were male. In his female case he first of all carried out transurethral resection of the bladder neck, which had only a slight effect on the residual urine, but considerable benefit was found after removal of two-thirds of the distended bladder. This case suggests that the primary pathology may be in the bladder itself.

Discussion

It is suggested that there are two types of bladder atony, the myogenic and the neurogenic, or possibly a combination of the two, in which some muscle as well as nerve degeneration takes place in the bladder wall.

Crabtree and Muellner, and later Houtappel, found, as we did in Case 1, that an increase in fibrous tissue around the smooth-muscle bundles is absolutely characteristic of the histology of the resected bladder wall. The absence of nerve-ganglion cells also seen in Case 1 may be of significance here.

The theory is advanced that there is either a nerve degeneration or a muscle degeneration in the bladder wall in these cases, and that atony and distension occur simultaneously so that no renal back-pressure effects are seen. In our experience the condition is predominantly found in females; most of the male cases reported have had either prostatism or some organic obstructive lesion. We have, in fact, experience of one male patient, aged 54, whose bladder contained on occasion as much as 80 oz. (2,275 ml.) of urine, but who micturated quite normally and could be catheterized easily. The absence of full investigations in this case, however, precludes its inclusion with confidence in the present series.

It is generally agreed that the ideal treatment in these cases, after careful exclusion of any of the common factors causing bladder distension, is subtotal cystectomy, removing two-thirds or three-quarters of the redundant bladder wall. Transurethral resection of the bladder neck by itself has no effect on the residual urine. There appears to be some chance of the residual urine increasing slightly in amount after partial cystectomy.

Summary and Conclusions

Four female cases of a hitherto neglected condition—primary atony of the urinary bladder—are described. Most of the sparse literature on the subject is quoted.

The classical clinical picture of the condition is a palpable distended bladder with large residual urine and often little in the way of symptoms except occasionally frequency. The patient really has an overflow retention. On cystoscopy no obstruction of the bladder neck is to be found, and a bladder wall thrown into numerous smooth folds is typical. The absence of hydronephrosis or hydro-ureter on pyelography and the absence of disturbance of blood chemistry or blood pressure are also constant features.

Subtotal cystectomy is the treatment of choice, and this was done in one case, but no great harm appears to result if the condition is left in the older patients, as no progressive renal damage is likely to occur. Cystometric findings are also characteristic in these cases.

There is no obvious reason why a comparable condition should not occur in the male.

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TREATMENT OF CHRONIC NON-SPECIFIC DIARRHOEA A CLINICAL COMPARISON

BY

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There are a number of persons who suffer perennially from chronic non-specific diarrhoea. The aetiology in these cases is no doubt diverse, but they are similar in that they form a symptomatic group in which no organic lesion can be discovered. Various forms of symptomatic relief are attempted, among which the use of a derivative of opium or one of the various antispasmodics on the market are popular at present. It seemed important that a clinical comparison should be made of the effectiveness of such treatment.

The selection of an antispasmodic was difficult, for there is no comparative study of the effectiveness of the many preparations available. Tricyclamol has been shown to be effective in decreasing gastric motility in balloon motility studies (Anderson 1955) and also in barium studies (Aylett and Douthwaite, 1955). Claims have also been made for its effectiveness in the control of "hypercholinergic" bowel symptoms (Schwartz *et al.*, 1955). However, the final selection of tricyclamol was arbitrary and was made largely on the ground that a supply was readily available. It is believed, however, that it may be representative of the group of antispasmodics. For comparison, codeine was selected because it has been used for many years in the treatment of diarrhoeal states and has been found effective in the hands of many clinicians. Codeine was used in a dosage of 30 mg. t.i.d. and tricyclamol in a dosage of 50 mg. t.i.d.

Material and Method

Selection of Subjects.—The subjects for the trial were patients attending the routine hospital out-patient department. All of them had bowel symptoms for at least six months prior to the commencement of the study. Immediately preceding admission to the trial all had at least 14 bowel actions a week, with loose or watery motions, often associated with abdominal discomfort. Examination by barium meal, barium enema, and sigmoidoscopy was negative in all cases. In

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the four subjects tested the faecal fat was normal. There was no gross evidence of steatorrhoea in any case. In all, nine persons agreed to co-operate in the trial. Of these, six suffered from constant diarrhoea and three had intermittent attacks with only brief periods of remission. The group was a heterogeneous one. The aetiology must be a matter of some dispute in any individual case. While in some of the patients the condition may have been determined by emotional disturbances, in others no such factors were seen to be present. In the absence of a satisfactory classification of the chronic diarrhoeas no attempt has been made to categorize these subjects. They are presented as a symptomatic group—probably of mixed aetiology—in which a trial of symptomatic control has been undertaken.

Plan of Trial.—Before the administration of either of the preparations each subject was observed over a period of at least 14 days. During this time each completed a daily stool chart giving full details of the number and consistency of the stools. A full record was also made of any abnormality such as the presence of blood, pus, or mucus, and a brief note of the general condition on that particular day. In fact, most persons were observed for much longer periods before beginning the trial, as the preliminary examinations were not completed within a fortnight. The subjects understood the objective of the trial, but they did not know the nature of the drugs being employed. Each drug was administered for a period of 14 days, during which time stool charts were completed in full. Five subjects received codeine in the first fortnight of the trial, followed by tricyclamol in the second fortnight. For the remaining four subjects the order was reversed. Assessment of the effectiveness of the drugs was made first of all on the average number of stools passed per week and, secondly, on the patient's subjective reactions to the drug.

Results

The Table sets out the results of the trial. The figures in the "control" column refer to the average number of stools passed per week during the observation period of a fortnight prior to administration of the drugs. Comparative figures for the fortnight during which codeine and tricyclamol were administered are also given.

Average Number of Bowel Actions per Week

Subject	Control	Codeine	Tricyclamol
L.P. ..	16	5	Stopped on day 3
W.R. ..	17	10	40*
E.W. ..	25	11	25
K.D. ..	18	7*	Stopped on day 2
G.G. ..	17	8	15
P.K. ..	31	7	32
D.K. ..	19	14*	40
J.S. ..	21*	9	Stopped on day 3
M.E. ..	21*	12	23
Average	21	9	29

* Approximate figures: patients failed to maintain detailed records.

Using the number of stools passed per week as the objective measure of the effectiveness of these drugs, it is seen that codeine reduced the number of bowel actions to a normal figure in most subjects. Tricyclamol, however, did not do so in any member of the group.

Patients' Subjective Reactions

The patient's subjective reaction was strongly in favour of codeine in all cases but one. In addition to

reducing the number of bowel actions codeine also decreased the urgency and precipitancy of defaecation. The subjects had an unaccustomed sense of well-being and security, and felt more able to lead a normal social life without fear or embarrassment.

It was remarkable that all but one subject expressed themselves strongly against tricyclamol. These persons were not only increasingly handicapped and embarrassed by frequent urgent bowel actions, but in some cases experienced general symptoms of an unpleasant nature. Three felt sufficiently unwell to discontinue the drug after two or three days of treatment. These subjects described their symptoms as profound malaise, depression, and lack of ability to concentrate. One patient appropriately described himself as being "washed out."

Five of the subjects complained of severe abdominal colics while taking the antispasmodic. One complained of a dry mouth and two of blurring of vision. While taking codeine two of the subjects complained of drowsiness, which, however, was not sufficient to interfere with normal work. It seemed clear, even using such a small experimental group, that codeine was an effective drug in the symptomatic control of the group, while the antispasmodic not only failed to control the symptoms but exaggerated most of them.

Discussion

The number of subjects used is small, but in view of the clear result we did not think it necessary or justifiable to investigate a larger group. It is clear that the administration of tricyclamol is not effective in controlling this group of non-specific diarrhoeas. Even in those subjects in whom side-effects directly attributable to the antispasmodic were present and in whom it would not be desirable to increase the dose of the drug, there was no effective control of the colonic symptoms. In one subject the dosage of tricyclamol was increased to 300 mg. a day without effecting any control of diarrhoea. We have used other antispasmodics in an attempt to effect symptomatic control of diarrhoea, both before and since this trial, but without success, and we are satisfied that tricyclamol is not a particularly unfortunate choice of antispasmodic. The results of the trial probably apply in general to other preparations.

It may be that the use of antispasmodics will be beneficial to a limited number of these sufferers, as possibly certain of the persons who at present are grouped as cases of non-specific or nervous diarrhoeas will in the future be proved to be patients suffering from autonomic imbalance of the bowel. In these the administration of an anticholinergic or antispasmodic might be effective. However, until such time as this nebulous group of conditions can be satisfactorily broken down into aetiological categories, it would not seem to be rewarding to administer anticholinergics indiscriminately. On the other hand, codeine is cheap and effective, and remarkably free from untoward reactions or side-effects in the dosage used. Symptomatic control of the symptoms, using codeine, has been continued in a large number of patients for many months. As the diarrhoea in many of these cases tends to clear up spontaneously after a varying period of time the use of codeine in doses of 30 mg. two or three times daily is a very effective method of tiding a patient over the acute phase of the bowel disorder.

Summary

A clinical comparison is presented of the use of an opium derivative, codeine, and an antispasmodic, tricyclamol, in the treatment of chronic non-specific diarrhoea.

The antispasmodic failed to control the symptoms and in a number of subjects exaggerated them.

Codeine is an effective symptomatic remedy for chronic non-specific diarrhoea.

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Medical Memorandum

Dequalinium in Myasthenia Gravis

During the course of treatment of a severe case of myasthenia gravis the patient developed a pharyngitis and was given decamethylenebis-4-aminoquinaldinium chloride (dequalinium chloride; "dequadin"). This compound was discovered to have antimicrobial activity by Babbs *et al.* (1956). They also found that, like other heterocyclic polymethylene bis-quaternary ammonium salts, there was a neuromuscular blocking activity, and that mice receiving it intravenously were paralysed. Clinically this drug is used as an oral antiseptic, and whilst being given on this account marked improvement was noted in the patient's myasthenia. The following case is reported because the problem may be worthy of further specialized study. The initial diagnosis in this instance was reached after marked resistance to suxamethonium ("scoline").

CASE HISTORY

A woman aged 62 was admitted to hospital on March 10, 1957, with a three-days history suggestive of a bulbar palsy. She had first developed difficulty in speaking. Progression of this disability with the onset, the previous day, of inability to swallow had made special care necessary. A vascular cause was at first suspected in view of the acute onset and the finding of a blood pressure of 230/120 mm. Hg. Her previous health had been good apart from some weakness in the left leg of six to eight months' duration on climbing stairs.

During her first day in hospital laryngeal stridor with difficulty in breathing led to anxiety. Preparations were made for a tracheotomy under general anaesthesia. Suxamethonium up to 9 ml. (450 mg.) did not paralyse the vocal cords, and, myasthenia gravis being suspected, she was allowed to come out of the anaesthetic and given intravenous neostigmine, 2 ml., which produced immediate relief of all symptoms.

The full-blown syndrome of myasthenia became obvious during the first week, with ocular palsy, drooping of the lids, and weakness of the neck and arms in addition to the initial symptoms. These were relieved by neostigmine and pyridostigmine bromide ("mestinon") for about two hours. After 11 weeks she was discharged on neostigmine, 30 mg. every three hours by mouth. She was able to get around quietly, although weakness became obvious two hours after her neostigmine.

One month after discharge the patient complained of a sore throat and, associated with this, a deterioration of her

voice. Examination showed some inflammation of the fauces, and dequalinium, one tablet (0.25 mg.) every three hours, to be sucked, was prescribed. In 24 hours there was marked improvement in her condition, and for the first time since the onset she felt almost normal. Before this she had felt herself needing head support even 20 minutes after neostigmine. Her voice, swallow, and general strength also improved and she felt able to go for short walks. After three days the dequalinium was stopped and immediately her condition deteriorated, to cause concern.

As a result of this, a trial was begun as follows. (1) Dequalinium, 0.25 mg., was given four-hourly for one week and then withdrawn the next week. This was repeated five times. It appeared that whilst on the drug the patient was considerably improved and had no symptoms. It was in fact possible to reduce the dosage of neostigmine to every four instead of three hours, and between doses of this drug she was much stronger. When off dequalinium she felt tired within half an hour after neostigmine, and before each dose was due felt very weak, unable to talk or swallow, and had double vision. (2) A blind trial with dummy tablets was performed on three separate occasions. Three days on dequalinium were alternated with three days on dummy tablets. Whilst on dequalinium there was considerable improvement and a relapse during the control periods. In fact, the relapse was enough to require almost three days on dequalinium before a return to normal.

The patient has been on dequalinium continuously for six months without ill effect and is asymptomatic on all counts with a steadily reducing dosage of neostigmine. At present she is having dequalinium, 1 tablet six-hourly, and neostigmine, 30 mg. six-hourly.

COMMENT

The basic pathology of myasthenia gravis is still far from clear. It is difficult, therefore, to give a simple explanation of the findings in the case reported above. The present position regarding the physiological action of neuromuscular blocking agents has been reviewed by Burn (1957). It would seem in myasthenia that there is a competitive block and the muscle and plate respond abnormally. Grob, Johns, and Harvey (1956) suggest the possibility that the defect could be due to choline or an abnormal product of acetylcholine. Potassium is known to be of great importance in the production of the end-plate potential, and Bülbring and Burn (1942) have investigated how sensitivity may be increased by adrenaline.

It is known that myasthenia gravis may remit spontaneously. However, there was sufficient immediate benefit in this case to suggest that dequadin might be responsible. It could act as a mild depolarizer or anticholinesterase potentiating the action of acetylcholine, or it might resensitize the plate.

The marked resistance to suxamethonium in myasthenia gravis is also not fully understood, but it too may be affected by the competitive block reaction. An adequate explanation is still required.

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