

## A CLINICAL TRIAL OF A CONTACT LAXATIVE: REPORT OF 250 CASES IN A SURGICAL UNIT

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One of the more unpleasant procedures in the routine pre-operative preparation of the surgical patient is the evacuant enema to prevent faecal contamination owing to loss of sphincteric control when under anaesthesia and, in the case of operations on the bowel, to ensure that the bowel is empty. Besides being unpleasant and often causing distress, it can sometimes give rise to the dangerous complication of bowel perforation owing to existing pathology or careless administration with grave consequences. This complication, though rare, is one of the causes of iatrogenic and avoidable fatalities.

The administration of the enema is also one of the less pleasant duties of the nurse. It is time consuming, taking at least thirty minutes between the time of administration and the clearing of the bed-pan and longer if the time taken to boil up the apparatus and its subsequent cleaning is taken into consideration. All this imposes demands on the nurse whose training befits her to other more beneficial aspects of patient care.

In the post-operative period gas colic and constipation are common problems. The enema is usually contraindicated in the early post-operative period particularly in the cases where these complications are most likely to arise; and the flatus tube, the "small" enema and the inert rectal suppository are the alternatives which often afford only partial relief.

Cases of chronic constipation especially in geriatric patients eventually require regular enemata for satisfactory evacuation after all the various bulk, lubricant and irritant laxatives and purgatives fail to produce an effective response owing to toleration. This imposes further demands on the nursing staff in a group of patients already requiring more than the usual nursing care.

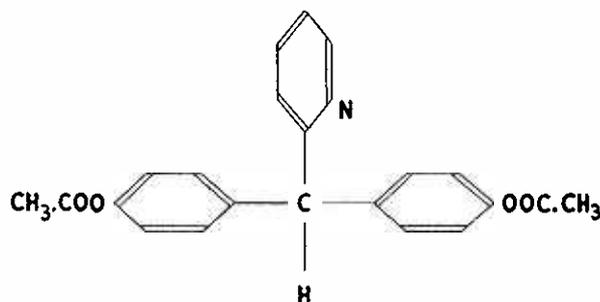
Because of all these difficulties, a substance that can be administered both orally and rectally and which will bring about a satisfactory bowel evacuation is highly desirable and should help overcome some of these problems. Such a substance has been discovered in recent years after a search of four years involving over 200 synthetic chemicals, and has been imported into Singapore under the trade name of Dulcolax.

### DEFINITION

A contact laxative is defined as a substance which acts by contact with the mucosa of the bowel resulting in increased peristaltic activity; this action is not dependent on any absorption of the substance and hence on enteral administration there is no action via the systemic circulation.

### CHEMISTRY

Dulcolax is (4, 4' — diacetoxy — diphenyl) — (pyridyl — 2) — methane with the following structural formula:—



It is the most active among the diphenyl-pyridyl-methane group of substances owing to the presence of a nitrogen atom in the alpha position on the pyridine ring. It is colourless, odourless and tasteless. It is insoluble in water and alkaline media but soluble in dilute mineral acids and organic solvents.

### PHARMACOLOGY

In 1953, Schmidt drew attention to the fact that laxatives being often taken for a long time without medical supervision should be thoroughly tested with regard to their toxicity and observed for any latent undesirable effects arising from prolonged usage. He conducted a series of experiments and showed that Dulcolax acted only on contact with the mucosa of the large bowel. Perfused isolated segments of jejunum and ileum showed no increase in peristaltic activity when Dulcolax was added; similar isolated segments of colon showed a marked peristaltic response when so exposed to the substance. He further demonstrated it is a true "contact laxative" by

giving it orally to animals whose small intestine had been tied off to prevent the substance from reaching the colon; no increase in peristaltic activity resulted. These tests were carried out carefully with the necessary controls and the bowel was later examined for evidence of cumulative damage that may result from the "tying off" the bowel. He also found that with subcutaneous administration, eight times the oral dose was necessary to evoke a response of similar degree. Further evidence of the contact nature of action was furnished by Göing and Schaumann (1955) who used a system of two balloons in the rectum or sigmoid colon; the function of the lower or more distal balloon was to occlude the lumen, the upper or more proximal balloon was to record changes resulting from peristaltic activity before and after the introduction of the drug into the large bowel. They showed that the stimulant effect was abolished by the topical application of a local anaesthetic. When the anaesthetic was applied after the Dulcolax suppository, peristalsis ceased within two to three minutes; when the anaesthetic was applied to the rectum or colon below the lower balloon there was no inhibitory action. They also found that morphine suppressed the peristalsis induced by the drug; this inhibition was reversed in some cases by the administration of Nalorphine (NAL), a morphine antagonist.

Schlegel (1954) added 15 mgm. of the drug to a standard barium enema and observed the resulting peristaltic activity fluoroscopically; activity started in the proximal ascending colon and progressed slowly to the sigmoid in waves; no local spasm was seen to occur. Göing and Schaumann (1955) also found that the increased peristaltic activity was not associated with spasmodic activity by their system of balloons.

Meyer-Burgdorff and Eichler (1954) and Ganz and Zindler (1955) have demonstrated that the level of intestinal tone did not appreciably affect the action of the substance; it is also effective in cases of partial ileus. The former workers also found that Dulcolax suppositories brought on bowel movement in all 17 patients in whom limited hypothermia had been induced by chlorpromazine and analgesics. As chlorpromazine has an adrenergic ganglion-blocking action, it suggests that Dulcolax works independently of a segmental reflex. Hobbs (1958) and Keogh and Fraser (1958) have reported satisfactory results in the treatment of megalocolon.

All these observations suggest that the drug works by a local reflex arc brought on by neurogenic stimulation of sensory nerve endings in the colonic mucosa and involving the Auerbach's and Meissner's plexuses. If such is the case, it should

have no effect in cases of Hirschprung's disease when it is given rectally and confined to the aganglionic segment of bowel; the opportunity of making this test is awaited.

#### Normal Action

Generally the drug acts within 15-60 minutes after contact with colonic mucosa. When given as suppositories action follows within 30-60 minutes. When given orally it acts in 8-10 hours. It is best taken at night with a glass of water and its effect takes place the following morning. It is non-irritant to the alimentary tract. Even after prolonged administration and high dosage the colonic mucosa shows no change when examined sigmoidoscopically. (Bath, 1953; Hauff, 1954; Scott, 1956). Schmidt using laboratory animals could detect no changes in the mucous membrane of the gastrointestinal tract after being subject to double the effective dose for three months; neither could he find any demonstrable changes in any other organs. The stool produced is usually soft and formed, watery stools or diarrhoea being uncommon. There is little or no associated colic.

#### Safety Factor

The normal effective dose in animals is 15 mgm/kg. (Schmidt, 1953). In acute toxicity tests all rats survived doses as high as 3 gm/kg. It was therefore concluded that the drug has the extremely high therapeutic index of 1:200. The lethal dose has never been established on laboratory animals: no animal has ever been killed by the drug.

#### Side Effects

No local or systemic effects have been observed so far. Systemic side effects are rather unlikely as the drug is not absorbed. The blood sedimentation rate, renal and hepatic functions are unaffected. (Frankl, 1953).

#### Contraindications

There appears to be no contraindications except when intestinal activity is undesirable, such as in the acute abdomen.

Twice the effective dose has no effect on the gravid uterus in rats, (Schmidt, 1953). Förtsch (1953) came to the same conclusion on obstetric patients. He also found that it is well tolerated by patients with hyperemesis. As it is not absorbed, it is not excreted in the milk and is hence the ideal laxative in post-partum mothers. (Förtsch, 1953; McGregor, 1960). Bath (1953) found it well tolerated by patients with peptic ulceration; he also found it is not habit forming. There is no loss of potency even after prolonged usage. (Meyer-Burgdorff and Eichler, 1954).

### Other Features

The saving in nursing time is much stressed by Sowerbutts (1960). He also compared the cost of patient preparation by an enema with that by Dulcolax and found the latter to be substantially cheaper. Both Rutter (1959) and Sowerbutts (1960) stressed the advantages of saving the patient from an "onslaught by water" and concluded that patients are spared a great amount of apprehension and discomfort.

The substance has been used extensively with satisfactory results as a preparatory procedure in radiological examinations of the abdomen, when faecal and gas shadows often prevent a satisfactory interpretation and which may necessitate repeat examinations, leading to undesirable increase in exposure to irradiation. (Schlegel, 1954; Kolshorn, 1954; Mies, 1957; Keogh and Fraser, 1958; Poppel and Bangappa, 1959; Kaye, 1959 and Sowerbutts, 1960). Clark (1957) used it on geriatric cases. Aue (1954) reported its efficacy in chronic intractable constipation occurring in children. It has also been used successfully in adult cases of chronic constipation by Frankl (1953). Brandt and Brandt (1954) reported its use on 100 cases of Parkinson's disease which were treated by the Italo-Bulgarian regime of increasing dosage of belladonna—one of the side effects of which is increasing constipation owing to decreased intestinal tone; he recorded no failures. Mandel and Silinsky (1960) found it well tolerated by patients with myocardial infarction and reliably effective in relieving constipation. Its use in gynaecological and obstetrical patients have been recorded by Förtsch (1953) who found it reliable even in obstinate cases of constipation and there were no undesirable side effects.

In 1954, Hauff reported its use post-operatively on over 200 patients. After abdominal surgery he advised its use with an enema on the third post-operative day and that the enema can be dispensed thereafter. Meyer-Burgdorff and Eichler in the same year published their results on 124 post-operative cases where they found it effective without being used in association with an enema. In cases of operations on the bladder and bladder neck, Dulcolax suppositories brought about an evacuation on the second instead of the usual fourth or fifth post-operative day. Ohling (1955) reported his experiences on 647 cases following abdominal and orthopaedic operations. He found that bowel movement followed in 15-30 minutes in male patients and in female patients it usually took about 60 minutes. No evacuation occurred only in a few cases and several of these were examined by X-rays which showed the bowel already empty of gas or faeces. The first series

on surgical patients published outside Germany was that of Scott (1956), who reported that 90% of 87 patients (of the Middlesex Hospital, London), who were allowed out of bed on the first post-operative day had a normal bowel action after rectal administration of the drug. Rutter (1956) found its efficacy impressive; out of 380 admissions into surgical wards over a period of one year only five enemata were given. Of the 187 pre-operative patients only one was recorded as a failure. Lavoie and Murat (1959) found it effective in 69 of 74 post-operative patients.

While in London in 1959-60, my attention was drawn to this new laxative as it has been recently introduced to the surgical wards of some of the London hospitals with satisfactory results to the patient, surgeon and anaesthetist and delight to the nursing staff as I have personally observed. In view of the acute shortage of nursing staff afflicting Singapore which promises no easy or early solution, and the other advantages of doing away with the enema at least in the majority of cases in surgical wards, a clinical trial of Dulcolax was embarked upon in the Professorial Surgical Unit, General Hospital, Singapore.

### METHOD AND MATERIALS

Dulcolax is supplied in 5 mgm. enteric coated tablets and 10 mgm. suppositories. The dosage used in the various series reported has varied from 2 to 6 tablets orally and 1 to several suppositories in various combinations. In the interests of costs, it was decided to use the smallest dosage-formula in this trial as a start and to increase it if necessary as the trial proceeded. As it turned out, this proved unnecessary.

### Modes of Administration

Two regimes were adopted:—

- A. Pre-operative Cases: Two 5 mgm. tablets orally the night before operation followed by one 10 mgm. suppository on the morning of the operation.

(If no bowel action followed, the routine pre-operative enema is administered prior to sending the patient to the theatre).

- B. Post-operative and Other Cases: One 10 mgm. suppository which was repeated if there was no bowel action after two hours.

No bed-pans were necessary except in non-ambulant patients.

### Patients

With the exception of one group of pre-operative patients, all other patients in the Professorial Surgical Unit during the period of trial had one

of the two modes of administration of Dulcolax described above instead of an enema, laxative or purgative customarily prescribed. The group of excepted pre-operative patients are those having operations on the colon, rectum and anus. It was felt that owing to the decision to use the minimum dosage, these cases would not receive a fair trial as such cases are normally prepared with repeated rectal washouts in addition to enemata. It is hoped that this group of cases will be the subject of a further trial later. The trial covered a period of six weeks.

The results were carefully recorded by the nurse on a proforma which besides the identification data (e.g. name, age, etc.) includes the following items: diagnosis; date of operation; date of administration of Dulcolax; nature of operation; time interval between administration and evacuation (in relation to the suppository); the quantity of the evacuation; the absence or presence of associated colic and, if present, the degree of colic. The proformas were collected by the ward sisters and checked by them to see that they had been fully and accurately filled up. It is gratifying to record that all the nursing staff gave their full co-operation in carrying out this trial.

In order to assess more accurately the subjective sensation of colic two groups of fourth and fifth year medical student volunteers were tested with one and two 10 mgm. tablets of oral Dulcolax respectively. The number of bowel motions and their consistency were noted in addition to the degree of colic experienced.

**RESULTS**

**Definitions:** A case is put in the post-operative group when he or she required a bowel stimulation within the first 10 days of an operation and for which a Dulcolax suppository had been administered. The pre-operative group is self-explanatory; so are the miscellaneous groups described below.

A total of 250 cases are available for study made up as follows:—

**TABLE I. SHOWING THE TYPES OF CASES.**

Group		No.
A.	Pre-operative Cases	111
B.	Post-operative Cases	92
C.	Miscellaneous	47
Total		250

**A. Pre-operative Cases**

Of this group of 111 patients only 5 had no bowel action; this gives a failure rate of 4.5%. The other 106 cases (95.15%) were completely satisfactory, there being no instance of faecal soilage at any stage during or after operation. (See Table II).

**TABLE II. PRE-OPERATIVE GROUP.**

Effect	No. of Cases	%
No effect	5	4.5
Good evacuation	83	} 95.5
Very good evacuation	23	
Totals	111	100

All the surgeons in the Unit were consulted and they noticed no difference with regard to the efficacy of bowel preparation during the period of the trial compared to that obtaining prior to the inception of the trial.

16 cases were operated under local anaesthesia: 5 biopsies; 7 endoscopies; 2 excisions of fibroadenoma of breast; 1 excision of submandibular mixed tumour and 1 enucleation of thyroid adenoma. (It is the practice of the Unit to have all patients going for operation, including those to be performed under local anaesthesia, prepared for general anaesthesia in case such a need arises). The remaining 95 cases had a general or spinal anaesthetic.

**Types of Operation**

The pre-operative group of patients had operations shown in Table III.

**TABLE III. SHOWING THE TYPES OF OPERATION PERFORMED ON THE 111 PRE-OPERATIVE CASES.**

<b>Biopsies:</b>	
Fibrosarcoma, chest wall	1
Needle biopsy, breast carcinoma	2
Needle biopsy, thyroid carcinoma	1
Needle biopsy, lung carcinoma	1..... 5
<b>Endoscopies:</b>	
Cystoscopy (G.A.)	2
Bronchoscopy	1
Gastrosocopy	1
Peritoneoscopy	4..... 8
<b>Skin and Jaw:</b>	
Skin graft	6
Repair of harelip	1
Excision of maxillary cyst	1

Excision of submandibular mixed tumour	1
Excision of lipoma	1
Drainage of abscesses and carbuncles	5.....15
Thyroid Gland :	
Thyroidectomy, partial and sub-total	5
Enucleation of adenoma	1..... 6
Breast :	
Mastectomy	5
Excision of fibroadenoma	2
Excision of chronic sinus	1..... 8
Chest :	
Lung resections	3
Oesophageal transection	1
Ligation of P.D.A.	1
Cervical sympathectomy	2..... 7
Abdominal Wall :	
Herniorrhaphy	13
Suture of burst abdomen	1
Secondary suture of wound	2.....16
Abdomen :	
Roux en Y bypass of stomach	1
Gastrectomy, all types	5
Gastroenterostomy	1
Drainage, subphrenic abscess	1
Appendicectomy	1
Cholecystectomy	10
Ovarian cystectomy	1
Spleno-renal anastomosis	1
Laparotomy only	4.....25
Genito-urinary :	
Nephrectomy	1
Nephroureterectomy	1
Nephrostomy	1
Prostatectomy	6
Litholapaxy	2
Urethroplasty	2
Drainage of Periarethral sinuses	1
Circumcision	4
Orchidectomy	2.....20
Others :	
Inferior vena cava-venogram	1
<b>TOTAL</b>	<u>111 cases</u>

**Time Taken to Act:** The time response, i.e. the interval between administration of the suppository and bowel action was recorded and the results are given in Table IV.

It will be seen that the bowels were opened within 60 minutes in 88% of cases. In more than half the cases (52%), action occurred in the 30-60 minute period. The fact that in about 12% of cases evacuation did not occur till over one hour suggests that the suppository should be given at least an hour before the scheduled

operation time. In practice this gave rise to little difficulty as only the first case on the operation list may be pressed for time but the usual ward activities wake the patient up a good two hours before the earliest scheduled operation, hence this difficulty was not a problem.

**TABLE IV. TIME RESPONSE. PRE-OPERATIVE GROUP.**

Time Response	No. of Cases	%
Less than 15 minutes	16	15
15-30 minutes	22	21
30-60 minutes	55	52
More than 60 minutes	13	12
<b>Total</b>	106	100

**Colic:** The incidence of associated colicky pain is given in Table V. Mild colic means the presence of colic that was neither unpleasant nor distressing. Moderate colic means pain that was definitely unpleasant but not severe. Severe colic means pain that was sufficient to cause distress to the patient.

**TABLE V. INCIDENCE OF COLICKY PAIN IN PRE-OPERATIVE GROUP.**

Degree	No. of Cases	%
No colic	64	60.4
Mild colic	36	33.9
Moderate colic	5	4.8
Severe colic	1	0.9
<b>Total</b>	106	100.0

6 patients experienced moderate or severe colic. The majority had no colic (60.4%) and the rest (33.9%) had only mild colic. The drug therefore rarely gives rise to distressing degrees of colicky pain.

#### B. Post-operative Cases

There are 92 cases in this group but fewer than 92 individual patients as some of them required bowel stimulation on more than one occasion in the post-operative period. Of these, 21 "cases" had a spinal anaesthetic and 61 "cases" had a general anaesthetic. No case operated under a local anaesthetic appeared to need bowel stimulation; this may of course be due to the nature of the operation rather than the anaesthetic.

There are no "failures" in this group but 6 cases needed a second suppository as the first had no effect after 2 hours. (See Table VI).

TABLE VI. POST-OPERATIVE GROUP.

Effect	No. of Cases	%
No effect	0	0
Flatus only	9	11
Good evacuation	73	77
Very good evacuation	9	11
Total	91	99

Types of Operation: The types of operation performed on this group of cases are listed in Table VII.

TABLE VII. SHOWING THE TYPES OF OPERATION PERFORMED ON THE 92 POST-OPERATIVE CASES.

Skin:		
Saucerization of carbuncle	1.....	1
Head:		
Craniotomy		3
Parotidectomy	1.....	4
Thyroid Gland:		
Thyroidectomy	2.....	2
Breast:		
Mastectomy		1
Excision of fibroadenoma	1.....	2
Chest:		
Lobectomy	1.....	1
Abdominal Wall:		
Herniorrhaphy		3
Burst Abdomen	2.....	5
Abdomen:		
Appendectomy		20
Gastrectomy		25
Cholecystectomy with or without		
Choledochostomy		16
Cholecysto-jejunostomy		1
Repair of perforated gastric ulcer		1
Gastroenterostomy		1
Splenectomy		1
Reduction of intussusception		1
Hemi-hepatectomy		2
Laparotomy only	22.....	66
Genito-urinary:		
Nephrectomy		1
Nephroureterectomy		1
Prostatectomy		2
Repair of ruptured urethra		1
Orchidectomy	2.....	6

Skeletal, amputation of toe 1..... 1

TOTAL \*93 cases

\*One patient had both gastrectomy and cholecystectomy.

It is interesting to note that cases where the bowel had been handled such as in abdominal operations, or disturbed, such as in retroperitoneal operations, form the majority of cases needing bowel stimulation for evacuation in the post-operative period.

Time Taken to Act: These observations are given in Table VIII.

TABLE VIII. TIME RESPONSE. POST-OPERATIVE GROUP.

Time Response	No. of Cases	%
Less than 15 minutes	7	9
15-30 minutes	18	11
30-60 minutes	26	32
More than 60 minutes	31	37
Total	82	100

There are more cases in the over 60 minutes category — 31 cases (37%) — than in the pre-operative group of patient, where only 12% of the cases took longer than 60 minutes for evacuation to occur. The difference is significant and is probably due to the depressed intestinal activity following anaesthesia and operation.

Colic: There was no instance of severe colic. 9 cases experienced moderate colic. The majority, 72 cases (88%), had mild or no colic. The results are tabulated in Table IX. The general impression was gained that the majority of patients were relieved of unpleasant or painful post-operative gas colic or abdominal distension with minimal discomfort.

In recording the degree of colic, care was taken to exclude the effect of pain due to the operation by careful questioning.

The following is one of several cases of post-operative ileus which has responded satisfactorily: Case I: L.K.M. an 18 year old Chinese youth was admitted on 8/11/61 with a one day history of severe epigastric pain. On examination he was found to have generalized peritonitis with a rigid abdomen and intestinal ileus. There were no localizing signs. Laparotomy was performed immediately through a lower right paramedian

incision and a gangrenous perforated appendix was found and removed. There was much free pus and the bowel was grossly distended with gas and intestinal secretions. The bowel was decompressed and the incision closed. The ileus persisted in the post-operative period and this was treated by continuous intragastric suction and intravenous fluid replacement for 72 hours by which time bowel sounds were heard. Flatus was not passed till the 4th post-operative and by the 5th day the bowels were still not opened and the abdominal distention was causing restlessness to the patient and some concern for the integrity of the wound. A Dulcolax suppository was inserted and a very large quantity of stool and flatus was passed within 15 minutes with only mild associated colic. He opened his bowels spontaneously thereafter and was discharged on the 8th post-operative day on a full diet and quite well.

TABLE IX. INCIDENCE OF COLICKY PAIN IN POST-OPERATIVE GROUP.

Degree	No. of Cases	%
No colic	40	49
Mild colic	32	39
Moderate colic	9	12
Severe colic	0	0
Total	81	100

### C. Miscellaneous Group

This group includes the following categories:—

- |   |   |                |
|---|---|----------------|
| (a) Constipation in the absence of operation                        | — | 37 cases       |
| (b) Subacute intestinal obstruction due to post-operative adhesions | — | 4 cases        |
| (c) Prior to radiographic examination                               | — | 6 cases        |
|   |   | Total 47 cases |

(a) All the 37 cases of constipation had a single suppository only, there being no case without response, and the results are summarized in Table X.

One patient in this group with paraplegia and associated constipation is worth recording.

Case II: C. H. a 23 year old Chinese man with an osteoclastoma of the 9th rib with vertebral and cord involvement giving rise to paraplegia

was operated on 16.9.60 when the tumour, involved rib and underlying pleura were excised. He remained paraplegic after operation and developed intractable constipation which needed daily enemata to prevent faecal impaction. He was put on Dulcolax suppositories nightly since 19.10.61 and had spontaneous bowel evacuation varying 2-7 hours after each suppository. He far preferred the suppository to the enema and the nursing staff were pleased to be relieved of an unpleasant routine.

TABLE X. RESULTS OF CONSTIPATION GROUP.

Effect	No. of Cases	%
No effect	0	0
Flatus only	2	5
Good evacuation	30	81
Very good evacuation	5	14
Total	37	100
Time Response		
Less than 15 minutes	7	18
15-30 minutes	8	22
30-60 minutes	14	38
More than 60 minutes	8	22
Total	37	100
Colic		
None	20	54
Mild	14	38
Moderate	3	8
Severe	0	0
Total	37	100

(b) The four cases listed under post-operative adhesions are cases who had previous abdominal operations and who were later admitted with signs of subacute intestinal obstruction. In all cases the obstruction was judged to be due to post-operative adhesions. In no case was the obstruction judged to be total. The general condition was good in all cases, the presenting and chief symptom being abdominal colic, and a two-enema test was considered unnecessary.

The results are summarized in Table XI.

TABLE XI. RESULTS OF SUBACUTE INTESTINAL OBSTRUCTION GROUP.

Effect	No.	Time Response	No.	Colic	No.
No effect	1	Less than 15 minutes	0	None	1
Flatus only	0	15-30 minutes	1	Mild	2
Good evacuation	3	30-60 minutes	2	Moderate	0
Very good evacuation	0	More than 60 minutes	0	Severe	0
Total	4	Total	3	Total	3

The case with no effect had an enema administered and the obstruction proved to be due to faecal impaction. It is possible that this case would have responded to orally administered Dulcolax.

(c) All six cases in the group prepared for radiographic examination had a good evacuation within 60 minutes of insertion of the suppository. Half of them had no colic and the other half had mild colic. Satisfactory films were obtained in all cases with no interference from gas or faecal shadows. The radiographic procedures performed were:

Intravenous pyelogram	3
Barium enema	1
Trans-hepatic cholangiogram	1
Trans-splenic porta-venogram	1
Total	<u>6 cases</u>

D. Medical Student Volunteers

39 students volunteered to try out the drug. These were divided into two groups; the first group of 14 students was given one 5 mgin tablets; the second group of 25 students had two 5 mgm. tablets. The tablets were taken at night and the effects were noted the next morning. The number of motions, their character and the degree of colic experienced were recorded and the results are tabulated in Tables XII and XIII.

In the "one tablet" group, two students experienced an unpleasant degree of colic; the rest had mild or no colic. One student had four motions consisting of loose but not watery stools; one had watery stools not associated with colic.

In the "two tablet" group about half had two motions; one had three motions consisting of soft or loose stools associated with a moderate degree of colic and tenesmus. Two had urgency.

TABLE XII. STUDENT VOLUNTEERS: ONE TABLET GROUP.

No. of Motions	No.	Degree of Colic	No.
None	0	None	8
1 motion	7	Mild	4
2 motions	6	Moderate	2
More than 2	1	Severe	0
Total	14	Total	14

TABLE XIII. STUDENT VOLUNTEERS: TWO TABLET GROUP.

No. of Motions	No.	Degree of colic	No.
None	0	None	6
1 motion	11	Mild	12
2 motions	13	Moderate	6
More than 2	1	Severe	1
Total	25	Total	25

28% had moderate or severe colic, a rather higher figure than those of the patients. In both groups the stools were formed and soft in the majority of cases.

Male-Female Time Response

It was noticed that male patients generally had a longer time interval between administration of a suppository and its effect in the post-operative period. It was decided to look into this difference in time response in greater detail and Table XIV shows the male-female time interval in the pre-operative group, post-operative group and total cases, i.e. including the miscellaneous group.

TABLE XIV. MALE-FEMALE TIME RESPONSE.

Time Interval	Males			Females		
	Pre-op.	Post-op.	All Cases	Pre-op.	Post-op.	All Cases
Less than 15 minutes	9	5	18	7	3	14
15-30 minutes	10	14	27	12	9	29
30-60' minutes	36	19	61	19	10	40
More than 60 minutes	8	29	43	5	3	11
Totals	63	67	149	43	25	94

To enable ready comparison the percentages occurring within 60 minutes and those occurring after 60 minutes are given in Table XV. by sexes for each group of cases with evacuation

TABLE XV. PERCENTAGES.

Time Interval	Pre-op Group		Post-op Group		All Cases	
	M	F	M	F	M	F
Less than 60 minutes	87.3	88.4	56.7	88.0	67.1	88.3
Longer than 60 minutes	12.7	11.6	43.3	12.0	32.9	11.7

It will be seen from the table that there is little difference between the sexes in time response in the pre-operative group of cases. On the other hand, in the post-operative group of cases there are, proportionally, almost four times as many males compared to females with a time response of longer than 60 minutes. Such a big difference appears unlikely to be due to mere chance. Cases

having had intra-abdominal, pelvic, extra-peritoneal and retro-peritoneal operations are probably more likely to have some degree of ileus in the post-operative period and therefore a longer time response and to take this factor into account, corresponding figures for cases after such operations are tabulated in Table XVI.

TABLE XVI. TIME RESPONSE AFTER "ABDOMINAL OPERATIONS".

Time Interval	Males		Females	
	No.	%	No.	%
Less than 60 minutes	34	54.8	14	87.5
Longer than 60 minutes	28	45.2	2	12.5
Totals	62	100	16	100

It will be seen that the great difference still holds. The chi-square is 5.6717, and  $P = < 0.02$ , where  $n = 1$ . This sex difference is therefore unlikely to be due to chance.

### CONCLUSIONS

The results show that a Dulcolax regime can effectively replace the pre-operative enema in patients going for a wide variety of operations. The failure rate is very low being less than 5%.

The experience gained in this trial shows that a second suppository inserted when the first suppository had no effect after a period of one or two hours will always produce a bowel movement. Owing to the standardization of the dosage to that of the minimum in this trial, cases having colonic, rectal and anal surgery have been excluded, but there is no reason to think that such cases cannot be as effectively prepared, without

enemata and rectal washouts, if the dosage and duration of the regime are increased.

In the post-operative period Dulcolax suppositories can be relied upon to produce the expulsion of gas or a bowel movement. This is of the greatest help when the nature of the operation precludes the administration of an enema.

In the pre-operative group, evacuation occurred within one hour in 88% of cases; in the post-operative group only 52% of cases had the desired effect within an hour of insertion of the suppository. This delay is probably due to depressed intestinal activity following operation (seen particularly after abdominal operations) and anaesthesia.

The effect of Dulcolax is normally not associated with abdominal colic—90% of patients of all groups experienced no colic or only mild colic. The incidence of colic is significantly higher among medical students.

It must be stressed that the most beneficial effects are the saving of the patient from unpleasantness and distress, the saving in nursing time and the great reduction of the use of the bed-pan with its attendant difficulties. It also has the advantages of ease of administration and great safety.

### SUMMARY

1. A "contact" laxative is defined. The chemistry, pharmacology and various clinical application elsewhere of such a contact laxative imported under the trade name of Dulcolax are described.
2. A trial has been conducted on 250 patients in the Professorial Surgical Unit, Singapore, covering 111 pre-operative cases, 92 post-operative cases, 37 cases of constipation, 4 cases of subacute intestinal obstruction and 6 cases of abdominal radiographic examinations.
3. It has been found to be effective, work usually within an hour after contact with colonic mucosa, not often associated with colic and safe in all groups of patients. No side effects apart from colic were noted.
4. A group of medical students were tested to assess more accurately the action of the drug, particularly with regard to the subjective side effect of colic. Their experience is essentially similar to that of the patients, except that they had a higher incidence of colic—28% had moderate or severe colic against 5.7% in the pre-operative group of patients.
5. Male patients in the post-operative period have a significant delay in response to Dulcolax suppositories compared to female patients. This difference in response is not present in the pre-operative group of patients.
6. The benefits to patients and nurses are stressed.

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