Does single application of topical chloramphenicol to high risk sutured wounds reduce incidence of wound infection after minor surgery? Prospective randomised placebo controlled double blind trial

Clare F Heal, senior lecturer,1 Petra G Buettner, senior lecturer,2 Robert Cruickshank, general practitioner,3 David Graham, general practitioner,3 Sheldon Browning, general practitioner,4 Jayne Pendergast, practice nurse,3 Herwig Drobetz, staff orthopaedic surgeon,5 Robert Gluer, medical student,1 Carl Lisec, surgical registrar6

ABSTRACT

Objective To determine the effectiveness of a single application of topical chloramphenicol ointment in preventing wound infection after minor dermatological surgery.

Design Prospective randomised placebo controlled double blind multicentre trial.

Setting Primary care in a regional centre in Queensland, Australia.

Participants 972 minor surgery patients.

Interventions A single topical dose of chloramphenicol (n = 488) or paraffin ointment (n = 484; placebo).

Main outcome measure Incidence of infection.

Results The incidence of infection in the chloramphenicol group (6.6%; 95% confidence interval 4.9 to 8.8) was significantly lower than that in the control group (11.0%; 7.9 to 15.1) (P = 0.010). The absolute reduction in infection rate was 4.4%, the relative reduction was 40%, and the relative risk of wound infection in the control group was 1.7 (95% confidence interval 1.1 to 2.5) times higher than in the intervention group. The number needed to treat was 22.8.

Conclusion Application of a single dose of topical chloramphenicol to high risk sutured wounds after minor surgery produces a moderate absolute reduction in infection rate that is statistically but not clinically significant.

Trial registration Current Controlled Trials ISRCTN73223053.

INTRODUCTION

Chloromycetin ointment consists of 10 mg/g of chloramphenicol in plastibase 30W and soft white and liquid paraffin.12 Chloramphenicol has a broad spectrum of activity against Gram positive and Gram negative bacteria, rickettsias, and Chlamydia.3 Chloramphenicol ointment is indicated for treatment of bacterial conjunctivitis, but little evidence exists for its effectiveness in prophylaxis or treatment of wound infection. Despite this, it is regularly used in areas outside its main indication. Before our study, several of the investigating general practitioners had applied it to sutured wounds as prophylaxis against wound infection. A survey of UK plastic surgeons reported that 66% used chloramphenicol eye ointment in their practice, mainly as prophylaxis against infection.4 The ointment has been used as an adhesive for replacement of the nail bed.5 A comprehensive Medline search found only one other study relating to the use of topical chloramphenicol ointment on wounds; this study investigated the application of chloramphenicol ointment to wounds after hip replacement.6 The incidence of wound infection in the intervention group was reduced (4% v 8%), but the sample size was small and the results were not statistically significant.

Topical ocular chloramphenicol is widely used in the United Kingdom and Australia for the treatment of conjunctivitis, but is very rarely prescribed for this indication in the United States.7 Some controversy previously existed about the link between aplastic anaemia and topical ocular chloramphenicol, on the basis of a small number of single case reports,7 but two international case-control studies provided no support for this association. Although the association between ocular chloramphenicol and aplastic anaemia cannot be excluded, the risk is less than one in a million per treatment course.8 No incidences of aplastic anaemia after dermatological application have been reported, despite widespread use.

A previous study of wound infection after minor surgery involving general practitioners in Mackay, Queensland, showed an overall incidence of wound infection of 8.6%.910 This incidence was higher than expected on the basis of the published results of a similar Australian general practice cohort (1.9%), a skin cancer clinic cohort (1.5%), and a European dermatology clinic cohort (2%).11-13 The acceptable rate of infection after clean minor surgery is suggested to be
nurses invited consecutive patients presenting for minor skin excisions to take part in the trial. The nurses collected demographic information on all patients, as well as clinical information on the presence of diabetes or any other predetermined important medical conditions. They used a body site map to define the excision site. At the end of the study we asked the practice nurses to re-examine computer records to fill in any missing data. The principal researcher visited participating general practitioners and practice nurses to provide training and ensure that recording was standardised.

Eligibility criteria
All patients presenting to a participating general practitioner for “minor skin excision” from all body sites were eligible to participate in the study. Skin flaps and two-layer procedures were recorded and included. We excluded patients who were already taking oral antibiotics, for whom oral or topical antibiotics were clinically indicated immediately postoperatively, or who were on immunosuppressive drugs. Other exclusion criteria were excision of sebaceous cyst, history of allergy to any of the ingredients of Chloromycetin ointment, and personal or family history of aplastic anaemia.

Surgical wound management protocol
We ran a workshop for participating general practitioners to develop guidelines to ensure that excisions were managed in a standardised manner. We were unable to reach consensus about skin preparations, so normal saline was used at one centre and chlorhexidine at two centres. The procedure shown in box 1 was agreed.

Intervention
We could not get information about the exact proportions of the constituents of the base of Chloromycetin ointment from the manufacturer. The principal investigator visited a compounding pharmacist to develop a close match to the vehicle of the Chloromycetin ointment by using a mixture of soft white and liquid paraffin, prepared single doses of the ointment in sterile jars, and stored them in a refrigerator. Immediately after suturing, the doctor applied either paraffin ointment or chloramphenicol ointment to the sutured wounds by using sterile forceps. Sufficient ointment was applied to cover the surface of the wound.

Recruitment, randomisation, and blinding
We used computer generated random numbers and opaque sealed envelopes to randomise patients. Only the principal investigator was aware of the identity of the coded ointments. The practice nurses enrolled patients and assigned participants to their groups. All participating patients received written instructions on postoperative wound care. Both groups were asked to
take their dressing off after 24 hours and to avoid the using antiseptics (fig 1).

Clinical outcomes
The practice nurse or the doctor assessed wounds for infection on the agreed day of removal of sutures or sooner if the patient re-presented with a perceived infection. Practice nurses and doctors assessing outcome were blinded to the allocation of intervention and control groups. We adapted our definition of wound infection from standardised surveillance criteria for defining superficial surgical site infections developed by the Centre for Disease Control’s National Nosocomial Infection Surveillance System (box 2). We also developed our own wound scale, after reviewing several existing scales in the literature, in order to improve rigour. This wound scale differentiated no infection or erythema; stitch abscess; less than 1 cm erythema from the wound margin; greater than 1 cm erythema from the wound margin; and deep infection or systemic symptoms. The primary researcher briefed all participating doctors and nurses on the definition of infection and also gave them written information. We asked practice nurses to swab any discharging infections to investigate any pattern of antimicrobial resistance.

Sample size
We calculated sample size on the basis of our previous study, which showed an infection rate of 8.6%. On the basis of a projected infection rate of 10%, we decided that an absolute decrease in incidence of infection of 5% would be clinically significant. To come to this conclusion with statistical confidence—a power in excess of 80% and a significance level of 0.05—we needed a total of 473 patients in the intervention group and 473 patients in the control group.

Statistical analysis
We based all analysis on the intention to treat principle. Depending on the distribution, we describe numerical data as mean value and standard deviation or median value and interquartile range. We present percentages with 95% confidence intervals. Because the sample was recruited through 15 different general practitioners and outcome might be more similar for patients from one medical professional (clustering) than from several, we adjusted confidence intervals and P values for this cluster sampling approach. Participating doctors were the primary sampling unit, and we applied the survey commands of Stata (release 8). We considered P values less than 0.05 to be statistically significant.

RESULTS
Practice and study characteristics
Of the total of 1246 patients who attended for skin excisions during the period from June 2007 to March 2008, 232 patients were excluded (table 1). Of the remaining 1014 patients, 509 were randomised to the intervention (chloramphenicol) group and 505 to the placebo (paraffin) group. A total of 42 patients were eventually lost to follow-up because they had their sutures removed elsewhere. Follow-up was completed in 972 (95.9%) randomised patients (fig 2).

Comparisons at baseline
Large differences existed between the intervention and the control groups at baseline (table 2). In the intervention group, 71.7% of patients were diagnosed with non-melanoma skin cancer or solar keratosis compared with 65.1% in the control group.

Incidence of infections
Infection occurred in 85 (8.7%) of the 972 excisions. The incidence of infection in the chloramphenicol group (6.6%; 95% confidence interval 4.9 to 8.8) was significantly lower than the incidence in the control group (11.0%; 7.9 to 15.1) (P=0.010; adjusted for cluster sampling). The relative risk of infection was 1.7 times higher in the control group compared with the intervention group (table 3). The number needed to treat (number of wounds treated for each infection prevented) was 22.8 (488/21.4).

We found no significant difference in the wound score between the control and intervention groups (P=0.253), although 5.5% of patients showed erythema greater than 1 cm in the intervention group compared with 9.1% of patients in the control group (table 3).

Communications to the editor
Staphylococcus aureus infections that were resistant to benzylpenicillin but sensitive to all other antibiotics in 22 cases. In one case, additional resistance to erythromycin but sensitivity to all other antibiotics was noted. In another case, Pseudomonas

Box 2 Definition of surgical site infection
- Infection must be within 30 days of excision
- Purulent discharge from the wound must be present, or
- The general practitioner must diagnose a wound infection, or
- The general practitioner prescribes antibiotics
- Stitch abscess must not be counted as an infection
Table 1 | Reasons for exclusion from study

| Reasons                                      | No (%) patients (n=232) |
|----------------------------------------------|------------------------|
| Patient declined participation              | 139 (60)               |
| Patient on oral antibiotics                  | 39 (17)                |
| Doctor did not follow study protocol         | 20 (9)                 |
| History of allergy to Chloromycetin          | 2 (1)                  |
| Patient did not plan to return for removal of sutures | 12 (5)               |
| Shave biopsy done                            | 6 (3)                  |
| Patient on immunosuppressive drug            | 4 (2)                  |
| Patient with infected sebaceous cyst         | 10 (4)                 |

DISCUSSION

The results of this study suggest that a single dose of topical chloramphenicol to sutured wounds can produce a relative reduction in infection rate of about 40%. The absolute reduction was 4.4%, which fell short of our pre-determined reduction for clinical relevance (5%), so this was essentially a negative trial. The incidence of infection in our control group (11%) is much higher than reported in the published literature looking at similar cohorts. The intervention thus may not produce a worthwhile absolute reduction in infection in low risk settings where infection rates are already low; the number needed to treat in these circumstances would be much higher than our figure of 22.8.

Limitations

The study had several limitations. Various characteristics influence the occurrence of infections; although we recorded information on as many variables as possible, ensuring that the baseline data were comparable proved difficult. For example, inadequate data were recorded on suture size and occupation, so we could not compare these factors. In addition, the prevalence of diabetes and of other medically important conditions was probably under-recorded, and power to analyse these subgroups was limited. Surgical training and technique of the general practitioners involved is a potential confounder that would be difficult to quantify and was not recorded. However, we adjusted the statistical analysis for the cluster sampling, taking the doctor as the primary sampling unit. The type of skin preparation used by the three participating practices differed, but we found no previously published evidence that this makes any difference to infection rates. A total of 42 participants were lost to follow-up. If all 21 participants who were lost to follow-up in the intervention group had developed an infection, the rates of infection in both groups would have been similar (10.4% and 11.0%); however, we believe that this scenario is extremely unlikely.

Diagnosis of infection—even when guidelines are used—is still subjective, and inter-observer and intra-observer variation may occur. The definition we used is the most widely implemented standard definition of wound infection, and by developing our own wound assessment scale we hoped to reduce the subjectivity of diagnosis of infection. We have no evidence to support the intra-practice and inter-practice reproducibility of measurement and recording procedures.

The study did not have an arm in which no ointment was applied, so we do not know if the ointment itself had any pro-infective or anti-infective properties. The ointment base of Chloromycetin consists of a mixture of soft white paraffin, liquid paraffin, and plastibase 30W, which is a plasticised hydrocarbon gel consisting of 95% mineral oil and 5% polyethylene glycol. We could not get information about the exact proportions of these constituents from the manufacturer. Our placebo ointment consisted of 50% soft white paraffin and 50% liquid paraffin and was not completely identical to the ointment base of Chloromycetin as it did not contain plastibase 30W. We cannot determine if this substance has an effect on infection, although we think that this is unlikely. Our trial used only a single dose of chloramphenicol ointment. We have no reason to surmise that repeated doses might lead to a greater reduction in infection rate.

Table 2 | Baseline comparisons of intervention (chloramphenicol) and control (paraffin) groups. Values are numbers (percentages) unless stated otherwise

| Characteristics | Intervention group (n=488) | Control group (n=484) |
|-----------------|---------------------------|-----------------------|
| Patients        |                           |                       |
| Mean (SD) age (years) | 59.5 (23.2)       | 59.0 (27.5)           |
| Male            | 266 (54.5)                | 262 (54.1)            |
| Smoking status: |                           |                       |
| Never smoked    | 298 (61.1)                | 299/483 (61.9)        |
| Ex-smoker       | 109 (22.3)                | 108/483 (22.4)        |
| Current smoker  | 81 (16.6)                 | 76/483 (15.7)         |
| Diabetes mellitus | 37 (7.6)                | 50/483 (10.4)         |
| With medical condition* | 79/478 (16.5)   | 86/475 (18.1)         |
| Lesions         |                           |                       |
| Body site:      |                           |                       |
| Neck and face   | 166 (34.0)                | 152 (31.4)            |
| Upper extremities | 139 (28.5)             | 140 (28.9)            |
| Trunk           | 108 (22.1)                | 102 (21.1)            |
| Lower extremities | 75 (15.4)              | 90 (18.6)             |
| Histology:      |                           |                       |
| Melanoma and naevi | 64 (13.1)              | 74 (15.3)             |
| Non-melanoma skin cancer and precursor | 350 (71.7)   | 315 (65.1)            |
| Other†          | 74 (15.2)                 | 95 (19.6)             |
| Procedures      |                           |                       |
| Mean (SD) length of excision (mm) | 20.9 (25.6)   | 21.0 (28.8)           |
| Median (interquartile range) No of days until removal of sutures | 7 (7-9)      | 8 (7-10)              |
| With flap       | 1 (0.2)                   | 3 (0.6)               |
| With two level procedure | 4 (0.8)          | 4 (0.8)               |

*Chronic obstructive pulmonary disease (n=14), aspirin or clopidogrel (n=120), oral steroids (n=3), continuous inhaled steroids (n=9), warfarin (n=42), ischaemic heart disease (n=7), peripheral vascular disease (n=6), and current cancer (n=21).
†Included sebhoenar keratosis, re-excisions of melanoma and basal cell carcinoma, sebaceous cyst, epidermal cyst, wart, and dermatitis.
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WHAT THIS STUDY ADDS

A single application of topical chloramphenicol to high risk sutured wounds reduced infection by 40%.

WHAT IS ALREADY KNOWN ON THIS TOPIC

A survey of UK plastic surgeons showed that 66% use chloramphenicol ointment in some capacity

A small pilot study suggested that chloramphenicol ointment might reduce the incidence of wound infection

No published studies have been done in a primary care setting

Table 3 | Incidence of wound infections in intervention (chloramphenicol) and control (paraffin) groups

| Infections | Intervention group (n=488) | Control group (n=484) | Combined results (n=972) |
|------------|---------------------------|-----------------------|--------------------------|
| No of infections | 32                        | 53                    | 85                       |
| Incidence of infection | 6.6%                      | 11.0%                 | 8.7%                     |
| Relative risk (95% CI) of infection | 1 (reference category) | 1.7 (1.1 to 2.5) | NA                       |
| Wound score: | (n=487) | (n=483) | (n=970) |
| Stitch abscess | 14 (2.9%) | 14 (2.9%) | 28 (2.9%) |
| <1 cm erythema | 67 (13.8%) | 62 (12.8%) | 129 (13.3%) |
| >1 cm erythema | 27 (5.5%) | 44 (9.1%) | 71 (7.3%) |

NA=not applicable.

Generalisability

Some limits to generalising these findings exist. The population of Mackay is slightly older than the general Australian population and has a lower median household income.22 Mackay is a provincial town in tropical North Queensland. The climate is hot and humid, with a mean daily maximum temperature ranging between 24.2 °C and 30 °C during the summer months and a relative humidity of 75-79%.23 These tropical conditions could increase sweat production and produce damp dressings, which might reduce the effectiveness of wound dressings as a potential barrier against exogenous bacteria.24-26 This would make wounds more prone to infection in a tropical environment, so the results may not necessarily be generalisable to a temperate climate, although no published evidence shows that heat and humidity increase infection rates. This might also explain why our infection rates were higher than suggested by previous data from temperate climates.27-31

Antibiotic use

Some concern exists about the overuse of topical antibiotics resulting in antibiotic resistance. British and Australian guidelines suggest that use of topical antibiotics should be restricted because of the capacity of most topical drugs to select resistant micro-organisms and to cause sensitisation. The guidelines also suggest that antimicrobials recommended for topical use should be selected from classes not in use for systemic treatment.32 33 A contrary argument says that the potential for antimicrobial resistance with topical antibiotics is actually lower than with systemic antibiotics because of the higher local concentration achieved by topical delivery.34 Patterns of antimicrobial activity and resistance have been examined for other antibiotic ointments.70-30 However, no evidence exists, over three decades of extensive use worldwide, to show that, with the exception of mupirocin, topical antibiotics administered on an outpatient basis contribute to any emerging resistance pattern.28 Chloramphenicol eye drops have been shown to be effective in the treatment of meticillin resistant Staphylococcus aureus ocular surface infections.31

Some concern also exists about the incidence of allergic contact dermatitis with use of topical antibiotics. For topical neomycin, this has been shown to be as high as 11% in a population referred for diagnostic patch testing.32 However, some evidence shows that the incidence of this reaction is as low as 1% when the ointment is used in the general population.28 The reaction is much more common among patients previously exposed to neomycin ointment.22 Contact allergy has been reported with the use of chloramphenicol ointment, but the incidence is thought to be low.32 34 Although any connection between the use of topical chloramphenicol and aplastic anaemia is unlikely,7 8 our study was not large enough to fully assess the risk in this setting.

Antibiotic prophylaxis is probably prescribed excessively or inappropriately for dermatological surgery and is thought to be best reserved for patients at high risk.19 35 36 No data are available on the current prescribing habits of Australian general practitioners regarding oral or topical antibiotic prophylaxis for minor excisions. Although no evidence is available on what reduction in the rate of infection we might reasonably expect from the use of oral prophylactic antibiotics for minor excisions, some evidence shows a 50% reduction in risk of infection when perioperative oral antibiotic prophylaxis is used after clean surgery.17 A similar reduction in infection rate from a single dose of topical antibiotic, as in this study, may encourage a reduction in the use of oral antibiotics.

The decision to prescribe antibiotic prophylaxis is complicated; in addition to efficacy, the antibiotic costs, adverse effects, and resistance should be taken into account. However, in some circumstances, topical delivery of antibiotic may be preferable to systemic administration.32 37 The results of this study could encourage the judicial use of topical antibiotics after minor skin surgery. However, topical
chloramphenicol would be unlikely to produce a worthwhile absolute reduction in infection rates in low risk settings in developed countries. Future research could explore the possibility that important reductions may be seen in higher risk wounds or in more resource poor settings.

Conclusion
This study suggests that application of a single dose of topical chloramphenicol to high risk sutured wounds after minor surgery produces a moderate absolute reduction in infection rate.

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1 Allen LV. Compounding gels. Secundum Artem. 2007;4(5) (available at www.picosearch.com/cgi-bin/ts.pl?index=406555&query=Gel&SEARCH=GO).

2 Pfizer. Product information: Chloramycetin eye ointment. Pfizer, 2005 (available at www.pfizer.com.au/ProductInfo.aspx).

3 Therapeutic guidelines: antibiotic. Version 13. North Melbourne, Victoria: Therapeutic Guidelines, 2006.

4 Erel E, Platt A, Ramakrishnan V. Chloramphenicol use in plastic surgery. Br J Plast Surg 1995;52:326-7.

5 Pasapula C, Strick M. The use of chloramphenicol ointment as an adhesive for replacement of the nail bed after simple nail bed repairs. J Hand Surg (Br) 2004;29:634-5.

6 Kamath S, Sinha S, Shariati E, Young D, Campbell AC. Role of topical antibiotics in hip surgery: a prospective randomised study. Injury 2005;36:783-7.

7 Rayner SA, Buckley RJ. Ocular chloramphenicol and aplastic anaemia: is there a link? Drug Saf 1996;14:273-6.

8 Laporte JR, Vidal X, Bailan E, Ibanez L. Possible association between ocular chloramphenicol and aplastic anaemia—the absolute risk is low. Br J Clin Pharmacol 1996;48:181-4.

9 Heal C, Buettner P, Raasch, Browning S, Graham D, Campbell M, et al. “Can sutures get wet?” A randomised controlled trial of wound management in general practice. BMJ 2006;332:1053-4.

10 Heal C, Buettner P, Browning S. Risk factors for infection after minor surgery in general practice. Med J Aust 2006;185:255-9.

11 Lathlean S. Skin cancer in general practice in South Australia. Aust Fam Physician 1999;28(supp 1):S28-31.

12 Dixon AJ, Dixon MP, Askew DA, Wilkinson D. Prospective study of wound infections in dermatological surgery in the absence of prophylactic antibiotics. Dermatol Surg 2006;32:826-7.

13 Amici J, Rogues A, Lasheras A, Gachi JP, Guillot P, Beylot C. A prospective study of the incidence and complications associated with dermatological surgery. Br J Dermatol 2005;153:967-71.

14 Culver DH, Horan TC, Gaynes RP, Martone WW, Jarvis WR, Emori TG, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index: National Nosocomial Infections Surveillance System. Am J Med 1991;91:112-7S.

15 Haas AF, Grekin RC. Antibiotic prophylaxis in dermatological surgery. J Am Acad Dermatol 1995;33:155-76.

16 Cruse JE, Foad R. The epidemiology of wound infection. Surg Clin North Am 1980;60:27-39.

17 Platt R. Antibiotics prophylaxis in clean surgery: does it work? Should it be used if it does? New Horiz 1998;6(2 suppl):s53-7.

18 Heal C, Buettner P, Raasch B, Browning S. Minor skin excisions in general practice in north Queensland. Aust Fam Physician 2006;35:825-8.

19 Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for the prevention of surgical site infection. Infect Control Hosp Epidemiol 2002;24:267-78.

20 Bruce J, Russell EM, Mollison L, Krukowski ZH. The quality of measurement of surgical wound infection as a basis for monitoring: a systematic review. J Hosp Infect 2001;49:99-108.

21 Edwards PS, Lipp A, Holmes A. Preoperative skin antisepsics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev 2004;(3):CD003949.

22 Australian Bureau of Statistics. Census of population and housing, basic community profiles. 2006. www.abs.gov.au/.

23 Australian Government, Bureau of Meteorology. Climate data online. 2008. www.bom.gov.au/climate/averages/B/ClimateMaps.

24 Edlich RF. Biochemical and clinical aspects. In: Cohen IK, Diegelman RF, Lиндblad WJ, eds. Wound healing. Sydney: WB Saunders, 1992;581-600.

25 Thomas S. Wound management and dressings. London: The Pharmaceutical Press, 1990:9-19.

26 Colebrook L, Hood AM. Infection through soaked dressings. Lancet 1948;2:682-3.

27 British Medical Association, Royal Pharmaceutical Society of Great Britain. British national formulary. London: BMA, RPS, 2006:605-6 (No 52).

28 Leyden JJ, Kligman AM. Contact dermatitis to neomycin sulfate. JAMA 1979;242:1276-8.

29 Bradley SF, Ramsey MA, Morton TM, Kauffman CA. Mupirocin resistance: clinical and molecular epidemiology. Infect Control Hosp Epidemiol 1995;16:354-8.

30 Miller MA, Dascal A, Portnow J, Mendersen J. Development of mupirocin resistance among MRSA after widespread use of nasal mupirocin ointment. Infect Control Hosp Epidemiol 1996;17:811-3.

31 Fukuda M, Ohashi H, Matsumoto C, Mishima S, Shimomura Y. Methicillin-resistant Staphylococcus aureus and methicillin-resistant coagulase-negative Staphylococcus ocular surface infection efficacy of chloramphenicol eye drops. Cornea 2002;21(7 suppl):S86-9.

32 Marks JG, DeLeo VA, Fowler JF, Fransway AF, Maibach HI, Smialowicz S, et al. North American contact dermatitis group patch test results for the detection of delayed-type hypersensitivity to topical allergens. J Am Acad Dermatol 1998;38:911-8.

33 Blondeel A, Oleffe J, Achten G. Contact allergy in 330 dermatological patients. Contact Dermatitis 1978;4:270-6.

34 Buckley S. Survey of patients taking topical medication at their first consultation. Med J Aust 1999;300:1497-8.

35 Messingham MJ, Arpey CJ. Update on the use of antibiotics in cutaneous surgery. Dermatol Surg 2005;31:1068-78.

36 Cho CY, Lo JS. Dressing the part. Dermatol Clin 1998;16:25-47.

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