Coronary thrombolysis — clinical guidelines and public policy: results of an Ontario practitioner survey

C. David Naylor, MD, DPhil, FRCPC; A. Andrew Hollenberg, MA, MBA; Anne Marie Ugnat, MSc; Antoni Basinski, MD, PhD, CCFP

The Ontario Medical Association (OMA) guidelines for intravenous thrombolysis in acute myocardial infarction were released in March 1988 and contributed to a government decision against special per-case funding to assist hospitals using tissue-type plasminogen activator (tPA). In October 1988, 1512 cardiologists, internists and physician-administrators who were OMA members were mailed a questionnaire seeking their views on the OMA guidelines and related issues. Of the 419 questionnaires (28%) that were returned, 392 contained usable responses. Among the respondents 268 (68%) had used thrombolytic drugs in the preceding 12 months; the mean number of cases was 10.6 (standard deviation 12.9). A strong or a mild preference for tPA over streptokinase was registered by 64% of the respondents; 28% had no preference. However, the self-reported ratio of actual streptokinase:tPA use was about 3:1, and 73% indicated that the government's funding policy had limited the availability of tPA in their hospital. The respondents were almost equally divided as to whether the policy should be changed. The guidelines were deemed helpful by 85% of the noncardiologists, as opposed to 52% of the cardiologists (p < 0.005). OMA involvement in developing and circulating such guidelines was supported by 74% of the respondents and opposed by 18%; opposition was more likely to come from those who found the guidelines unhelpful (p < 0.001). Support for involvement by the College of Physicians and Surgeons of Ontario was much weaker (supported by 32%, opposed by 62%). Overwhelming opposition to government involvement was evident.

La publication, en mars 1988, des normes de l'Association medicale de l'Ontario (AMO) sur la thrombolyse endoveineuse pour infarctus aigu du myocarde a joué dans la décision du gouvernement de ne pas fournir aux hôpitaux une assistance pécuniaire spéciale pour chaque cas où l'on utilise l'activateur tissulaire du plasminogène (AtP). Dès octobre 1988 nous sondions par la poste 1512 cardiologues, spécialistes en médecine interne et médecins administrateurs, tous membres de l'AMO, sur leurs opinions quant aux normes précitées et aux questions y afférentes. On a retourné 419

Dr. Naylor is with the Clinical Epidemiology Unit and the Division of General Medicine, Toronto Western Division, Toronto Hospital, and the departments of Medicine, Health Administration and Behavioural Science, University of Toronto. Mr. Hollenberg is a policy analyst with the Ontario Medical Association (OMA), Toronto. Ms. Ugnat is an analyst with the Clinical Trials Unit, Centre for Cardiovascular Research, Toronto Hospital. Dr. Basinski is with the Clinical Epidemiology Unit and the Department of Family Medicine, Toronto Western Division, Toronto Hospital, and the departments of Family and Community Medicine and of Preventive Medicine and Biostatistics, University of Toronto.

Dr. Naylor was supported by a Career Scientist Award from the Ontario Ministry of Health. The views expressed herein are those of the authors and should not be attributed to either the Ontario Ministry of Health or the OMA.

Reprint requests to: Dr. C. David Naylor, Rm. 1-West 821, Toronto Hospital (Toronto Western Division), 399 Bathurst St., Toronto, Ont. M5T 2S8

(28%) des questionnaires, dont 392 sont utilisables. Parmi les répondants retenus 268 (68%) ont eu recours à des thrombolytiques dans les 12 mois précédents; le nombre moyen des cas est 10,6 (écart-type 12,9). Les 64% disent préférer (fortement ou faiblement) l'AtP à la streptokinase; 28% n'ont pas de préférence. Mais les réponses font état d'un rapport effectif d'utilisation streptokinase/AtP d'environ 3 à 1; 73% des répondants disent que la politique de financement susdite a limité la disponibilité de l'AtP dans leur hôpital. L'ensemble des répondants se divise en parts presque égales sur la question de savoir si on devrait changer cette politique. Quant aux normes 85% des non cardiologues les tiennent utiles, contre 52% des cardiologues (p < 0,005). L'initiative prise par l'AMO dans la rédaction et la diffusion de telles normes est approuvée par 74% des répondants et blâmée par 18%; ces derniers se trouvent surtout parmi ceux à qui les normes n'ont pas paru utiles (p < 0,001). Une intervention sur cette question par le Collège des médecins et chirurgiens de l'Ontario serait accueillie par 32% des répondants mais rejetée par 62%. Quant à l'intervention du gouvernement on s'y oppose très fortement.

In November 1987 tissue-type plasminogen activator (tPA) was released for use in Canada as an intravenous thrombolytic agent. Streptokinase had earlier received federal approval for similar indications, but the availability of tPA catalyzed interest in the potential benefits of coronary thrombolysis for acute myocardial infarction. Accordingly, in January 1988 the Ontario Medical Association (OMA) convened a panel to develop guidelines for the use of intravenous thrombolytic drugs in acute myocardial infarction. The resulting guidelines¹ were approved by the OMA Board of Directors and were mailed Mar. 31, 1988, to cardiologists, internists and OMA members in hospital administrative capacities, such as chiefs of staff and medical directors.

Although the guidelines reviewed diverse aspects of thrombolytic therapy, the sections dealing with choice of thrombolytic agent captured the greatest attention. These sections indicated that insufficient evidence had accumulated to permit designation of tPA over streptokinase as the drug of first choice for routine use in acute myocardial infarction.

At the time the OMA guidelines were developed, tPA was being reviewed by a governmental advisory body to determine whether it merited special funding arrangements. Whereas inpatient drugs are conventionally covered within the global budgets negotiated annually for general hospitals, the high cost of tPA led to the consideration of funding per case in addition to usual budgetary allocations. The advisory body used the OMA policy in rendering a verdict and recommended against special funding, albeit with the proviso that the decision be reviewed as evidence accumulated from major comparative trials.

Although the guidelines had emphasized uncertainty about the best choice of thrombolytic drug, the OMA press release² and statements by the OMA spokesman led Toronto's *Globe and Mail* to report that the OMA was specifically recommending against the use of tPA because of its higher price (Apr. 6, 1988: A1-A2); the story was then carried nationally on the Canadian Press wire service. Coverage extended to the British journal *Nature*, which repeated the errors in the Canadian Press story.³ Confusion also arose because some physicians and hospital pharmacists misinterpreted the government policy as a proscription on the use of ordinary hospital funds to purchase tPA (Dr. Anthony Schincariol, tPA product manager, Genentech Canada, Burlington, Ont.: personal communication, 1988).

Intraprofessional controversy was augmented by the failure of the OMA board to put the guidelines before the OMA Section on Cardiology. Many cardiologists and internists were apparently already convinced of the superiority of tPA on the basis of its better side-effect profile and greater efficiency as a lytic agent at the doses in common use.

In October 1988 a survey was arranged under the auspices of the OMA to learn more about the views of practitioners on issues related to coronary thrombolysis specifically and dissemination of practice guidelines in general. We herein report the results of that survey and discuss the implications of these findings for further initiatives in technology assessment and guideline formulation.

Methods

A brief questionnaire was designed by us and produced by the OMA. There was no funding or need for previous field testing before distribution. The questionnaire was mailed in October 1988 to the 1277 members of the OMA sections of Cardiology and Internal Medicine and to the 235 physicians on the OMA's list of hospital chiefs of staff, medical directors or equivalent physician-administrators. The mailing was structured to eliminate overlap whenever possible. The covering letter from the OMA president acknowledged the issues that had arisen in the development and the dissemination of the guidelines and requested cooperation in completing the questionnaire. A prepaid, addressed envelope Use of thrombolysis accompanied each questionnaire.

Membership in the OMA sections on Cardiology and Internal Medicine is open to any member with internal medicine certification who indicates these respective section preferences on a membership information form. We expected a low response by internists from the outset since many members of the Section on Internal Medicine would have practices confined to noncardiologic subspecialties. However, we could not predetermine which internists were active in coronary care.

The data entry for every response was doublechecked. In most of the cases two people reviewed each entry. The OMA undertook a preliminary descriptive analysis. Before the final analysis every 10th record was checked again against the data file; no errors were found. We used standard chi-squared tests, logistic regression and $2 \times k$ contingency table analyses with tests for trend. Although various prespecified hypotheses were used to guide the analysis, the multiplicity of statistical tests and the systematic univariate review of the database substantially increased the chances of type I errors. A p value of 0.01 or less would suggest a low risk of a type I error: p values of 0.001 or less are strongly reassuring that the result is unlikely to be due to random error alone. No directionality of any hypothesis was assumed (i.e., p values are either nondirectional, as in chi-squared tests, or two-sided).

Results

Response rate

Of the 1512 questionnaires 419 (28%) were returned. Of these, 27 did not include any usable data; they were from retirees and medical subspecialists not involved in coronary care or represented a double return. Thus, there were 392 respondents, who represented an estimated 149 general hospitals.

Designated position

The physicians surveyed were asked to designate their position(s). Cardiologists, internists or both accounted for 75% of the total. For analytic purposes we classified as cardiologists the minority who designated themselves as both cardiologists and internists. The overall sample included 45 coronary care unit (CCU) directors (all but 2 of whom were also internists, cardiologists or both) and 59 chiefs of staff. Of the chiefs of staff 88% did not indicate another position. Only 9% of the respondents marked "other" as their sole designation; this group included many medical subspecialists, but its composition cannot be further specified.

The respondents were asked to estimate how many times they had administered a thrombolytic agent to a patient with an acute myocardial infarction in the preceding 12 months; 268 (68%) recorded one or more cases and 124 (32%) no use. A categorical breakdown of the frequency of use is shown in Table 1. The mean number of cases was 10.6 (standard deviation [SD] 12.9); the median was 6 and the total 2834. Cardiologists showed significantly greater average use than internists (16.2 [SD 16.4]

v. 6.7 [SD 7.0], p < 0.001). The 268 respondents who had used streptokinase or tPA in the preceding 3 months were asked to indicate, within deciles, in what proportion of cases they had used tPA (Fig. 1). They indicated far more frequent use of streptokinase than of tPA. To produce an appropriately weighted estimate of the overall use of tPA each respondent's self-reported 12-month use of any thrombolytic drug was multiplied by the midpoint of the self-reported decile for the 3-month proportionate use of tPA. If 20 missing values for the proportionate use of tPA were consid-

Ontario*	normoto and physic	ian-administrators in
No. of cases	No. (and %) of respondents	Cumulative frequency (and %)
0	124 (32)	124 (32)
1-5	120 (31)	244 (62)
6-10	73 (19)	317 (81)
11-20	42 (11)	359 (92)
21-40	26 (7)	385 (98)
≥ 41	7 (2)	392 (100)

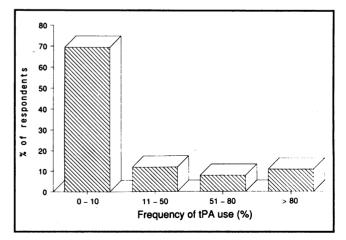


Fig. 1: Frequency of use of tissue-type plasminogen activator (tPA) by 268 respondents who had administered thrombolytic drugs during the 3 months before receipt of questionnaire.

ered to be 0 (analogous to assuming 100% streptokinase use) the total tPA caseload would be projected at 694 (24% of all cases). If these practitioners were assigned the average proportionate tPA use from the other 248 respondents rather than 0 the total tPA caseload would be 735 (26%). Thus, the overall tPA use was around 25%. We found no significant relation between the frequency of use and the proportion of tPA use.

Protocols

Asked whether their hospital had a defined, written protocol on thrombolysis use in myocardial infarction 90% (329 of 367) of the respondents answered "Yes". However, 60% did not believe their CCU or hospital had a policy defining subsets of patients who should receive tPA rather than streptokinase or vice versa.

Since multiple records were often received from practitioners at the same hospital, we deleted the records without a specific hospital affiliation and grouped the remainder by hospital. Simple decisionmaking rules were applied to resolve disagreements among practitioners in the same centre. The CCU director's record was used when available; failing that, cardiologists and internists were used to define the policy, and in the event of disagreement simple majority rule was used. If neither had reported for a given centre the chief of staff's record took priority. Ties were decided by coin toss.

This method produced a centre-specific set of 149 records. The proportion reporting a written protocol for thrombolysis use was 85%. However, 70% did not have a policy defining differential use of

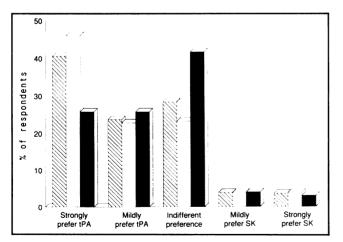


Fig. 2: Thrombolytic preferences of respondents if they were to suffer myocardial infarction. Diagonally striped bars represent all respondents, white bars represent those who reported use of thrombolytic drugs during the 12 months before receipt of questionnaire, and black bars represent those who did not administer such drugs. SK = streptokinase.

tPA versus streptokinase. Both results were consistent with the findings in the overall data set.

Personal thrombolytic preferences

The respondents were asked which agent they would prefer to receive if they suffered an acute myocardial infarction and were an appropriate candidate for thrombolytic treatment with either streptokinase or tPA. Fig. 2 shows the much greater preference for tPA and compares the preferences of physicians reporting use of thrombolysis versus nonusers. Those who actually prescribed thrombolytic drugs were significantly more likely to show a preference for tPA (p = 0.002).

Awareness and responses to the OMA guidelines

Of 381 respondents only 12% had been unaware of the OMA guidelines before receiving the questionnaire; of 335, 91% reported having read them. We did not check for knowledge of the contents. Those reporting any thrombolysis use in the preceding 12 months were significantly more likely than the others to be aware of the guidelines (92% v. 80%, p = 0.001) or to have read them (95% v. 81%, p = 0.0002).

For comparison we asked the respondents whether they had read the guidelines for deep venous thrombosis released under the auspices of the College of Physicians and Surgeons of Ontario (CPSO) in 1988. Of 390 respondents 85% had done so.

Table 2 illustrates the differences in views by position (i.e., cardiologist, internist or other).

Awareness of cost differences

We asked the respondents to record how many times more expensive than streptokinase they believed tPA to be. In October 1988 the respective prices for 1.5 million units of streptokinase and 100 mg of tPA were \$289.50 and \$2900 (i.e., a factor of 10). Of 368 respondents 68% answered correctly.

Table 2: Views on Medical Association bolytic drugs by OMA	(OMA) guideli				
	Found guidelines helpful; no. (and %)				
Section	No	Yes	Total		
Cardiology	44 (48)	48 (52)	92		
Internal medicine	23 (16)	120 (84)	143		
Other	8 (13)	54 (87)	62		
Total	75 (25)	222 (75)	297		

The respondents showed strong digit preference for multiples of 5 as follows: 10 (249 respondents), 5 (46), 15 (18) and 20 (15). The mean response was 11.3, but there was substantial variation, as suggested by the standard deviation of 10.5. Cardiologists reported a similar mean, 10.8. However, their superior precision was evident, the standard deviation being only 3.3; 95% of the responses fell between 5 and 15.

Impact of the thrombolysis funding policy

There was some divergence in the perception of the impact of the government's funding policy for the use of tPA in the respondents' hospital (Table 3). We estimated that 60% to 70% of hospitals did indeed adopt limited use of tPA as a result of the lack of additional funding from the government.

Among those who used thrombolytic agents in the past year 54% (138 of 255) reported that the funding policy had not directly changed their pattern of use, and 46% (117 of 255) reported that it had; this contrasts with the 73% in this subgroup who stated that the funding policy had constrained the availability of tPA in their centre. The discrepancy is compatible with two complementary hypotheses: the funding decision occurred before these practitioners could adopt tPA (so that they would simply continue using streptokinase), or some hospitals used standard operating funds to purchase tPA in quantities sufficient to maintain a given practitioner's established preferences. (The drug supplies provided free for Genentech or Burroughs-Wellcome studies may also have supported continued use by some practitioners.)

When asked whether the government should defray the costs of routine use of tPA rather than streptokinase the respondents were more or less evenly divided (Table 4); the approximate 50:50 split was maintained in the subgroups, including CCU directors, cardiologists and chiefs of staff.

On the other hand, we postulated that practitioners' preference in the treatment of acute myocardial infarction should be reflected in their view of government funding. A striking relation between strong or mild preference for tPA and the likelihood of favouring full funding was evident (p < 0.0009). In addition, cross-tabulation of the data suggested that those practitioners using tPA more frequently might be more likely to favour full funding (Table 5). The chi-squared test for trend confirmed a significant relation between increasing use of tPA and increasing probability that a given respondent would favour funding (p < 0.001). Although this was a data-driven hypothesis its plausibility is obvious.

Source of clinical policy and guidelines

Table 6 shows the respondents' preference for the development and circulation of clinical policies by the OMA rather than the CPSO and overwhelm-

Table 4: Views o funding to defra streptokinase					
Use of	Government should defray tPA costs; no. (and %) of respondents*				
thrombolytic drugs	No	Yes	Tota		
No	53 (56)	42 (44)	95		
Yes	115 (46)	135 (54)	250		
Total	168 (49)	177 (51)	345		

A Martine Martine Martine and	Formal or informal policy of limited use adopted; no. (and %) of respondents*		
Category of response	No	Yes	
Internists (n = 157)	25	75	
Thrombolytic drug users ($n = 253$)	27	73	
Cardiologists ($n = 101$)	29	71	
CCU directors $(n = 44)$	32	68	
Centre-specific set $(n = 141)$	36	64	
Chiefs of staff $(n = 48)$	46	54	
Total (n = 334)	30	70	

ing opposition to the setting of guidelines by the government.

Because of controversy about the CPSO guidelines on deep venous thrombosis we had hypothesized that respondents familiar with those guidelines would be more likely to oppose CPSO involvement in guideline setting. The chi-squared test for trend offered some support for this relation (p = 0.03). Although no such pattern was demonstrable for all the respondents who had read the OMA guidelines, a greater probability of opposition to OMA involvement was noted among those who did not find the thrombolysis guidelines to be helpful (p < 0.001).

Discussion

Despite a low overall response rate we obtained responses from 268 physicians across Ontario who had used intravenous thrombolytic drugs for acute myocardial infarction in the preceding 12 months. The 2834 cases of use suggested by the responses would clearly constitute most of the cases of myocardial infarction treated with thrombolytic drugs in Ontario in any 12-month period during 1987-88; hence, the responses were from a large and pertinent sample of physicians. The OMA guidelines were apparently well known to physicians in general and thrombolysis users in particular, and they were found to be helpful by most of the respondents.

Our results are compatible with the view that the OMA guidelines and the government funding policy sharply limited the diffusion of tPA. Despite the clear preference for tPA, practitioners reported using the drug in only about 25% of cases in the 3 months before October-November 1988. Moreover. a substantial number reported that the government's funding policy had limited the availability of tPA in their hospital or CCU.

These findings should perhaps be interpreted in the light of the experience with the cesarean section guidelines released by the Society of Obstetricians and Gynaecologists of Canada (SOGC) in April 1986. In that instance practitioners were aware of the guidelines, and about 50% reported that they followed them, but a review of the hospital discharge data failed to substantiate the degree of drop in cesarean section rates that would be expected from these self-reported practices (Professor Jonathan Lomas, Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ont .: personal communication, 1989). Could our selfreported results also be misleading?

We think not, for three reasons. First, the OMA guidelines did not specifically recommend against the use of tPA. Hence, given the respondents' own preferences there would be little reason for them to underreport their use of tPA. Second, the OMA guidelines were accompanied by a government funding policy that militated against the purchase of tPA by hospitals. No financial incentives or disincentives accompanied the SOGC cesarean section guidelines. Third, even if a hospital were to adopt policies that

Frequency, %	Government should defray costs; no. (and %) of respondents				
of respondents	No	Yes	Total		
< 10	89 (51)	84 (49)	173 (70)		
11-50	17 (57)	13 (43)	30 (12)		
51-80	5 (29)	12 (71)	17 (7)		
81-100	2 (8)	24 (92)	26 (11)		

*Durina	the 3	3 months	before	receipt	ot	questionnaire.	
5							

	Group; no. (and %)				
View	OMA	CPSO*	Government		
Strongly opposed	32 (8)	125 (32)	294 (76)		
Opposed	37 (10)	115 (30)	68 (18)		
Indifferent	31 (8)	25 (6)	7 (2)		
Supportive	190 (49)	106 (27)	13 (3)		
Strongly supportive	98 (25)	17 (4)	5 (1)		
Total	388	388	387		

would reduce cesarean section rates (e.g., specific endorsement of trials of labour in selected patients who had previously undergone cesarean section) the ultimate decision would remain in the hands of the obstetrician. In contrast, if a hospital does not purchase tPA its practitioners will simply be unable to use it.

Although 85% to 90% of the centres appear to have had a written protocol for the use of intravenous thrombolytic drugs, 60% to 70% had no policy defining subsets of patients who should receive tPA rather than streptokinase; this is compatible with the distribution of use in Fig. 1. Streptokinase was apparently used almost exclusively by most of the centres, a smaller number predominantly using tPA.

Given the patterns of use the persistence of a strong preference for tPA is noteworthy. Our results were obtained in October-November 1988, after the publication of two landmark placebo-controlled studies of intravenous thrombolysis. The Anglo-Saxon Study of Early Thrombolysis (ASSET) revealed a relative reduction of 26.3% in the 30-day all-cause mortality rate for patients given tPA within 5 hours after the onset of chest pain.⁴ No acetylsalicylic acid (ASA) was used. The Second International Study of Infarct Survival (ISIS-2) used a 2×2 factorial design, the subjects receiving streptokinase, ASA, both or neither.⁵ Its outcome measure — the 35-day vascular mortality rate - was similar to the measure in ASSET. ISIS-2 actually showed a greater effect than ASSET in the subgroup treated within 5 hours. However, its results might be more accurately interpreted as a reduction of 23.3% in the mortality rate for streptokinase versus placebo and a reduction of 43.8% for streptokinase plus ASA versus ASA.^{6.7} Thus, these placebo-controlled trials supported the concept that a final judgement on the agent of choice should be reserved pending the results of direct comparative studies now under way. We speculate that practitioners continued to be swayed by tPA's somewhat superior side-effect profile and, above all, its greater clot-lysing efficiency at standard doses.^{8,9} Certainly these two themes have figured prominently in the advertisements for tPA.

In both the original¹ and the updated guidelines¹⁰ the OMA panelists noted tPA's promise but were unwilling to predicate formal recommendations about drug choice on an intermediate outcome measure such as arterial recanalization rates. One inconsistency in the survey responses suggested that a proportion of the practitioners took the same view as the OMA panel. Whereas 69% of the thrombolysis users and 64% of the respondents overall would either strongly or mildly prefer to receive tPA if they had a myocardial infarction, significantly fewer — 54% and 51% respectively — favoured government funding to defray the costs of routine tPA use. Such findings emphasize the many issues still to be resolved concerning the nature and the strength of evidence needed to formulate clinical policies or render verdicts on new technologies. A set of explicit decision-making rules is clearly needed.

In the absence of such rules different interpretations of inconclusive evidence are inevitable. For example, the Alberta Cardiovascular Society approved a set of thrombolysis guidelines in the spring of 1988 that indicate a preference for tPA.¹¹ In June 1988 the heads of cardiology at the two main Winnipeg hospitals affiliated with the University of Manitoba drafted a position paper on thrombolysis for the Manitoba minister of health that recommended tPA on the basis of its superior side-effect profile and lytic efficacy.¹² In contrast, the Quebec Pharmacology Advisory Board issued a task force report in June 1988 that concluded "it is impossible to recommend one thrombolytic agent or the other", although selective use of tPA was suggested.¹³ Some degree of provincial pluralism in clinical policy may be desirable, since health care administration remains primarily a provincial responsibility. However, these interprovincial discrepancies do emphasize the interpretive problems in determining clinical policies and assessing technologies.

We turn finally to the respondents' view on the development of guidelines by different bodies. The OMA and the CPSO disagreed about which organization should have the primary responsibility for developing guidelines for clinical practice.^{14,15} In March 1989 the CPSO sent a questionnaire on these matters to a random sample of 5000 physicians. The results, on preliminary analysis, were interpreted as providing a mandate for the CPSO to proceed with greater activity in this field.¹⁶ The discrepancy from our findings may be attributable to question-framing differences or to sampling bias. Surveys by a neutral organization may be preferable to determine how practitioners view guidelines and what organizations they think should be involved in developing and circulating guidelines.

The Ontario experience with the guidelines for intravenous thrombolysis, diagnosis of deep venous thrombosis and, most recently, detection and management of asymptomatic hypercholesterolemia¹⁷⁻²⁰ illustrates the controversies that can surround technology assessment and clinical policy formulation. This experience and our survey results suggest that alternative processes and clearer standards of evidence would be helpful to reduce the risk of alienating individual practitioners or special interest groups within the profession. One option may be to establish a widely representative and independent council, at a federal or a provincial level, to assess the technology and to draft clinical policy. A neutral agency would be best suited to undertake or commission the necessary background studies, to establish standards of evidence and to promote or facilitate the attainment of a consensus among concerned groups of practitioners in medicine and other health care fields.

We thank the many physicians who took time from their busy schedules to complete the questionnaire; their cooperation made the study possible.

References

- 1. Guidelines for the Use of Coronary Thrombolysis, Ontario Medical Association, Toronto, Mar 1988
- 2. Fletcher D: OMA guidelines urge fiscal responsibility in use of drugs for heart attacks. *Ont Med Rev* 1988; 55 (4): 24-25
- 3. Ezzell C: TPA too costly for medical use. *Nature* 1988; 332: 577
- 4. Wilcox RG, von der Lippe G, Olsson CG et al for the ASSET study group: Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. *Lancet* 1988; 2: 525-530
- ISIS-2 (Second International Study of Infarct Survival) Collaborative Group: Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988; 2: 349-360
- 6. Basinski A, Naylor CD: Aspirin and fibrinolysis [C]. Ibid: 1188-1189
- Naylor CD, Basinski A: Tissue plasminogen activator [C]. N Engl J Med 1989; 320: 318
- TIMI Study Group: The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. N Engl J Med 1985; 312: 932-936
- Verstraete M, Bernard R, Bory M et al: Randomised trial of intravenous recombinant tissue-type plasminogen activator versus intravenous streptokinase in acute myocardial infarction. Lancet 1985; 1: 842-847
- Naylor CD, Armstrong PW for the Ontario Medical Association Consensus Group on Thrombolytic Therapy: Guidelines for the use of intravenous thrombolytic agents in acute myocardial infarction. *Can Med Assoc J* 1989; 140: 1289– 1299
- 11. Thrombolytic Therapy for Acute Myocardial Infarction, Alberta Cardiovascular Society, Edmonton, July 1988
- 12. Position Paper on Thrombolytic Therapy for Treatment of Acute Myocardial Infarction, Section of Cardiology, University of Manitoba, Winnipeg, June 1988
- 13. Task Force on Thrombolysis: Thrombolysis in the Management of Myocardial Infarction, Pharmacology Advisory Board, Quebec, June 1988
- 14. Advisory Group on Strategy: Guidelines for Medical Practice, supplementary report to OMA Council, May 1989
- 15. Borsellino M: OMA at odds with college over clinical parameters. *Med Post* 1989; 25 (26): 2, 54
- 16. Annual Report, 1988-89, College of Physicians and Surgeons of Ontario, Toronto, 1989: 7
- 17. Horlick L: Managing hypercholesterolemia [C]. Can Med Assoc J 1989; 141: 861-862
- Naylor CD, Basinski A for the Toronto Working Group on Cholesterol Policy: Managing hypercholesterolemia [C]. Ibid: 862-863
- 19. Steiner G, Angel A, Wolfe B et al: Asymptomatic hypercholesterolaemia: viewpoint of the lipid research groups in Ontario. Ont Med Rev 1989; 56 (10): 7-10
- 20. Naylor CD, Basinski A for the Toronto Working Group on Cholesterol Policy: A rebuttal from the Working Group on Cholesterol Policy. Ibid: 12-13, 16, 21

Conferences continued from page 1051

Sept. 13-15, 1990: New Brunswick Medical Society Annual General Meeting

- Hotel Beauséjour, Moncton
- Ms. Judy Orem, annual general meeting coordinator, New Brunswick Medical Society, 176 York St., Fredericton, NB E3B 3N8; (506) 458-8860

Sept. 13-15, 1990: Ontario Medical Association and Canadian Anaesthetists' Society Annual Fall Meeting Niagara Falls, Ont.

Dr. F. Halliday, OMA/CAS Annual Fall Meeting, c/o Greater Niagara General Hospital, PO Box 1018, Niagara Falls, Ont. L2E 6X2; (416) 358-0171, ext. 474

Sept. 14-16, 1990: Canadian Hospital Association 7th Annual Invitational Seminar on Health Care Directives Millcroft Inn, Alton, Ont.

Conferences, Canadian Hospital Association, 100–17 York St., Ottawa, Ont. K1N 9J6; (613) 238-8005, FAX (613) 238-6924

Sept. 14–17, 1990: Royal College of Physicians and Surgeons of Canada Annual Meeting (held in conjunction with the Annual Meeting of the Canadian Pediatric Society and Canadian Society for Clinical Investigation)

Metro Toronto Convention Centre

Anna Lee Chabot, coordinator, Royal College of Physicians and Surgeons of Canada, 74 Stanley St., Ottawa, Ont. K1M 1P4; (613) 746-8177, FAX (613)746-8833

Sept. 14–17, 1990: 67th Annual Meeting of the Canadian Paediatric Society (held in conjunction with the Annual Meeting of the Royal College of Physicians and Surgeons of Canada)

Metro Toronto Convention Centre

Dr. Victor Marchessault, executive vice-president, Canadian Paediatric Society, 401 Smyth Rd., Ottawa, Ont. K1H 8L1; (613) 737-2728

Sept. 15-23, 1990: British Medical Association Annual Scientific Meeting

Edinburgh

Meetings Department, PO Box 8650, Ottawa, Ont. K1G 0G8; 1-800-267-9703, FAX (613) 731-9013

Sept. 21-23, 1990: Dermatology '90: Therapeutic Update New World Harbourside, Vancouver

Dermatology '90, 204-402 W Pender St., Vancouver, BC V6B 1T6; (604) 669-7175, FAX (604) 669-7083

continued on page 1085