restriction, questioned if it was an over-reaction to a few case reports, and debated if the time would come when topical chloramphenicol could be a viable treatment option in the American market (which would require an appropriate clinical indication).[13]

Conclusion

We believe a rational antibiotic policy will reduce the emergence of resistance, and suggest that 1 week of topical chloramphenicol should be the cheap, effective and safe first-line treatment for MRSA blepharoconjunctivitis, with systemic eradication therapy to reduce reinfection, and vancomycin reserved for only severe or resistant cases. In a world of sparse novel antibiotics, this small study demonstrates that there is still the potential for other countries to identify, revive and utilise already existing antibiotics, which are not currently licensed or available to their populations.[2,4,7,13] This clinical conundrum is currently the case with topical chloramphenicol and the management of MRSA positive ocular swabs.

Conflict of interest

The authors declare no conflict of interest.

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References

1 Haas W, Pillar CM, Torres M, Morris TW, Sahm DF. Monitoring antibiotic resistance in ocular microorganisms: results from the Antibiotic Resistance Monitoring in Ocular micRorganisms (ARMOR) 2009 surveillance study. *Am J Ophthalmology* 2011; **152**(4): 567–574.e563.
2 Spellberg B, Powers JH, Brass EP, Miller LG, Edwards JE Jr. Trends in antimicrobial drug development: implications for the future. *Clinical Infect Dis* 2004; **38**(9): 1279–1286.
3 World Health Organisation. Antibacterial agents in clinical development. 2017. WHO/EMP/IAU/2017.11. 7. Available at: http://www.who.int/medicines/areas/rational_use/antibacterial_agents_clinical_development/en/ (accessed on 9 October 2017).
4 Buckland D. Antimicrobial resistance and the race to find new antibiotics. *Prescriber* 2017; **28**: 12–15.
5 Bush K, Page MG. What we may expect from novel antibacterial agents in the pipeline with respect to resistance and pharmacodynamic principles. *J Pharmacokinet Pharmacodyn* 2017; **44**(2): 113–132.
6 Falagas ME, Mavroudis AD, Vardakas KZ. The antibiotic pipeline for multi-drug resistant gram negative bacteria: what can we expect? *Expert Rev Anti Infect Ther* 2016; **14**(8): 747–763.
7 Theuretzbacher U, Van Bambeke F, Cantón R, Giske CG, Mouton JW, Nation RL *et al.* Reviving old antibiotics. *J Antimicrob Chemother* 2015; **70**(8): 2177–2181.
8 Both L, Botgros R, Cavaleri M. Analysis of licensed over-the-counter (OTC) antibiotics in the European Union and Norway, 2012. *Euro Surveill* 2015; **20**(34): pii = 30002.
9 Lam RF, Lai JS, Ng JS, Rao SK, Law RW, Lam DS. Topical chloramphenicol for eye infections. *Hong Kong Med J* 2002; **8**(1): 44–47, Review.
10 Robaei D, Naunton M, Watson S. Seeing red: over-the-counter chloramphenicol. *Clin Exp Ophthalmol.* 2015; **43**(2): 99–100.
11 Thomseth V, Cejvanovic V, Jimenez-Solem E, Petersen KM, Poulsen HE, Andersen JT. Exposure to topical chloramphenicol during pregnancy and the risk of congenital malformations: a Danish nationwide cohort study. *Acta Ophthalmol.* 2015; **93**(7): 651–653.
12 Wiholm B-E, Kelly JP, Kaufman D, Issaragrisil S, Levy M, Anderson T *et al.* Relation of aplastic anaemia to use of chloramphenicol eye drops in two international case-control studies. *BMJ* 1998; **316**(7132): 666–666.
13 Fraunfelder FW, Fraunfelder FT. Restricting topical ocular chloramphenicol eye drop use in the United States. Did we overreact?. *Am J Ophthalmol* 2013; **156**(3): 420–422.
14 Sotozono C, Fukuda M, Ohishi M, Yano K, Origasa H, Saiki Y *et al.* Vancomycin Ophthalmic Ointment 1% for methicillin-resistant *Staphylococcus aureus* or methicillin-resistant *Staphylococcus epidermidis* infections: a case series. *BMJ open* 2013; **3**(1): e001206.
15 Fridkin SK, Hageman J, McDougal LK, Mohammed J, Jarvis WR, Perl TM *et al.* Epidemiological and microbiological characterization of infections caused by Staphylococcus aureus with reduced susceptibility to vancomycin, United States, 1997-2001. *Clinical Infect Dis* 2003; **36**(4): 429–439.
16 Limbago BM, Kallen AJ, Zhu W, Eggers P, McDougal LK, Albrecht VS. Report of the 13th Vancomycin-Resistant Staphylococcus aureus Isolate from the United States. *J Clin Microbiol* 2014; **52**(3): 998–1002.

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Sir,

The importance of immunosuppression as risk and prognostic factor for periorbital non-melanoma skin cancers

We read with great interest the article by RC Gerring *et al*[1] regarding prognostic factors and survival rates in a retrospective case series of patients who underwent orbital exenteration for non-melanoma skin cancers (NMSC). The authors have thoroughly described the correlation between survival rates and some factors which are thought to influence the prognosis after orbital exenteration.

Their article does not make any reference to the important relation between immunosuppression and the

behaviour of NMSC. There is a good deal of evidence that shows that azathioprine and cyclosporin, as well as other agents, adversely affect such cancers.[2,3] A direct carcinogenic effect has been described in transplant patients for both azathioprine and cyclosporin, beside their primary immunosuppressive role. The former acts as mutagen and photosensitizer by increasing the level of its metabolite 6-thioguanine, while the latter seems to upregulate the transforming growth factor β (TGF-β), a cytokine implicated in cells proliferation and transformation.

Immunological cancer surveillance systems in patients using these drugs in the long term are known to be impaired in the detection and eradication of precancerous lesions. Finally, evidences suggest that also immunosuppression related to HIV/AIDS, non-Hodgkin lymphoma and chronic lymphocytic leukaemia may increase the risk of developing more aggressive SCCs.[4,5]

Even assuming that no immunosuppressed individuals were present in Gerring *et al*'s[1] sample, we believe that considering immunosuppression among the potential prognostic factors is mandatory as far as NMSC are concerned. This is extensively outlined in many studies, including major reviews and meta-analysis.

Conflict of interest

The authors declare no conflict of interest.

References

1 Gerring RC, Ott CT, Curry JM, Sargi ZB, Wester ST. Orbital exenteration for advanced periorbital non-melanoma skin cancer: prognostic factors and survival. *Eye* 2017; **31**: 379–388.
2 Jiyad Z, Olsen CM, Burke MT, Isbel NM, Green AC. Azathioprine and risk of skin cancer in organ transplant recipients: systematic review and meta-analysis. *Am J Transplant* 2016; **16**: 3490–3503.
3 Berg D, Otley CC. Skin cancer in organ transplant recipients: epidemiology, pathogenesis, and management. *J Am Acad Dermatol* 2002; **47**(1): 1–17.
4 Wilkins K, Turner R, Dolev JC, LeBoit PE, Berger TG, Maurer TA. Cutaneous malignancy and human immunodeficiency virus disease. *J Am Acad Dermatol* 2006; **54** (2): 189–206.
5 Otley CC. Non-Hodgkin lymphoma and skin cancer: a dangerous combination. *Australas J Dermatol* 2006; **47**(4): 231–236.

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Sir,

Response to 'The importance of immunosuppression as risk and prognostic factor for periorbital non-melanoma skin cancers'

We would like to thank Dr Albanese for his interest in our recent publication, RC Gerring *et al.*[1] Although there is no data specifically looking at periorbital skin malignancies, there is significant evidence to support an increased risk for the development of nonmelanoma skin cancer after solid organ transplant at an approximate rate of 65–250-fold for squamous cell carcinoma and 10-fold for basal cell carcinoma as compared to the general population.[2,3]

The pathophysiology underlying these significantly increased skin cancer rates is thought to be through both the carcinogenic action of immune suppressive agents,[4,5] as well as impaired eradication of precancerous changes related to immune suppression.[6] Among transplant patients, known risk factors for the development of skin cancer after transplantation include fairer skin type, level of immune suppression, and degree of ultraviolet exposure.[3,7] Bone marrow transplantation has also been shown to increase the risk of nonmelanoma skin cancers in both children[8] and adults.[9] Given the increasing incidence of both solid organ and bone marrow transplantation, and increased survival after these therapies, immune suppression state in relation to skin cancer is an especially important topic of interest.

Unfortunately, we were not able to obtain this historical patient information consistently as part of our retrospective chart review (study time period of 2002–2012). We were able to obtain historical patient data with regards to skin cancer history, however, significant prior medical history data was often limited. For this reason, we were not able to include immune suppression as part of our analysis. We do, however, appreciate its importance as a potential prognostic indicator and will consider this upon any potential future research.

Conflict of interest

The authors declare no conflict of interest.

References

1 Gerring RC, Ott CT, Curry JM, Sargi ZB, Wester ST. Orbital exenteration for advanced periorbital non-melanoma skin cancer: prognostic factors and survival. *Eye* 2017; **31**: 379–388.
2 Moloney FJ, Comber H, O'Lorcain P, O'Kelly P, Conlon PJ, Murphy GM. A population-based study of skin cancer incidence and prevalence in renal transplant recipients. *Br J Dermatol* 2006; **154**: 498–504.
3 Euvrard S, Kanitakis J, Claudy A. Skin cancers after organ transplantation. *N Engl J Med* 2003; **348**: 1681.
4 Jiyad Z, Olsen CM, Burke MT, Isbel NM, Green AC. Azathioprine and risk of skin cancer in 55 organ transplant recipients: systematic review and meta-analysis. *Am J Transplant* 2016; **16**: 3490–3503.
5 O'Donovan P, Perett CM, Zhang X, Montaner B, Xu YZ, Harwood CA *et al.* Azathioprine and UVA light generate