Review of published recommendations and guidelines for the transfusion of allogeneic red blood cells and plasma

Special Supplement

Supplément spécial

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Abstract

Objective: To evaluate published guidelines and recommendations for the transfusion of allogeneic red blood cells and plasma in terms of content and methods.

Evidence: Bibliographic search of MEDLINE database for articles making therapeutic recommendations regarding erythrocyte and plasma transfusion, between January 1966 and July 1996; manual search of bibliographies from relevant reviews, guidelines and textbooks.

Data synthesis: Evaluation focused on how the evidence was identified, selected and incorporated. Therapeutic recommendations were compared and contrasted. Time trends related to transfusion triggers were also examined.

Results: The 59 references that met our criteria consisted of 17 clinical practice guidelines (CPGs) and 42 reviews. Five CPGs addressed the use of allogeneic red blood cells, 4 focused on fresh frozen plasma and 8 did both. All CPGs were based on the recommendations of an expert panel, although no specific consensus process was described. Among the 17 CPGs, only 1 used a computerized literature search and grading of the evidence and the strength of the individual recommendations. None of the CPGs cited or discussed the few available randomized, controlled clinical trials published at least 6 months earlier. For red blood cells, only 1 set of guidelines recommended a transfusion trigger; 6 advocated a range of transfusion thresholds based on clinical judgement; 1 recommended using only clinical judgement; the 5 remaining guidelines did not comment on either. For plasma, guidelines recommended an assessment of the coagulation cascade and the risk of ongoing bleeding before administration.

Conclusions: Although several agencies have published guidelines for the use of red blood cells and plasma, rigorous, evidence-based guidelines in this area are still needed.

Historically, the hemoglobin concentration or hematocrit value at which physicians transfuse allogeneic blood products during acute anemia, that is, the transfusion trigger or threshold, has been 100 g/L or 30%.[1–6] Plasma transfusions to correct coagulation abnormalities (and in the past, to expand intravascular volume) have also been guided by standard protocols and specific triggers rather than an assessment of the individual patient's overall risks and benefits. Since 1985, concerns about the transmission of HIV and other viruses through blood products have significantly modified both real and perceived risks and benefits. Many agencies have responded by issuing clinical practice guidelines (CPGs) advocating a more restrictive approach to the use of allogeneic red blood cells and plasma.[7–9]

Like most clinical decisions, the administration of allogeneic red blood cells and plasma is based on the balance of benefits, risks and costs. However, physicians making such decisions are faced with massive amounts of sometimes conflicting information. Increasing oxygen delivery through allogeneic red blood cell transfusion to avoid the potential complications of anemia must be balanced against the infectious and noninfectious complications of transfusion. Similarly, the decision

to administer plasma requires an assessment of the coagulation defect that is present in the patient, and the ongoing risk of bleeding must be weighed against infectious and noninfectious risks, such as pulmonary edema.

Guidelines have been issued to guide clinical decision-making in the controversial area of transfusion medicine. Traditionally, guidelines have represented a consensus of expert opinion, often defining a standard of practice. More recently, however, they have come to mean evidence-based recommendations that have been carefully developed by organizations using well-established methods.[10,11] For this review, we systematically selected, evaluated and summarized guidelines for the transfusion of allogeneic red blood cells and plasma published over the past 30 years. We then examined supporting evidence for each recommendation as well as the methods by which they were derived.

Methods

Literature search

A computer search of the MEDLINE database (January 1966 to July 1996) was conducted using the medical subject headings (MeSHs) "blood transfusion," "erythrocyte transfusion," "plasma," "plasmapheresis," "plasma exchange," "plasma substitute" and "blood component transfusion." The search strategy involved looking for these terms, as key words and text words, in the titles and abstracts of all citations. The results were combined with a previous MEDLINE search (1989–93) that used the following MeSHs: "blood transfusion," "adverse effects," "post-operative complications," "aged," "immunosuppression" and "infection." No limits were placed on either search; therefore, all languages as well as animal studies were included.

The collection of transfusion medicine publications of one of the reviewers (PH) supplemented the results of these searches. A manual search was conducted of the bibliographies of 3 major surgery texts,[12–14] 4 anesthesia texts,[15–18] 2 texts of transfusion medicine,[19,20] a hematology text,[21] an internal medicine text[22] and 4 critical care texts.[23–26] The references of all review articles and guidelines were also searched manually. Unpublished material was not included.

Literature selection

In total, 8426 articles were identified through computer and manual searches. Of these, 1424 were determined to be relevant to CPGs on transfusion of red blood cells and plasma. These were categorized as reviews, guidelines, editorials or book chapters. Abstracts from these selected citations were evaluated independently by 2 reviewers (LC,PH) to determine their eligibility for this study. Of the 1424, 118 were broadly categorized as reviews or guidelines; 59 were rejected because they did not make treatment recommendations regarding allogeneic red blood cell or plasma transfusions, leaving 42 reviews and 17 guidelines for the systematic review. Primary studies describing original research and other articles based on a neonatal population were excluded. Disagreements over selection were resolved by consensus. The 59 selected articles were further categorized according to the definitions outlined below.

Definitions

We defined "reviews" as articles that generally represented an assessment of the literature related to allogeneic blood transfusion. They were further divided into "narrative reviews," which combined expert opinion with evidence[27] without an explicit question or method, or "systematic reviews," which addressed a specific question and used an explicit, structured method to identify, select and provide an unbiased synthesis of the relevant evidence (meta-analyses were included in this category). Within the narrative review category, articles were further classified as "textbook reviews" (reviews published as textbook chapters), "historical reviews" (describing the role of the intervention in medicine over time) or "background reviews" (providing a general discussion of a topic).

CPGs have been defined by the Institute of Medicine as "systematically developed statements to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances."[28] For our purposes, CPGs had to have cited primary studies, included recommendations on the clinical indications for the use of red blood cells and plasma and been sponsored or endorsed by a medical society or organization. We also distinguished between guidelines and recommendations. For the purposes of this overview, "recommendations" were statements within guidelines, which gave practical, unambiguous advice about a specific aspect of transfusion therapy[29] whereas "guidelines" consisted of 1 or more therapeutic recommendations within a document.

Among the guidelines, 5 addressed the use of allogeneic red blood cells, 4 focused on fresh-frozen plasma and 8 did both. All guidelines were based on the recommendations of an expert panel, although no specific consensus process was described.

Data synthesis

The therapeutic recommendations in each article were categorized according to topic and examined to de-

termine the strength of evidence supporting them. Guidelines were evaluated using a checklist that focused primarily on how the evidence was identified, selected and incorporated. The use of a transfusion trigger and the role of clinical judgement over time were also compared.

The checklist was adapted from several articles describing how to develop and use guidelines.[10,11,28–32] Objective criteria from each article were compiled and modified to examine several different aspects of guideline development methods. The checklist was used to evaluate relevance, objectives, methods, results, the strength of the evidence and the final recommendations. Each guideline was evaluated independently by 2 authors (AC,PH).

Results

Reviews

Among the 42 reviews, 2 were classed as systematic,[33,34] 31 narrative,[35–65] 5 historic,[2,66–69] 3 text chapters[70–72] and 1 pamphlet.[73] Most reviews (15) focused on the perioperative setting, 6 addressed allogeneic transfusions in trauma situations, 5 focused on chronic anemia and 13 covered both nonoperative and operative settings as well as chronic and acute anemia. Until about 1987, reviews generally advocated the use of a transfusion trigger. Subsequently, most authors denounced this idea; however, a few continued to support the transfusion trigger concept, often citing the National Institutes of Health (NIH) consensus conference guidelines published in 1988 as a source advocating the 70 g/L threshold.

Red blood cell guidelines

Of the 13 guidelines addressing red blood cell transfusions, only 8 fulfilled all aspects of the CPG definition.[7,9,74–79] The 3 guidelines developed by the Canadian Red Cross Society[80–82] were published as pamphlets without any reference to published research. The guidelines endorsed by the American Association of Blood Banks (AABB)[83] were developed to provide standard criteria for utilization reviews and were not to be used to guide clinical practice. Finally, the surgical red blood cell transfusion practice policies[84] were not endorsed by a medical society or organization. Despite these limitations and concerns, these 5 guidelines were included in this review.

Target populations for the guidelines were quite diverse: 7 addressed general patient populations;[7,76,78,80–83] 3 focused on specific patient populations (i.e., patients undergoing coronary artery bypass grafting,[79] those with leukemia[75] and obstetric patients[77]); and 3 addressed the administration of red blood cells solely in the perioperative period.[9,74,84] Many of the recommendations from the AABB primarily addressed the issue of chronic anemia.[76]

The issue of a transfusion trigger was addressed in the text or the recommendations of all published guidelines. If we define a transfusion trigger or threshold as a hemoglobin concentration or hematocrit below which most patients should receive at least 1 unit of red blood cells, then only 1 guideline[75] recommended a transfusion trigger. Six guidelines[7,9,74,76,77,83] advocated a range of transfusion thresholds based on clinical judgement or specific risk factors; 1 guideline[84] recommended using clinical judgement without any specific trigger and the other 5[78–82] did not make any recommendation about clinical judgement or a transfusion trigger. The number of recommendations within each guideline ranged from 1[9] to 31[84] (Table 1). The 31 detailed recommendations within the surgical red blood cell transfusion practice policies[84] were devoted to perioperative patients. A significant number of recommendations in this report addressing the use of alternatives to red blood cell transfusions (e.g., autologous programs, erythropoietin and other medications), the perioperative use of anticoagulants and antiplatelet medications as well as anesthetic and surgical technique.

In contrast, the guidelines of the American College of Physicians (ACP)[7] contained 26 recommendations focused primarily on red blood cell transfusion, with a few advocating alternatives. Of the 26, 7 were general recommendations about transfusion and 19 were directed at specific patient populations. In this guideline, the avoidance of allogeneic red blood cells was one of the overriding principles.

The guidelines developed by the American Society of Anesthesiology[74] included not only recommendations regarding red blood cells but also for plasma, platelet and cryoprecipitate. For red blood cells, they state that transfusions are particularly beneficial when hemoglobin concentration is between 60 and 100 g/L. In addition, the transfusion decision should incorporate an assessment of risks for complications resulting from inadequate oxygenation. Alternatives were also mentioned as potentially beneficial.

One of the first guidelines regarding red blood cell transfusion from the NIH addressed 4 issues: the criteria for transfusions, the morbidity associated with anemia, the risks of transfusion and acceptable alternatives in the perioperative setting.

Plasma guidelines

Twelve CPGs addressing the use of plasma were published between 1985 and 1996.[8,74,76,77,79–83,85–87] Of these,

Table 1: Summary of 17* guidelines for the transfusion of red cells and plasma

Guideline	Sponsor	Setting	Methods			Recommendations		Comments
			Electronic search	Literature selection criteria	Grading of evidence	Number	Grading	
Red cells Surgical red blood cell transfusion practice policies[84] (1995)	None	Perioperative	No	No	No	31	Yes	Evidence inconsistently applied. Many recommendations. Very detailed.
Consensus statement on red cell transfusion[78] (1994)	Royal College of Physicians of Edinburgh	All patients	No	No	No	4	No	Report from consensus conference. Not evidence based.
Pratiques transfusionelles en hématologie clinique[75] (1993)	Collège français des hématologistes	Acute leukemia	No	No	No	1	No	Only guideline recommending trigger (80 g/L). Use of platelets addressed.
Practice strategies for elective red blood cell transfusion[7] (1992)	American College of Physicians	All patients	Yes	No	No	26	No	Focus on blood avoidance. Literature search not reproducible.
Perioperative red blood cell transfusion[9] (1988)	National Institutes of Health	Perioperative	No	No	No	5	No	Broad recommendations. Focus on blood avoidance.
Plasma Practice parameters for the use of fresh frozen plasma, cryoprecipitate and platelets[85] (1994)	American College of Pathologists	All patients	No	No	No	16†	No	Does not advocate assessment of ongoing bleeding.
Guidelines for the use of fresh frozen plasma[86] (1992)	British Society for Haematology	All patients	No	No	No	17	No	Limited to pathologists. Defines fresh-frozen plasma, indications and dosing. Not evidence based.
Hospital blood transfusion audit systems[87] (1988)	British Society for Haematology	Massive bleeding	No	No	No	8‡	No	Specific to massive blood loss.
Fresh-frozen plasma: indications and risks[8] (1985)	National Institutes of Health	All patients	No	No	No	9§	No	Defines fresh-frozen plasma, indications and dosing. Expert panel.
Red cells and plasma Practice guidelines for blood component therapy[74] (1996)	American Society of Anesthesiologists	Perioperative obstetrics	Yes	Yes	Yes	11	Yes	Most rigorously developed guidelines. Evidence limited to clinical studies.
Blood component therapy[77] (1995)	American College of Obstetricians & Gynecologists	Obstetrics, gynecology	No	No	No	10	No	All blood components mentioned. Indications used; contraindications stated. No primary evidence cited.
Criteria for transfusion of blood components[80,81] (1992, 1993)*	Toronto, Vancouver regional Red Cross centres	All patients	No	No	No	9	No	Locally developed. Recommendations limited, not graded. No literature review.
Clinical guide to transfusion[82] (1993)	Canadian Red Cross Society	All patients	No	No	No	13	No	All blood components mentioned. No literature review. Detailed product information.
Guidelines for transfusion support in patients undergoing coronay artery bypass grafting[79] (1990)	American Association of Blood Banks	Coronary artery bypass grafting‡	No	No	No	8	No	Vague recommendations.
Strategies for the review of transfusion practices[83] (1989)	American Association of Blood Banks	All patients	No	No	No	13	No	Audit criteria only. Not a CPG. Not evidence based.
Contemporary transfusion practice[76] (1987)	American Association of Blood Banks	All patients	No	No	No	12§	No	Position paper review more than a CPG. Consensus process not mentioned.

*These 2 guidelines[80,81] were treated as 1 as they were virtually identical.
†In this guideline, there were 8 clinical indications and approximately 8 recommendations on dosing.
‡The number of recommendations was based on the subheadings, not on the number of specific statements addressing therapeutic interventions.
§Only refers to red cell or plasma recommendations.

3 were dedicated to plasma transfusions in specific clinical settings: massive transfusion,[87] coronary artery bypass grafting[79] and perioperative use.[74] The remaining guidelines provided general indications for use, particularly the appropriate clinical settings.[8,85,86] All guidelines were developed and endorsed by major United States or British medical societies.

None of the guidelines advocated the routine use of plasma to treat coagulation abnormalities. Rather they recommended that the administration of plasma be guided by an assessment of the coagulation cascade. With the exception of those of the College of American Pathologists,[85] the guidelines recommended an assessment of the risk of ongoing bleeding as well as the elucidation of specific coagulation abnormalities.

Appraisal of the CPGs

The methods used to develop 17 of the guidelines were evaluated using a checklist of 26 criteria (Table 2). The 2 reviewers disagreed on only 8 (1.9%) of 416 potential interpretations of these criteria. Seven guidelines reported a method, but with insufficient details. Only 2 guidelines reported a computer search of the literature,[7,74] and only 1[74] graded the evidence and the strength of individual recommendations in a systematic fashion. Regarding the completeness of the evidence reviewed, none of the guidelines cited or discussed the small number of available randomized, controlled clinical trials that had been published at least 6 months before the publication of the guideline. None of the guidelines described a specific consensus process in the formulation of recommendations by expert panels. Only 1 guideline clearly indicated the expertise (or representation) of its committee members[74] and none described the membership selection process. Thus, we were unable to determine the committee composition for most guidelines.

Discussion

In this review of published CPGs on the transfusion of red blood cells and plasma, we noted that most of the 16 guidelines were weak in terms of the methods they used, compared with current norms.[28,29,88,89] Only 2 described a literature search and the selection and appraisal strategy in any detail, and none described important aspects of the guideline formulation process. These findings illustrate the need for rigorously developed, evidence-based guidelines in the area of allogeneic red blood cell and plasma transfusion.

Identifying all relevant evidence and subjecting it to critical appraisal are the most important elements of an evidence-based guideline process. Unbiased selection and evaluation of the published material assures the practitioner that practice guideline developers are reflecting the current state of knowledge rather than their opinions. Although 2 guidelines reported using electronic searches, the small number of published randomized, controlled clinical trials comparing transfusion practices were not cited, and insufficient information was reported to allow the searches to be reproduced.

CPG experts have indicated that several steps in the formulation of the recommendations or guidelines may be important in elucidating important values and biases interjected into the process.[28,32,90] To this end, aspects of the guideline formulation process were examined. All guidelines were developed using expert panels; however, none of the guidelines described the selection and expertise of the panelists, the mechanism used in resolving disagreements or how expert opinion rather than evidence was used in the formulation of individual recommendations. Despite these major shortcomings, the recommendations may not have been significantly affected by the various consensus processes because the clinical evidence is rather weak.

There is also some question as to which method is best; however, an explicit description of the method would make the process more transparent and perhaps more credible. The more rigorous reporting of guidelines, evident in recent publications, has only been advocated by experts in the field over the past few years.[28,29,88,89] Thus, older guidelines should not be expected to fulfill newer and more demanding standards.

The need for CPGs for the use of allogeneic red blood cells and plasma stems from a major change in the risks, both real and perceived, of contact with blood products following the realization that blood transmits viruses such as HIV and hepatitis. Because of these perceptions, many guidelines have promoted a philosophy of blood and plasma avoidance with less consideration for the consequences of withholding transfusions. The ACP recommendations,[7] for both chronic and acute anemia, espoused such an approach. Unfortunately, there have been very few clinical trials that adequately describe all clinically important benefits, risks and costs of various transfusion strategies in different patient populations. The paucity of randomized, controlled trials has ensured that the recommendations in published guidelines rely heavily on expert opinion, which has sometimes (particularly more recently) valued the risks of viral transmission through blood products above all other consequences of the transfusion decision.

Although guidelines have received increased attention in recent years, recommendations for allogeneic blood transfusion therapy were in existence as early as 1941.[1] In 1960, Graham-Stewart[91] published criteria for a justi-

fiable transfusion. Like many of the more recent guidelines, the author advocated the use of clinical judgement when making a decision to transfuse, going as far as declaring that all traditional dogma surrounding transfusion medicine should be abandoned in favour of evaluating each case on its own merit.

The most recently published guideline is also the most rigorously developed and methodologically sound.[74] Like several other guidelines, those of the American Society of Anesthesiology Task Force advise against a "transfusion trigger," although they suggest a range of hemoglobin levels that may guide the clinician. This task force recommended that the decision to transfuse should be based upon a patient's risk for complications from inadequate oxygenation, as well as all other important physiologic and surgical factors. Interestingly, the recommendations were fewer in number and less specific in guiding clinical decision-making compared with the surgical practice

Table 2: Evaluation of 17* guidelines by 2 reviewers using a checklist

Guideline evaluation criteria	Yes	No	Disagreement
Context			
Was the rationale for the guideline stated?	14	2	0
Were all appropriate health care professionals involved in guideline formulation?†	9	3	1
Methods, general			
How were the methods for guideline development described?			
1. Fully described and reproducible?	0	16	0
2. Refer to a process but insufficient detail to reproduce?	7	9	0
3. No method was described?	9	7	0
Was a target patient population specified?	8	5	3
Were all relevant outcomes identified (e.g., mortality, morbidity, quality of life)?	2	12	2
Were alternative interventions identified?	11	5	0
Does the guideline include a definition of the intervention and its optimal role in patient management?	6	10	0
Search strategy			
Was a computer search conducted?	2	14	0
Was a manual search of references from relevant articles conducted?	2	14	0
Is the search strategy reproducible?	0	16	0
Literature selection			
Were reasons for inclusion of literature explicitly stated?	1	15	0
Were reasons for exclusion of literature explicitly stated?	0	16	0
Data synthesis			
Was an attempt made to evaluate the strength of evidence? (i.e., Did the authors distinguish between randomized, controlled trials and animal studies?)	1	15	0
If so, was a system of evidence evaluation determined?	1	14	1
Recommendations			
Was the process of recommendation formulation specified?	2	14	0
Does each recommendation cite specific evidence bearing upon the conclusion?	9	7	0
Are each of the recommendations appropriate given the strength of the evidence?†	3	4	0
Does the guideline explicitly state the strength of the recommendation?	2	14	0
Guidelines			
Are all of the recommendations in the document consistent with each other?	13	2	1
Do the guidelines provide the option of choice for the patient, if appropriate?	3	13	0
Have the guidelines been peer reviewed?	12	4	0
Have the guidelines been pilot tested?	0	16	0
Is there a stated plan for revisions or renewal?	0	16	0
Has the effectiveness of the guidelines been evaluated?	0	16	0

Note: "Guidelines" refers to the entire document; "recommendations" refers to the individual statements in the document.
*Two guidelines[80,81] were treated as 1 as they were virtually identical.
†There was insufficient information provided to answer this question in the remaining guidelines.

policies[84] and the practice strategies for elective red blood cell transfusion from the ACP.[7]

One decision of the task force was to limit the available evidence to clinical outcomes-based studies, which clearly introduces a distinct bias in a field with such limited evidence. Although the guidelines were evidence-based, the recommendations on autologous transfusion, intraoperative salvage and hemodilution did not cite nor report on a considerable number of existing clinical trials.

Interestingly, 10 of the 17 guidelines were sponsored by organizations in the United States. Of the remaining 7, 3 were published Canadian transfusion guidelines that did not fully satisfy our definition because there was no synthesis of the available literature and they did not include any references. In addition, they were developed by transfusion specialists rather than a cross-section of potential users. They were also not subjected to any form of peer review, and they did not describe the methods used.

In conclusion, the concept of an arbitrary transfusion trigger for allogeneic red blood cell transfusions or standard protocols for plasma use was refuted by most guidelines; instead most advocated an assessment of clinical need or use of clinical judgement. There was a wide range in the number of recommendations and the breadth of content included in the various guidelines. The published allogeneic red blood cell and plasma transfusion guidelines thus have significant methodologic limitations, and it is unclear whether the values of Canadian patients and practitioners are reflected in their recommendations. We recommend that future guidelines in transfusion medicine be evidence-based and report in detail the methods used in their formulation.

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References

1. Adams RC, Lundy JS. Anesthesia in cases of poor surgical risk: some suggestions for decreasing the risk. *Surg Gynecol Obstet* 1941;71:1011-4.
2. Zauder HL. Preoperative hemoglobin requirements. *Anesth Clin N Am* 1990;8:471-80.
3. Stehling L, Simon TL. The red blood cell transfusion trigger: physiology and clinical studies. *Arch Pathol Lab Med* 1994;118:429-34.
4. Graves CL, Allen RM. Anesthesia in the presence of severe anemia. *Rocky Mt Med J* 1974;67:35-40.
5. Lundsgaard-Hansen P. The "critical hematocrit": a figure differing from patient to patient. *Beitr Infusionther* 1992;30:208-15.
6. Carson JL, Willett LR. Is a hemoglobin of 10g/dL required for surgery? *Med Clin North Am* 1993;77(2):335-47.
7. American College of Physicians. Practice strategies for elective red blood cell transfusion. *Ann Intern Med* 1992;116:403-6.
8. Consensus Conference (National Institutes of Health). Fresh-frozen plasma: indications and risks. *JAMA* 1985;253:551-3.
9. Consensus Conference (National Institutes of Health). Perioperative red blood cell transfusion. *JAMA* 1988;260:2700-3.
10. Woolf SH. Practice guidelines, a new reality in medicine: II. Methods of developing guidelines. *Arch Intern Med* 1992;152:946-52.
11. *Guidelines for Canadian clinical practice guidelines*. Ottawa: Canadian Medical Association; 1994.
12. Muakkassa FF. Transfusion therapy. In: Moylan JA, editor. *Surgical critical care*. St. Louis: Mosby; 1994:649-95.
13. Schwartz SI. Hemostasis, surgical bleeding, and transfusion. In: Schwartz SI, Shires GT, Spencer FC, Cowles Husser W, editors. *Principles of surgery*. 6th ed. New York: McGraw-Hill Inc; 1994:95-118.
14. Collins JA. Blood transfusions and disorders of surgical bleeding. In: Sabiston DC Jr. editor. *Textbook of surgery: the biological basis of modern surgical practice*. 14th ed. Philadelphia: Saunders; 1991:85-102.
15. Atkinson RS, Rushman GB, Davies NJH. *Lee's synopsis of anesthesia*. 11th ed. Oxford: Butterworth-Heineman; 1993.
16. Miller RD. Transfusion therapy. In: Miller RD, editor. *Anesthesia*. 4th ed. New York: Churchill Livingstone; 1994:1619-46.
17. Dripps RD, Eckenhoff JE, Vandam LD, editors. Blood component therapy. In: *Introduction to anesthesia: the principles of safe practice*. 7th ed. Philadelphia: Saunders; 1988:282-92.
18. Stoelting RK, Miller RD, editors. Fluid and blood therapy. In: *Basics of anesthesia*. 3rd ed. New York: Churchill Livingstone; 1994:238-45.
19. Mollison PL, Engelfriet CP, Contreras M. *Blood transfusion in clinical medicine*. 9th ed. London: Blackwell Scientific; 1993.
20. Blumberg N, Heal JM, Dodd RY. *Scientific basis of transfusion medicine: implications for clinical practice*. Philadelphia: Saunders; 1994.
21. Schroeder ML, Rayner HL. Transfusion of blood and blood components. In: Lee GR, Bithell TC, Foerster J, Athens JW, Lukens JN, editors. *Wintrobe's clinical hematology*. 9th ed. Philadelphia: Lea & Febiger; 1993:651-99.
22. Klein HG. Blood groups and blood transfusion. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. *Harrison's principles of internal medicine*. 13th ed. New York: McGraw-Hill; 1994:1788-93.
23. Ansell JE. Hematologic problems in the intensive care unit. In: Rippe JM, Irwin RS, Alpert JS, Fink MP, editors. *Intensive care medicine*. 2nd ed. Boston: Little, Brown; 1991:1013-61.
24. Yeston NS, Niehoff JM, Dennis RC. Transfusion therapy. In: Civetta JM, Taylor RW, Kirby RR, editors. *Critical care*. 2nd ed. Philadelphia: Lippincott; 1992:427-43.
25. Schiffer CA. Transfusion therapy in the critical care setting. In: Shoemaker WC, Ayres S, Grenvik A, Holbrook PR, Thompson WL, editors. *Textbook of critical care*. Philadelphia: Saunders; 1989:903-18.
26. Marino PL. Principles of transfusion therapy, editors. In: *The ICU book*. Malvern: Lea & Febiger; 1991:218-31.
27. Oxman AD, Cook DJ, Guyatt GH. Users' guides to the medical literature: VI. How to use an overview. *JAMA* 1994;272(17):1367-71.
28. Hayward RSA, Wilson MC, Tunis SR, Bass EB, Guyatt G. Users' guides to the medical literature VIII. How to use clinical practice guidelines A. Are the recommendations valid? *JAMA* 1995;274(7):570-4.
29. Wilson MC, Hayward RSA, Tunis SR, Bass EB, Guyatt G. Users' guides to the medical literature: VIII. How to use clinical practice guidelines. B. What are the recommendations and will they help you in caring for your patients? *JAMA* 1995;274(20):1630-2.
30. Hayward RSA, Wilson MC, Tunis SR, Bass EB, Rubin HR, Haynes RB. More informative abstracts of articles describing clinical practice guidelines. *Ann Intern Med* 1993;118:731-7.
31. Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature: IX. A method for grading health care recommendations. *JAMA* 1995;274(22):1800-4.
32. Cluzeau F, Littlejohns P, Grimshaw G, Feder G. The development of appraisal criteria for clinical guidelines [abstract]. 12th annual meeting of the International Society of Technology Assessment in Health Care, San Francisco: 1996 [unpublished].
33. Welch HG, Meehan KR, Goodnough LT. Prudent strategies for elective red blood cell transfusion. *Ann Intern Med* 1992;116:393-402.
34. Crosby ET. Perioperative haemotherapy: I. Indications for blood component transfusion. *Can J Anaesth* 1992;39:695-707.
35. Gould SA, Rice CL, Moss GS. The physiologic basis of the use of blood and blood products. In: Nyhus IM, editor. *Surgery annual*. New York: Appleton-Century Crofts, 1984:13-38.
36. Stehling LC. Recent advances in transfusion therapy. *Adv Anesthesiol* 1987;4:213-54.
37. Edelman B, Heyman MR. Blood component therapy for trauma patients. In: Stene JK, Grande CM, editors. *Trauma Anesthesia*. Baltimore: Willams &

Wilkins; 1991:133-76.
38. Stehling L. Indications for perioperative blood transfusion in 1990. *Can J Anaesth* 1991;38:601-4.
39. Hogman CF, Bagge L, Thoren L. The use of blood components in surgical transfusion therapy. *World J Surg* 1987;11:2-13.
40. Kruskall MS, Mintz PD, Bergin JJ, Johnston MFM, Klein HG, Miller JD, et al. Transfusion therapy in emergency medicine. *Ann Emerg Med* 1988;17:327-35.
41. Spence RK, Cernaianu AC, Carson JL, DelRossi AJ. Transfusion and surgery. *Curr Probl Surg* 1993;30:1104-80.
42. Kahn RA, van Aken WG. *Blood transfusion and problems of bleeding*. Boston: Martinus Nijhoff; 1982.
43. Kasprisin CA, Peschel MB. *Practical aspects of blood administration*. Arlington (VA): American Association of Blood Banks; 1986.
44. Greenwalt TJ, Zelenski KR. Transfusion support for haemoglobinopathies. *Clin Haematol* 1984;13(1):151-65.
45. Eisenbrey AB. Red blood cell transfusions. *J Fla Med Assoc* 1993;80(1):39-42.
46. Huestis DW, Bove JR, Busch S. *Practical blood transfusion*. 3rd ed. Boston: Little, Brown; 1981.
47. Rawstron RE. Preoperative haemoglobin levels. *Anaesth Intensive Care* 1976;3:175-85.
48. Collins JA. Current status of blood therapy in surgery. *Adv Surg* 1989;22:75-104.
49. Davies SC, Olatunji PO. Blood transfusion in sickle cell disease. *Vox Sang* 1995;68:145-51.
50. Rudowski WJ. Blood transfusion: yesterday, today, and tomorrow. *World J Surg* 1987;11:86-93.
51. Chaplin H. Packed red blood cells. *N Engl J Med* 1969;281:364-7.
52. Carson JL. Morbidity risk assessment in the surgically anemic patient. *Am J Surg* 1995;170(6A suppl):32s-6s.
53. McClelland DB, Inskip MJ, Sinclair CJ. *Uncertainties and variations in transfusion practice. Annual of Cardic Surgery.* Philadelphia: Current Science;1994:83-8.
54. Ellison N. 1991 Review course lectures: blood transfusion — when and what? Cleveland: International Anesthesia Research Society; 1991;7-13.
55. Lundsgaard-Hansen P. Treatment of acute blood loss. *Vox Sang* 1992;63:241-6.
56. McCullough J, Jacob HS. The chronically transfused patient: advances in treatment. Hosp Pract (Off Ed) 1985;20(7):77-84.
57. Rossi EC. Red cell transfusion therapy in chronic anemia. *Hematol Oncol Clin North Am* 1994;8(6):1045-52.
58. Goodnough LT, Despotis GJ. Establishing practice guidelines for surgical blood management. *Am J Surg* 1995;170(6A suppl):16s-20s.
59. Rosen NR. Current transfusion issues. *Indiana Med* 1989;764-6.
60. Sharon BI. Transfusion therapy in congenital hemolytic anemias. *Hematol Oncol Clin North Am* 1994;8(6):1053-86.
61. Jefferies LC. Transfusion therapy in autoimmune hemolytic anemia. *Hematol Oncol Clin North Am* 1994;8(6):1087-104.
62. Simon TL. Evolution in indications for blood component transfusion. *Clin Lab Med* 1992;12:655-67.
63. Coffin CM. Current issues in transfusion therapy: 2. Indications for use of blood components. *Postgrad Med* 1987;81:343-50.
64. Casteel Campbell L, Von Burton G, Holcombe RF. Transfusion therapy in sickle cell disease patients: methods and acute indications. *J La State Med Soc* 1993;145(12):515-21.
65. Sohmer PR, Dawson RB. Transfusion therapy in trauma: a review of the principles and techniques used in the MIEMS program. *Am Surg* 1979;45:109-25.
66. Fish H. The importance of blood examinations in reference to general anaesthetization and operative procedures. *Ann Surg* 1899;32:79-89.
67. Shields TW, Rambach WA. Whole blood transfusions in surgical practice. *Surg Clin North Am* 1959;39:121-31.
68. Kilduffe RA, DeBakey M. The blood bank and the technique and therapeutics of transfusions. St. Louis: Mosby; 1942.
69. Clark JH, Nelson W, Lyons C, Mayerson HS, DeCamp P. Chronic shock: the problem of reduced blood volume in the chronically ill patient. Part II. Hemoglobin and red blood cell deficits in chronic shock. *Ann Surg* 1947;125(5):626-37.
70. Marshall M, Bird T. *Blood loss and replacement*. London: Edward Arnold Ltd; 1983.
71. *Transfusion medicine in the 1990's*. Arlington (VA): American Association of Blood Banks; 1990.
72. *Clinical practice of transfusion medicine*. 2nd ed. New York: Churchill Livingstone; 1989.
73. *Questions and answers about transfusion practices.* In: Stehling LC, Berry AJ, Ellison N, Faust RJ, Lake CL, McCord ES, Mayers VR. Park Ridge (IL): American Society of Anesthesiologists; 1987:1-41.
74. American Society of Anesthesiologists Task Force on Blood Component Therapy. Practice guidelines for blood component therapy. *Anesthesiology* 1996;84:732-47.
75. Andreu G, Benbunan M, Boasson M, Bussel A, Cordonnier C, Dosquet P, et al. Pratiques transfusionnelles en hématologie clinique : recommandations de la Commission d'Evaluation du Collège français des hématologistes pour le support transfusionnel dans le traitement des leucémies aiguës en aplaisie thérapeutique. *Nouv Rev Fr Hematol* 1993;35:517-22.
76. Petz LD, Tomasulo PA. Red cell transfusion. In: Kolins J, McCarthy LJ, editors. *Contemporary transfusion practice*. Arlington (VA): American Association of Blood Banks; 1987:1-26.
77. ACOG technical bulletin: blood component therapy. *Int J Gynaecol Obstet* 1995;48:233-8.
78. Consensus statement on red cell transfusion. *Br J Anaesth* 1994;73:857-9.
79. Goodnough LT, Johnston MFM, Ramsey G, Sayers MH, Eisenstadt RS, Anderson KC, et al. Guidelines for transfusion support in patients undergoing coronary artery bypass grafting. *Ann Thorac Surg* 1990;50:675-83.
80. Bested AC, Francombe W, Freedman J, Herst R, Norman C, Medical Advisory Council of Canadian Red Cross Toronto Centre. *Criteria for transfusion of blood components*. Toronto: Canadian Red Cross Society; 1992.
81. *Criteria for blood components usage*. Vancouver: Canadian Red Cross Society; 1993.
82. Description of blood components and plasma fractions. In: *Canadian Red Cross Society clinical guide to transfusion.* 3rd ed. Ottawa: Canadian Red Cross Society; 1993.
83. Silberstein LE, Kruskall MS, Stehling LC, Johnston MFM, Rutman RC, Samia CT, et al. Strategies for the review of transfusion practices. *JAMA* 1989;262(14):1993-7.
84. Spence RK. Surgical red blood cell transfusion practice policies. *Am J Surg* 1995;170(6A suppl):3S-15S.
85. Development Task Force of the College of American Pathologists. Practice parameters for the use of fresh-frozen plasma, cryoprecipitate, and platelets: fresh-frozen plasma, cryoprecipitate, and platelets administration practice guidelines. *JAMA* 1994;271:777-81.
86. Contreras M, Ala FA, Greaves M, Jones J, Levin M, Machin SJ, et al. Guidelines for the use of fresh frozen plasma. *Transfus Med* 1992;2:57-63.
87. Ali AM, VanderGliessen B, Blajchman MA. Hospital blood transfusion audit systems. In: Smit Sibinga CT, Das PC, Heiniger HJ, editors. *Good manufacturing practice in transfusion medicine: proceedings of the 18th International Symposium on Blood Transfusion.* Dordrecht (Netherlands): Kluwer Acad Publ; 1994:269-79.
88. Woolf SH, Battista RN, Anderson GM, Logan AG, Wang E, Canadian Task Force on the Periodic Heath Examination. Assessing the clinical effectiveness of preventive maneuvers: analytic principles and systematic methods in reviewing evidence and developing clinical practice recommendations: a report by the Canadian Task Force on the Periodic Health Examination. *J Clin Epidemiol* 1990;43:891-905.
89. Jones J, Hunter D. Consensus methods for medical and health services research. *BMJ* 1995;311:376-80.
90. Grimshaw J, Freemantle N, Wallace S, Russell I, Hurwitz B, Watt I, et al. Developing and implementing clinical practice guidelines. *Qual Health Care* 1995;4:55-64.
91. Graham-Stewart CW. A clinical survey of blood transfusion. *Lancet* 1960;2:421-4.

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