you do it in the American knee-chest position?

CHAIRMAN. Well, can I dispose of these two semi-surgical question. Sigmoidoscopy: I do in the left lateral position, I have no experience of the other position, I have found this very satisfactory. Ileorectal anastomosis: people would argue a case for ileorectal in young children, to avoid ileostomy, but I would not make any exception to my general principles; I don't think ileorectal is a good operation, I have been disappointed in it and, as I say, I find ileostomy is well tolerated by children, if the rectum were diseased, I would not do an ileorectal anastomosis.

WATKINSON. I advised chloramphenicol orally, because I felt this was the drug least likely to produce diarrhoea on long-term usage. I have no experience of immunosuppressant properties of chloramphenicol. On the other hand I have seen one case with aplastic anaemia who had this perhaps a year before, but as the lady also had amyloid disease it is likely that these were not connected.

Toxic megacolon: in the early 1950s before Professor Goligher appeared in Leeds, I was the one who had difficulty in persuading surgeons to operate on ulcerative colitis. I did treat a number of patients with toxic megacolon, with success, with steroids. I would not do that now, the bowel is paper thin and there is a serious risk of perforation.

HANCOCK. Would you give them steroids just to bring the pulse down if it were up?

WATKINSON. I wouldn't, no. If toxic megacolon is present on admission I think it is an indication for urgent surgery, I would not embark on steroids.

GLICK. Professor Goligher, how much greater is the risk of surgery after a course of medical treatment in an acute case? There have been mentioned 3 days' treatment, 7 days' treatment. The great difficulty is that you often get a partial success in the treatment of an acute case. It is very difficult to decide when you are going to call the surgeon in. If you felt that the risk of operation was, say three times greater, then you would want to call the surgeon in sooner. Could you give us any sort of criterion for this?

CHAIRMAN. Well, it is difficult to be very precise but I would have thought that a short course of steroids and replacement therapy, for 5 or 6 days or a week, at the most. I don't think this would make very much difference; I think that it is when the treatment is allowed to carry on for a long while and perhaps the patient perforates without you realizing, that is when the risk arises. I would have thought that it is one's duty to give the patient a trial on medical therapy because, if you can get him to remit, this is a wonderful thing. But my point is that you should not prolong

this exercise more than, perhaps 5 or 6 days—perhaps a week.

GLICK. I think that in a previous article you once said up to a fortnight, I wondered why you have changed your mind?

CHAIRMAN. Well, we have become disturbed that we still have a high mortality with some of these patients. When you say a fortnight, it often is more than that by the time the patient comes to you, recently we have shortened the time and we have had an improvement in our mortality. But I must emphasize again that this could partly be due to a change in the type of case coming to us. I don't want to make exaggerated claims for this.

FOLLOWS. In view of the universal involvement of the rectum in ulcerative colitis, do you think, as a practical point, it is sufficient to use a proctoscope in making a diagnosis of ulcerative colitis, rather than a sigmoidoscope, or perhaps as well as a sigmoidoscope? Purely from the point of view of diagnosis.

CHAIRMAN. Well, actually proctoscopy is more uncomfortable for the patient than sigmoidoscopy. The proctoscope is usually rather bigger and a very narrow Lloyd Davies sigmoidoscope is much less disturbing to the patient than either a digital examination or a proctoscopy and gives you a far better view; a far more precise instrument I would have said.

FOLLOWS. I was thinking really—someone who is not used to using a sigmoidoscope could use a proctoscope without any danger.

CHAIRMAN. Well, that's true. I should have thought that it is not unreasonable to ask people to learn to use a sigmoidoscope, it is not a very sophisticated instrument.

FLETCHER. May I ask Dr Watkinson to define again, as I may have misunderstood him, his indications for steroid therapy. He just puts two classes I think, of absolute indication. A fulminating attack not responding to simple medical treatment, and an attack associated with systemic complications. But he then went on to show a slide which showed prednisone as the steroid he would use for mild cases.

WATKINSON. I try to work in an orderly progression. I try initially the effect of diet and simple measures, antispasmodics, in mild cases to see if that will help. I next try the effect of salazopyrin orally, next I try the effect of topical treatment and finally try the effect of systemic steroids. Now the rapidity with which one produces these treatments depends on the severity of the case. In the urgent fulminating cases one has to throw the whole lot at them in the hope of effecting a remission and start all these treatments simultaneously. For a milder case one gives these treatments over a matter of some weeks perhaps on an out-patient basis. My reason for giving ACTH or cortisone in the severe attack is because the remission rates have been shown to be much better, and, further, steroids do have fluid and salt retaining properties which this sort of patient wants. Prednisone gives good results in the milder cases, particularly the distal cases of proctocolitis, it has fewer side effects, fewer electrolyte problems, and is very suitable for an out-patient basis.

I have always felt the shock of an ileostomy to a patient who has only been ill for a couple of weeks

is a very serious one but, as Professor Goligher has said, the time for which we persist with the medical treatment has progressively shortened. Originally we tried to make it between 10 and 14 days, now we use the whole therapeutic armamentarium and, unless an unequivocal improvement occurs within a week, surgery is considered. I am afraid an improvement under present medical treatment only occurs in about 50% of this type of case and in the elderly patients if any deterioration occurs surgery is required much earlier.

PEARSON. We heard how unspecific the sigmoidoscope findings are in ulcerative colitis. I wonder what is the danger of misdiagnosing ulcerative colitis in patients with other causes of diarrhoea and what dangers are there. In other words, how much secondary mucosal change you get with say an infective diarrhoea or small bowel diarrhoea?

CHAIRMAN. Well, we certainly find that people who are having antibiotics sometimes have rather an excessive mucus, and this can be confusing. In people who have Crohn's disease higher up the intestinal tract, sometimes you are not quite sure about the appearance of the rectal mucosa, whether it is absolutely normal or not. But I am not sure whether this is due to the fact that there is already disease in the rectum. Though I have had very little experience of specific dysenteries, I imagine that in a bacterial dysentery the changes might look very like those of an ordinary ulcerative colitis; and in an amoebic dysentery there are changes.

ZAHRAI. I would like to ask Dr Watkinson what is the colonic flora like in ulcerative colitis, and if it is known if it makes any difference to the management of the acute case?

WATKINSON. No, I am afraid very little is known about the colonic flora in ulcerative colitis. Dr Tonkin of the Westminster Hospital has claimed clinical improvement by changing the intestinal flora by giving these patients lactobacillus preparations. It has been shown that a drug like Salazopyrine has no effect on the bacterial flora. This was shown by Dr Bagen of the Mayo Clinic nearly 20 years ago. So I think very little is known about this. I have no experience of these lactobacillus preparations myself.

CHAIRMAN. To come back to your question about sigmoidoscopy. I think a very important point I should make is that Crohn's disease of the large intestine is now terribly common, almost as common as ulcerative colitis in my experience. I get as many cases of Crohn's disease of the large bowel as I do of ulcerative colitis and it often presents appearances different from those of ulcerative colitis. To start with the rectum may not be involved at all, even though the colon is involved higher up, and whenever you get a patient with what appears to be colitis and the rectum is not involved—but the involvement is higher up, this makes diagnosis of Crohn's disease almost certain. Secondly, the rectum may be involved but, if it is, the changes are apt to be patchy, you may get little areas of normal mucosa, normal vessel pattern, and then areas of colitis or proctitis. In addition, you often get quite wide fissures and ulcers, which have been recognised as an important diagnostic sign of Crohn's Disease. Lockhart-Mummery

and Morson have emphasized this. So that sigmoidoscopy and rectal examination can often indicate that you are dealing with a Crohn's rather than a colitis. One can soon learn to recognize the typical anal ulcers characteristic of Crohn's disease which were previously confused with tuberculous ulcers both on clinical and histological grounds. However the finding of the typical non-caseating giant cells on histology helps to clinch the diagnosis. Radiological appearances are also suggestive, one gets skip lesions, spiculated ulcers and marked mucosal oedema. In my practice, so-called segmental colitis is awfully rare, if it exists at all. Granulomatous colitis is very common and it is becoming more and more common and constitutes 50% of the cases.

QUESTION. When we are faced with explaining to a patient or relative that they need a total proctocolectomy, as a last resort we explain to the relative that there is a danger of malignant change in later life if you persist without surgery. Now then, can you tell us categorically that we need not tell the patients with Crohn's disease that they are liable to neoplasm?

CHAIRMAN. Oh, you could not say that at all, we have had two cases of carcinoma with Crohn's disease, and it may be that there will be more as time goes by. After

all, Crohn's in the large bowel has only been seriously recognized in a big way for the last few years; there are not all that number of cases that have been followed up for 10, 15, 20 years. The thing that worries me in talking to patients who have Crohn's disease in the large bowel, in selling them an ileostomy and proctocolectomy, is can I tell them they will never have Crohn's in their small bowel? and of course I cannot. When it comes to colitis I can, I can promise them that they will not have any further trouble with colitis, but when you come to Crohn's you cannot say that. The indication at the moment is that they do remarkable well, much better than the small-bowel Crohn's, but you don't know and it is a very worrying thing; I have had several patients now who have had small-bowel Crohn's resected, and then got large bowel Crohn's and life is miserable so that eventually I had to do an ileostomy and proctocolectomy. I obviously had to be very alive to the possibility of a recurrence of this Crohn's in the small bowel. On the other hand, the patients were in a terrible state and they were treated by ileostomy and proctocolectomy, and they have done very well, but what is the future? I think we ought to be absolutely candid with these patients.