Testing control of radiationinduced diarrhea with a psyllium bulking agent: A pilot study

by Joseph Murphy, Dawn Stacey, Juanita Crook, Brian Thompson and Diane Panetta

Sixty cancer patients who were undergoing radiation therapy to the pelvis of at least 4,000 cGy in 20 fractions over four weeks were randomized to take or not take Metamucil[®]. Results were analyzed for the presence of radiation-induced diarrhea in two groups: patients taking Metamucil (n=30) or not taking Metamucil (n=30). The Murphy Diarrhea Scale was developed to assist in the synthesis of data collected in daily patient-reported diaries. Results were analyzed using ANOVA F-tests. Metamucil significantly decreased the incidence (p=0.049) and severity (p=0.030) of diarrhea and showed a strong trend in reducing the use of anti-diarrhea medication (p=0.062). According to this pilot study, Metamucil was an effective method of controlling radiation-induced diarrhea. Results of this pilot study have implications for clinical practice and nursing research.

• Key words: Radiation-induced diarrhea, pelvic radiation, Metamucil, psyllium

The majority of cancers of the pelvic area are carcinomas and most carcinomas are responsive to radiation therapy. Due to the radiation sensitivity of the intestinal mucosa, especially the small intestine, a risk of acute radiation injury is both expected and accepted in order to achieve tumour control (Yeoh & Horowitz, 1987). Therefore, cancer patients receiving radiotherapy to the pelvic region commonly suffer some degree of radiation enteritis and acute diarrhea (McAnena & Daly, 1986; Rutledge & Engelking, 1998).

In our institution, patients who experience radiation-induced diarrhea (RID) are managed by dietary manipulation and/or antidiarrhea medications such as loperadine or diphenoxylate; these treatments are consistent with the literature (Rutledge & Engelking, 1998). If symptoms are intolerable, radiotherapy treatments are interrupted (Capirci, Stevanin, Lavedar, & Polico, 1993; Kaanders & Ang, 1994).

Literature review

Radiation-induced diarrhea (RID) is a manifestation of histological changes to the intestinal mucosa brought about by radiation (Rutledge & Engelking, 1998; Tarpila, 1971; Trier & Browning, 1966; Wiernick, 1966). In addition to a temporary decrease in quality of life (Bye, Ose, & Kaasa, 1995; Yeoh & Horowitz, 1987), the patient may suffer malabsorption with compromise of their nutritional status (Kost, Keinert, & Glaser, 1998; Trier & Browning, 1966). There are few data on the prevalence of RID. In a review by Rutledge and Engelking, the incidence of diarrhea from pelvic abdominal radiation, as perceived by nurses, was reported at 20% to 49%. However, our clinical experience suggests that the incidence is even higher.

Diarrhea is defined as "abnormally frequent and fluid discharge of the bowels" (Boland & Stodden, 1986). However, a review of the literature on diarrhea in adults suggests that the methods for measuring diarrhea are varied and there is no "gold standard" (Belknap, Davidson, & Smith, 1997; Bosaeus, Anderson, Nystrom, 1979; Bounous, Lebel, Shuster, Gold, Tahan, & Baslin, 1975; Capirci et al., 1993; NCIC-CTG, 1991; Rutledge & Engelking, 1998; Smalley, Klish, Campbell, & Brown, 1982). Parameters that have been reported include frequency, texture, blood in stools, incontinence, patient selfreporting, use of medications, and stopping radiotherapy treatments. Bliss, Guenter, and Settle (1992) demonstrated that reporting diarrhea as the percentage of "days with diarrhea," compared to eight other definitions, minimized the influence of monitoring biases that may lead to over-reporting of diarrhea.

Several studies have demonstrated some success in controlling RID with low fat diets (Booth, MacIntyre, & Mullin, 1964; Bosaeus et al., 1979) and reducing bile salts with binding agents (Chary & Thomson, 1984) or with an elemental diet (Bounous et al., 1975; Capirci et al., 1993). Theoretically, all of these treatments should reduce the amount of bile salts to be



From left to right: Brian Thompson, Dawn Stacey, Joseph Murphy and Diane Panetta.

Joseph Murphy, RD, BSc, is a clinical dietitian in nutrition services at the Ottawa Hospital – General Campus, Ottawa, Ontario. Dawn Stacey, RN, BScN, OCN, is an education coordinator – nursing, at the Ottawa Regional Cancer Centre. Juanita Crook, MD, FRCP(C), is a radiation oncologist at Princess Margaret Hospital in Toronto, Ontario. Brian Thompson, PhD is a statistician in Ottawa. Diane Panetta, RN, is an oncology nurse at the Ottawa Regional Cancer Centre in Ottawa.

CONJ: 10/3/00

resorbed by the colon, thereby reducing the amount of stool. Capirci and colleagues used a very low fat, low fibre diet, plus an elemental supplement that provided 30% of energy requirements, to patients receiving pelvic radiation therapy. While a high success rate was reported, their definition of diarrhea was unclear and they did not define the "medical therapy" provided to 12% of the patients for management of RID. In addition, two of the 52 patients had their treatments interrupted due to diarrhea.

In another study (Chary & Thomson, 1984), 33 patients receiving pelvic radiation were placed on low fat diets (40g/day). In addition, 17 of the 33 also took cholestyramine, a bile salt binding resin. A diarrhea scale (very similar to the one in the current study) was used in the synthesis of results. Some control of RID was obtained, however, nine of the 17 patients taking cholestyramine complained of side effects such as nausea and abdominal cramps.

Bulking agents have also been used to control some forms of diarrhea. The most commonly used agent is psyllium hydrophilic

mucilloid (Metamucil[®]) which is a concentrated hydrophilic soluble fibre that absorbs water in the small and large intestines. There is some evidence that Metamucil is effective in cases of chronic, non-specific diarrhea of childhood (Smalley et al., 1982) and misoprostol-induced diarrhea (Bobrove, 1990). In addition, Metamucil has been recommended for treatment of some cancer-related causes of diarrhea (Bisanz, 1997; Hilderley, 1997).

To date, no studies have examined the use of psyllium in the management of RID. Yet based on clinical experience, it is a common recommendation to patients at the Ottawa Regional Cancer Centre.

Purpose

The purpose of this study was to compare the severity, frequency, and incidence of diarrhea experienced by patients randomized to take or not take Metamucil while receiving a course of radical pelvic radiation.

Abrégé: Test du contrôle de la diarrhée induite par les radiations à l'aide d'un agent d'imbibition à base de psyllium : une étude pilote

Les patients atteints de cancer et recevant un traitement de radiothérapie dans la région pelvienne souffrent habituellement, à des degrés variables, d'entérite de radiation et de diarrhée aiguë. La diarrhée de radiation (DR) entraîne une diminution temporaire de la qualité de vie, et le patient peut souffrir de malabsorption compromettant son état nutritionnel. L'incidence de la DR due à la radiothérapie pelvienne abdominale, telle que perçue par le personnel infirmier, est de l'ordre de 20 à 49 %.

Il existe une variété de méthodes pour mesurer la diarrhée sans qu'il n'existe d'étalon. Les paramètres notés comprennent la fréquence et la durée de la diarrhée, sa texture, la présence de sang dans les selles, l'incontinence, le compte-rendu des patients, la prise de médicaments ainsi que l'arrêt des traitements de radiothérapie. L'échelle de diarrhée de Murphy a été développée dans le cadre de l'étude pilote pour quantifier et consigner la fréquence et la texture des selles ainsi que l'usage de médication anti-diarrhéique dans le but d'attribuer une valeur numérique aux jours-avec-diarrhée.

L'agent d'imbibition le plus fréquemment utilisé dans le contrôle de la diarrhée est le muciloïde hydrophile de psyllium (Metamucil[®]) lequel est une fibre soluble hydrophile concentrée qui absorbe l'eau dans l'intestin grêle et le gros intestin. À ce jour, aucune étude n'a examiné l'usage du psyllium dans la gestion de la diarrhée de radiation. Cependant, sur la seule base de l'expérience clinique, il est régulièrement recommandé aux patients du Centre régional de cancérologie d'Ottawa.

Cette étude visait à comparer la sévérité, la fréquence et l'incidence de la diarrhée subie par des patients choisis au hasard pour la prise ou non de Metamucil dans le cadre d'une série de traitements de radiothérapie radicale en région pelvienne. Soixante patients recevant un traitement au bassin d'au moins 4 000 cGy en 20 fractions échelonnées sur quatre semaines ont été choisis au hasard pour la prise ou non de Metamucil. Les résultats ont été analysés pour vérifier la présence de DR dans les deux groupes : patients prenant du Metamucil (n=30) ou non (n=30). Les résultats ont été analysés à l'aide des tests ANOVA F. Le Metamucil a réduit de façon significative l'incidence (p=0.049) et la sévérité (p=0.030) de la diarrhée, et une tendance marquée de réduction de la prise de médicament anti-diarrhéique se dessinait (p=0.62). Selon cette étude pilote, le Metamucil représentait une méthode de contrôle efficace de la DR.

Comme il s'agissait d'une étude pilote, elle était d'une portée limitée. De plus, l'échelle de diarrhée de Murphy n'a pas encore été validée, quoiqu'elle soit similaire aux échelles de mesure de diarrhée publiées dans le passé et pertinentes à la pratique clinique. Il est possible que l'inclusion de « prise de médicament anti-diarrhéique » dans la définition d'une journée-avec-diarrhée limite davantage la portée de l'étude. Cependant, lorsqu'on a effectué l'analyse des résultats en excluant les données correspondant à la « prise de médicaments anti-diarrhéiques », les mêmes tendances notées pour l'incidence et la sévérité se sont précisées, quoique statistiquement non significatives. Dans cette étude pilote, aucune donnée n'a été recueillie quant au type ou à la dose de médicament anti-diarrhéique utilisé. Il pourrait s'avérer important de recueillir cette information dans le cadre d'études ultérieures.

Malgré ces limites, les résultats démontrent l'efficacité du Metamucil dans la réduction de l'incidence et de la sévérité de la DR. À notre institution, le Metamucil continue d'être offert aux patients, sur une base optionnelle, pour contrôler la DR et ce, à une dose d'une à deux cuillerées à thé par jour accompagnée d'une augmentation de liquides. Les professionnels de la santé sont encouragés à explorer plus à fond le rôle du Metamucil dans le contrôle de la DR subie par les patients recevant des traitements de radiothérapie dans la région pelvienne. On préconise de poursuivre les recherches sur l'impact du Metamucil et la validation de l'échelle de diarrhée de Murphy.

Definitions

Metamucil: primarily psyllium, a dietary fibre derived from the seed of the plant 'Phantago ovatu.'

Radiation-induced diarrhea (**RID**): a day-with-diarrhea on at least five per cent of the days reported, as determined by using the MDS (see Table One).

Time to onset of RID: the number of days from the start of treatment to the first day-with-diarrhea.

Duration of RID: the number of days from the first to the last day-with-diarrhea.

Severity of RID: mild, moderate, or severe, as determined by using the MDS (see Table Two).

Baseline bowel pattern: determined by the first five days of the patient's diary.

Method

Procedure

Patients with prostate or gynecologic cancer who were undergoing radiotherapy to the pelvis of at least 4000 cGy in 20 fractions were recruited from the two site locations of the Ottawa Regional Cancer Centre. Those with a history of gastrointestinal (GI) disease or who regularly used laxatives or anti-diarrhea medications were excluded. Patients with a tumour of the GI tract were also excluded in order to measure the effect of radiation and not the effect of cancer.

The convenience sample was obtained by consecutively recruiting patients with prostate or gynecologic cancer who were within three days of starting radiation. A table of random numbers was used to randomly assign patients into one of two groups - 1) take Metamucil and 2) do not take Metamucil. Informed written consent was obtained from all subjects. Accrual of subjects for this pilot study was limited by time and resource availability. However, there were sufficient numbers of patients in each group to allow for statistical analysis of the data.

Table	One:	De	fining	g a	day-with-diarrhea	

A day-with-diarrhea is any day with one of the following criteria:

- A. Four to six bowel movements more than normal
- B. One or more watery bowel movements
- C. Two to three loose or poorly formed bowel movements more than normal
- D. Use of anti-diarrhea medication

Table Two: Murphy Diarrhea Scale(MDS) for severity rating		
	Score	
Mild diarrhea (<11% days-with-diarrhea)	1	
Moderate diarrhea (11-20% days-with-diarrhea)	2	
Severe diarrhea (>20% days-with-diarrhea)	3	

A different researcher in each site location met the patient, performed the baseline assessment, gave diet teaching, and if appropriate, instructed subjects on the use of Metamucil. The "Nutritional guidelines to help control diarrhea" booklet (Clinical Nutrition/Nutrition Services, 1993) was used as the basis for teaching to ensure consistency between researchers, and a copy was given to all patients. This booklet advises patients to follow a low fibre diet and encourages them to limit their intake of fat, caffeine, and alcohol.

Data collection

All patients were asked to complete a diary from the first day of recruitment until their follow-up appointment, approximately 28 days post-treatment. In this diary, they recorded the number of bowel movements per day, the consistency of stools, the amount of anti-diarrhea medication taken, and if appropriate, the daily dose of Metamucil. Compliance with filling out the diaries was assessed weekly during the treatment period.

Data analysis

Moderate (2)

Mean score (p=0.03)

Severe (3)

98

The Murphy Diarrhea Scale (MDS) was used to assist in synthesis of the data collected in the pilot study. This instrument was developed by the first author to quantify and account for, as written in the diaries, frequency and texture of stools and the use of anti-diarrheal medication in determining days-with-diarrhea as a numerical score. Although this scale has not yet been validated, it is based on a pre-existing scale (Chary & Thomson, 1984) and the National Cancer Institute of Canada - Clinical Trials Group (NCIC-CTG) expanded toxicity criteria (NCIC-CTG, 1991).

The statistical package SAS (SAS, 1989) was used to analyze the scores generated by the MDS for use of antidiarrheal medication, as well as incidence, time of onset, duration, and severity of RID. The primary method of analysis was ANOVA using the F-test, with a significance level of p=0.05. All analyses were calculated allowing for differences in gender and site location by including these variables in the statistical model.

Table Three: Patient characteristics (n=60)				
	Metamucil	No Metamucil		
Males (n=51)	25	26		
Mean age in years (range)	63.7 (50-79)	66.7 (54-75)		
Mean weight in Kg (range)	83.6 (61-156)	83.1 (62-110)		
Average dose of radiation in cGy	6575	6585		
Females (n=9)	5	4		
Mean age in years (range)	56.3 (46-76)	64.7 (50-69)		
Mean weight in Kg (range)	70.0 (67-75)	68.6 (52-88)		
Average dose of radiation in cGy	6800	6850		
Table Four: Diarrhea severity scores				
MDS severity rating Metamucil No Meta				
	(n=30)	(n=30)		
Mild (1)	17	7		

2

11

1.80 +/- .96

RCSIO:	10/3/00
--------	---------

6

17

2.33 +/- .84

Results

Sample

Eighty-four patients were recruited over a period of 18 months. The majority were male (n=72) and ages ranged from 46 to 79 years. The most common treatment protocol was 200 cGy/day, five days a week for four to five weeks, followed immediately by eight to 10 additional treatments to a smaller area of the pelvis. Data from 24 subjects were subsequently excluded from the analysis because of voluntary withdrawal (n=1), inaccurate diary entries (n=6), incomplete diaries (n=2), failure to return diaries (n=13), and using Metamucil while in the non-Metamucil group (n=2).

Only nine of the remaining 60 patients were female. The final sample size was evenly distributed between the two groups, Metamucil or no Metamucil, although this distribution was purely coincidental. There were no significant differences between these two groups for mean age, age range, or weight (see Table Three).

Differences between Metamucil and no Metamucil groups

More than half the patients (n=17) reported mild diarrhea when taking Metamucil, whereas a similar number of patients who were not taking it had severe diarrhea (n=17). There was a significant difference between the groups on their average severity of diarrhea (p=0.03) (see Table Four).

The incidence of RID was significantly decreased from 83% in the non-Metamucil group to 60% in the Metamucil group (p=0.049). The mean percent days patients took anti-diarrhea medication was also reduced, from 15.1 in the non-treatment group to 6.7 for those taking Metamucil, although the results did not reach statistical significance (p=0.062). Average time to onset of RID was similar for both the Metamucil and non-Metamucil groups at approximately 14 days. Average duration of RID was also similar at close to 40 days. Neither of these variables reached statistical significance (see Table Five)

The analyses were then repeated with anti-diarrhea agents removed from the definition of a day-with-diarrhea (i.e. patients taking anti-diarrheal agents were only classified based on the number and consistency of bowel movements). Although statistical significance was not reached in any category, similar trends towards a decrease in incidence and severity of diarrhea when using Metamucil were evident (see Table Six).

Discussion

The use of Metamucil was associated with a reduction in the incidence and severity of RID and a decrease in the use of antidiarrhea medication. The pilot study results compare favourably with other published treatments of RID, such as elemental diets and bile salt binding resins (Bounous et al., 1975; Chary & Thomson, 1984).

Metamucil was very well-tolerated by patients, none of whom complained of gastro-intestinal side effects or an inability to take the Metamucil. In contrast, in one study where patients were placed on low fat diets and given cholestryramine to control RID, nine of the 17 patients complained of side effects such as nausea and abdominal cramps (Chary & Thomson, 1984). In addition, unlike a study by Capirci and colleagues (1993) where two of the 52 patients using a very low fat, low fibre diet and an elemental supplement had their pelvic radiation treatments interrupted due to diarrhea, none of the patients in this pilot study required treatment interruption.

Metamucil is a low-cost, well-tolerated product with minimal side effects that appears to reduce the incidence and severity of diarrhea. RID is believed to be partly due to damage to the lining of the intestinal tract that interferes with re-absorption of water and bile salts in the terminal ileum and large intestine (Kost et al., 1998; Tarpila, 1971; Trier & Browning, 1966; Wiernick, 1966). The dietary fibre, psyllium, found in Metamucil is a hydrophilic mucilloid that provides a bland, non-irritating bulk to the stools. Metamucil appears to absorb the excess liquid present as a result of radiation and helps form stools. Therefore, patients may have less frequent bowel movements, better formed

1		/			
stools,	and	use	fewer	anti-diarrhea	
medicat	ions.				

Т !	• 4	4.	
LIM	Ita	UO	ns

This study was a pilot study and, therefore, was limited in scope. In addition, the MDS has yet to be validated, although it is similar to previously published diarrhea measurement scales that have demonstrated relevance to clinical practice (Chary & Thomson, 1984; NCIC-CTG, 1991). The next step is to validate the MDS.

The inclusion of "use of anti-diarrhea medication" in the definition of a daywith-diarrhea may be a further limitation of the study. However, when the results were analyzed excluding "use of antidiarrhea medications," the same trends for incidence and severity were noted, although statistical significance was not reached. In this pilot study, data were not collected on the type or dose of the antidiarrhea medications used. This information may be important to collect in subsequent studies.

The diary reporting started at the beginning of treatment and continued for four weeks post-treatment. The baseline

Table Five: Differences between Metamucil and non-Metamucil groups				
	Metamucil	No Metamucil	Significance	
Mean severity score (MDS)	1.80	2.33	p=0.030**	
Incidence of diarrhea	60%	83%	p=0.049**	
Mean time to onset (days)	13.9	14.1	p=0.895	
Mean duration (days)	41.5	38.5	p=0.905	
Mean % days took anti-diarrhea medication	6.70	15.10	p=0.062*	

* not significant but a trend

** statistically significant

 Table Six: Differences between Metamucil and non-Metamucil groups excluding use of anti-diarrheal medication in definition of a day-with-diarrhea

	Metamucil	No Metamucil	Significance
Mean severity score (MDS)	1.70	2.10	p=0.078*
Incidence of diarrhea	57%	77%	p=0.107*
Mean time to onset (days)	14.9	16.8	p=0.500
Mean duration (days)	42.9	42.7	p=0.980
		•	•

CONJ: 10/3/00

* not significant but a trend

bowel patterns were taken from the first five days of treatment. This was considered acceptable given that the effects of radiation do not usually appear until the second week of treatment. However, several patients in both groups reported experiencing a day-with-diarrhea within the last three days of recording in the diary. It is possible that these patients may have been experiencing RID beyond the measurement period. In subsequent studies, data collection should be extended so that the diary begins one week prior to commencing radiation therapy and continues for six to eight weeks after treatment.

Clinical implications

Nurses play a key role in symptom management and should recognize that diarrhea is commonly experienced by patients receiving pelvic radiation. Nurses should discuss this possibility with patients before radiation begins and work with them to explore methods to monitor and control the diarrhea. Monitoring requires asking patients about changes in frequency and texture of stools, and use of anti-diarrheal agents. It also includes consistent documentation of incidence and severity of diarrhea, as well as the results of interventions.

Metamucil continues to be offered to patients as an option for controlling RID at our institution. The recommendations are to

References

- Belknap, D., Davidson, L.J., & Smith, C.R. (1997). The effects of psyllium hydrophilic mucilloid on diarrhea in enterally fed patients. **Heart and Lung, 26**, 229-37.
- Bisanz, A. (1997). Managing bowel elimination problems in patients with cancer. Oncology Nursing Forum, 24, 679-687.
- Bliss, D.Z., Guenter, P.A., & Settle, R.G. (1992). Defining and reporting diarrhea in tube fed patients - What a mess! American Journal of Clinical Nutrition, 55, 753-59.
- BoBrove, A.M. (1990). Misoprostol, diarrhea and psyllium mucilloid [letter to the editor]. Annals of Internal Medicine, 112, 386.
- Boland, D.O., & Stodden V.L. (Eds.), (1986). The new Webster's dictionary. New York: Lexicon Publications, Inc.
- Booth, C.C., MacIntyre, F., & Mullin, D.L. (1964). Nutritional problems associated with extensive lesions of the distal small intestine in man. **Quarterly Journal of Medicine**, **131**, 401.
- Bosaeus, I., Anderson, H., & Nystrom, C. (1979). Effect of a low fat diet on bile salt excretion and diarrhea in the gastrointestinal radiation syndrome. Acta Radiologica Oncology, 18, 460-64.
- Bounous, G., Lebel, E., Shuster, J., Gold, P., Tahan, W.T., & Baslin, E. (1975). Dietary protection during radiation therapy. **Stralentherapie**, **149**, 476-83.
- Bye, A., Ose, T., & Kaasa, S. (1995). Quality of life during pelvic radiotherapy. Acta Obstetricia et Gynecologica Scandinavica, 74, 147-52.
- Capirci, C., Stevanin, C., Laveder, F., & Polico, C. (1993). Diet therapy: An effective method to prevent radiation enteritis. Paper presented at the International Congress of Radiation Oncology, Kyoto, Japan.
- Chary, S., & Thomson, D.H. (1984). A clinical trial evaluation cholestyramine to prevent diarrhea in patients maintained on low-fat diets during pelvic radiation therapy. International Journal of Radiation Oncology, Biology, & Physics, 10, 1885-90.
- Clinical Nutrition/Nutrition Services, Ottawa General Hospital. (1993). **Nutrition guidelines to help control diarrhea** (P005). Ottawa, ON: Author.

start with one teaspoon of Metamucil each morning and to increase fluid intake by one to two extra glasses of water. If necessary, the Metamucil is increased to one teaspoon twice a day.

Conclusion

Despite the limitations of this pilot study, the results lend support to the effectiveness of Metamucil in reducing the incidence and severity of radiation-induced diarrhea. Health care professionals in various settings should be encouraged to further explore the role of Metamucil in the control of RID experienced by patients receiving radical pelvic radiation. Subsequent research on the impact of Metamucil, as well as further validation of the Murphy Diarrhea Scale is warranted.

Acknowledgements

The authors wish to thank and acknowledge the assistance of the following: Annette Bériault, RN, BScN, CON(C), Marjolaine Lortie, RN, and Rita Blattman, RN, of the Ottawa Regional Cancer Centre, as well as Judy Leeson, RD, and Stéphanie St-Hilaire, RD, of the Ottawa Hospital. Proctor & Gamble Corporation provided partial funding of this study through a research grant.

- Hilderley, L.J. (1997). Radiotherapy. In S.L. Groenwald, M.H. Frogge, M. Goodman, & C.H. Yarbro, (Eds.), Cancer nursing: Principles and practice (4th ed., pp. 808-22). Boston: Jones and Bartlett Publishers.
- Kaanders, J.H., & Ang, K.K. (1994). Early reactions as doselimiting factors in radiotherapy. Seminars in Radiation Oncology, 4, 55-67.
- Kost, S., Keinert, K., & Glaser, F.H. (1998). D-Xylose test of resorption as a method to determine radiation side effects in the small intestine. **Strahlentherapie und Onkologie**, **174**(9), 462-7.
- McAnena, O.J., & Daly, J.M. (1986). Impact of antitumour therapy on nutrition. Surgical Clinics of North America, 66, 1213-28.
- NCIC-CTG, National Cancer Institute of Canada Clinical Trials Group. (1991). **Expanded common toxicity criteria**. Toronto, ON: Author.
- Rutledge, D.N., & Engelking, C. (1998). Cancer-related diarrhea: Selected findings of a national survey of oncology nurse experiences. **Oncology Nursing Forum**, **25**, 861-73.
- SAS Institute Inc. (1989). Statistical Analysis System (version 6) [Computer software]. Cary, NC: Author.
- Smalley, J.R., Klish, W.J., Campbell, M.A., & Brown, M.R. (1982). Use of psyllium in the management of chronic nonspecific diarrhea in childhood. Journal of Pediatric Gastroenterology and Nutrition, 1, 361-63.
- Tarpila, S. (1971). Morphological and functional response of human small intestine to ionizing irradiation. Scandinavian Journal of Gastroenterology, 12, 1-52.
- Trier, J.S., & Browning, T.H. (1966). Morphological response of the mucosa of human small intestine to x-ray exposure. Journal of Clinical Investigation, 45, 194-204.
- Wiernick, G. (1966). Radiation damage and repair in the human jejunal mucosa. Journal of Pathology, 91, 389-93.
- Yeoh, E.K., & Horowitz, M. (1987). Radiation enteritis. Surgery, Gynecology and Obstetrics, 165, 373-79.