

Clinical Review

Clinical Review identifies issues in the medical literature of interest to clinicians in Africa. Essential references are given at the end of each section

Dermatology Review

Skin lightening agents: a widespread practice with potentially serious consequences

The aim of this review is to raise awareness of the widespread practice of skin lightening and the potential serious side effects associated with it. Skin lightening is commonly practiced in Africa, the Middle East, Asia, the Caribbean and Latin America. However, its practice is particularly common in sub-Saharan Africa, with reported prevalence rates of use between 26-67%.¹⁻³ The highest prevalence of use has been reported predominantly in West African countries.

The use of skin lightening agents to cosmetically lighten the skin has deep historical and cultural roots. It appears to be driven by social pressures as in some cultures lighter skin colour is perceived to be associated with success and social advantage. Skin lightening agents are also used in an attempt to make the skin appear more radiant as 'teint clair', or clear skin is often the standard of beauty promoted in West African magazines. A recent study from South Africa investigated women's perceptions of the benefits and risks associated with the use of skin lightening agents. Interestingly, the majority claimed awareness of the adverse effects, but this did not deter them from using them, and although 32% reported adverse effects, 90% expressed satisfaction with the results achieved.⁴

Skin lightening is practiced predominantly by women, but studies report that men use them regularly as well. All socio-professional groups are involved in this practice. Women admit to increasing their cosmetic use of skin lightening products before important events such as weddings. Of particular concern are reports of the continued use of these products by pregnant women, and even an increase in use by some pregnant and breastfeeding women in preparation for the baptism of their child.⁵ A recent study amongst Senegalese women of predominantly lower social class highlighted the economic impact of this practice on household income. It demonstrated that the monthly expenditure on skin lightening agents constituted 19% of their total income.⁶ Social pressures of maintaining a lighter skin colour together with a lack of understanding of the constituents of these products has led to them being associated with a high incidence of both local and systemic side effects.



Constituents of skin lightening agents

Skin lightening formulations contain a diverse range of agents. Those that commonly cause complications or potentially can cause serious complications include potent corticosteroids (often clobetasol propionate), high-dose hydroquinone (greater than the recommended 5% maximum concentration), and mercurial derivatives. They are present in varying concentrations and the product information is often misleading (Figure 1). A study conducted in Paris, France, which reported that skin lightening is widely practiced amongst immigrant communities originating from Africa, measured three samples of creams bought from markets and found hydroquinone concentrations of 4.5%, 9% and 16.7%.



Figure 1: A cream which suggests that it contains natural aloe vera actually contains clobetasol propionate.

The packaging of two of the products did not mention the presence of hydroquinone, and the third listed only a 2% concentration of hydroquinone.⁷ Samples analysed in Senegal found hydroquinone concentrations of 4-8.7%.¹ A recent study demonstrated that almost 50% of skin lightening creams used by a sample of Somali women in the USA contained mercurial derivatives at concentrations in excess of the recommended Food and Drug Administration threshold.⁸ Several studies in Africa have reported that the majority of products contain hydroquinone and/or potent topical steroids.^{1,3} However, a study from Togo reported that mercury derivatives were a more common constituent than either corticosteroids or hydroquinone, and were present in 31% of skin lightening agents. Approximately 25% of products used in Senegal and Togo were of unknown composition. Even when the constituents of skin lightening creams are correctly labeled, users are often unaware of the risks associated with them. Alternatively, if they recognise a constituent such as hydroquinone, they may not know what is considered to be a safe concentration to use.

Studies have demonstrated that those who practice skin lightening often use them on a daily basis. In some countries they are commonly used on the body as well as the face, a study in Senegal reported that 92% of users applied them to the whole body.¹ Long term use can cause both cutaneous and systemic side effects, and approximately 70% of users develop complications. Risk factors for developing complications include the type and concentration of lightening agent used, the use of several products at the same time, the length of time that they are used, application all over the body, and sun exposure.

Cutaneous side effects

There are numerous side effects affecting the skin and multiple complications are common. In particular, chronic use of skin lightening agents containing corticosteroids is associated with severe and widespread skin infections (fungal and bacterial), scabies infestation, and pigmentary problems. Skin infections in this context are often clinically atypical and severe, and they can be difficult to treat and may recur. Fungal infections affecting the face are usually a rare occurrence but they are a much more common problem in this group of patients (Figure 2). Dermatophyte fungal on the body can be widespread, inflammatory or pustular. Communities where skin bleaching with potent topical steroids is common practice suffer with high rates of scabies infestation, and scabies often presents with widespread pustular or crusted lesions.¹

Pigmentary problems can be particularly disfiguring and include hyperpigmentation, exogenous ochronosis,



Figure 2: Pityriasis versicolor (*Malassezia* infection) and hyperpigmentation.

and chemical leukoderma. Hyperpigmentation is usually post-inflammatory and often occurs because high dose hydroquinone can be photosensitizing as well as highly irritating producing an irritant contact dermatitis. Ochronosis, which is almost impossible to treat, is characterised by disfiguring blue/black pigmentation in sun exposed areas of the skin, and is a strong indication of the prolonged use of hydroquinone. Chemical leukoderma has mainly been linked to the use of monobenzylolether of hydroquinone, but can rarely be caused by hydroquinone as well.

Steroid induced acne is a very common problem and can be severe (Figure 3). In addition there is the problem of 'rebound acne' when potent topical corticosteroid containing skin lightening agents are abruptly withdrawn. Striae are a common complication and important marker of chronic corticosteroid use. Corticosteroid-induced skin atrophy can also lead to impaired wound healing and wound dehiscence.

Systemic side effects

There is a significant risk of percutaneous absorption with regular, long-term, and all over body application of high concentrations of skin bleaching agents. Adrenal suppression can be induced by a weekly dose of 50g of clobetasol propionate 0.05%.⁹ Studies report that the amount of corticosteroids applied to the skin for skin lightening purposes can reach 350g,² or even 480g⁵ per month. A study in Senegal reported that the average amount of corticosteroid applied every month was 95g (range 15-350g).⁵ Hypertension, diabetes, and low birth-for-weight babies have all been reported in association with potent corticosteroid use.^{5,10} In a hospital based study in Dakar, Senegal, patients who had used skin lightening products for more than 10 years had an odds ratio of 1.3 for developing hypertension, and an odds ratio of 3.6 for developing diabetes.¹⁰ There are reports of adrenal insufficiency when skin bleaching is suddenly stopped. The long-term application of potent topical



Figure 3: Steroid induced acne with hyperpigmentation.

steroids to the face can also increase the risks of cataracts, glaucoma and infections.²

Animal studies have demonstrated that hydroquinone can cause cancer. There has been only a single report from Senegal of the development of cutaneous squamous cell carcinoma in sun-exposed skin of two patients who practiced long-term skin bleaching. Although a direct carcinogenic effect of hydroquinone or other unidentified compounds is possible, the authors suggested that the mechanism of carcinogenesis was more likely to involve melanin destruction, solar exposure, and corticosteroid-induced immunosuppression.¹¹

The renal complications associated with the use of mercurials are well known. In the early 1970s they were the most common cause of nephrotic syndrome in adult women in Kenya. Mercury compounds have also been associated with neurological complications such as insomnia, memory loss and peripheral neuropathy, and there has been a case report of mercury intoxication in

a newborn, which was attributed to the mother's use of mercury containing soap during pregnancy and lactation.⁸

New cases of leprosy remain a problem in certain parts of Africa. There has been a reported case of a delay in the diagnosis of leprosy as a result of the application of a skin lightening agent by the patient to treat the hypochromic lesion of leprosy on her cheek.

The cosmetic use of skin lightening products has had a huge impact on dermatological services. In Dakar, Senegal, the proportion of dermatological visits related to complications of the use of bleaching products significantly increased from only 2% of dermatological consultations in 1976 to approximately 25% by 2003.¹ The high incidence of infections associated with this practice is a significant public health concern. It is important for clinicians to appreciate the dangers of skin lightening agents, and to be able to recognise clinical signs of its use in order to educate their patients and prevent serious sequelae. Patients often do not admit to using them. However, skin lightening agents produce characteristic changes to their skin, which can act as an indicator to the physician. At the early stages of use patients develop erythema, facial hypertrichosis, and hyperpigmentation, particularly affecting the cheekbones, forehead and periocular areas.

Public education campaigns are required to highlight the dangers associated with this practice. Government authorities need to be alerted to this problem and persuaded to clamp down on the production of bleaching agents, which have been incorrectly labeled and marketed, and which contain dangerous levels of bleaching agents. The media also need to understand their responsibility in reinforcing this practice by selecting images of fair skin and promoting this as a desirable attribute.

Mahreen Ahmeen, Department of Dermatology,
Royal Free Hampstead NHS Trust

References

1. Mahé A, Ly F, Aymard G, et al. Skin diseases associated with the cosmetic use of bleaching products in women from Dakar, Senegal. *Br J Dermatol* 2003; 148: 493–500.
2. Faye O, Keita S, Diakité FS, et al. Side effects of de-pigmenting products in Bamako, Mali. *Int J Dermatol* 2005; 44: 35–36.
3. Dadzie O, Petit A. Skin bleaching: highlighting the misuse of cutaneous depigmenting agents. *J Eur Acad Dermatol Venereol* 2009; 23(7): 741–50.
4. Dlova N, Hamed SH, Tsoka-Gwegweni J, et al. Women's perceptions of the benefits and risks of skin-lightening creams in two South African communities. *J Cosmet Dermatol* 2014;13(3):236–41.
5. Mahé A, Perret JL, Ly F, et al. The cosmetic use of skin-lightening products during pregnancy in Dakar, Senegal: a common and potentially hazardous practice. *Trans R Soc Trop Med Hyg* 2007; 101: 183–187.
6. Diongue M, Ndiaye P, Douzima PM, et al. Economic impact of skin-lightening products on household income in sub-Saharan Africa: the case of Senegal. *Med Sante Trop* 2013; 23(3): 308–12.
7. Petit A, Cohen-Ludmann C, Clevenbergh P, et al. Skin lightening and its complications among African people living in Paris. *J Am Acad Dermatol* 2006; 55(5): 873–8.
8. Adawe A, Oberg C. Skin-lightening practices and mercury exposure in the Somali community. *Minn Med* 2013; 96(7): 48–9.
9. Caruthers JA, August PJ, Staughton RC. Observations on the systemic effect of topical clobetasol propionate (Dermovate). *Br Med J* 1975; 4: 203–4.
10. Raynaud E, Cellier C, Perret JL. Dépigmentation cutanée à visée cosmétique. Enquête de prévalence et effets indésirables dans une population féminine sénégalaise. *Ann Dermatol Venereol* 2001; 128: 720–724 (French).
11. Ly F, Kane A, Dème A, et al. First cases of squamous cell carcinoma associated with cosmetic use of bleaching compounds. *Ann Dermatol Venereol* 2010;137(2):128–31.

Medicine Review

African type 1 diabetes - the epidemiology dilemma

It is generally recognised that the incidence of type 1 diabetes, particularly in childhood, is relatively low in sub-Saharan Africa, probably about 2 per 100 000 per year; compared with about 20 per 100 000 per year in Europe. In fact, there is good global evidence that from the equator, type 1 incidence rises the further north countries are situated, with particularly high rates in the Scandinavian countries of northern Europe. There are several theories which attempt to explain this interesting phenomenon, and these have recently been reviewed in an article in the journal *Diabetes Update* by Dr Eleanor Kennedy.¹ This publication will probably not be known to those outside the UK. It is the journal of Diabetes UK (the national patient organisation). UK diabetologists are invited members of this organisation, and also receive the journal. Dr Kennedy summarises four current theories for the north-south variation in type 1 diabetes incidence, as follows:

- The 'sunshine hypothesis'. There is clearly more sunshine in equatorial areas compared with the dark zones of northern Europe and America. This may lead to lower vitamin D levels in the north. There is quite strong evidence that vitamin D supplementation in infancy can protect against the later development of type 1 diabetes in a dose-dependent way.
- The 'hygiene hypothesis'. This theory is well known in asthma epidemiology, but may also apply to type 1 diabetes. The idea is that low exposure to bacteria and viruses in early childhood reduces the immune system's ability to resist later auto-immune attack, including islet cell antibodies and the pancreatic beta cell. Childhood infections are likely to be much more common in poorly-resourced equatorial areas, than in northern areas where the countries are richer, and children live in less crowded environments. Though this is an attractive idea, there is no direct supportive evidence at present.
- The 'cow's milk hypothesis'. It has been known for some time that prolonged breastfeeding can protect against the later development of type 1 diabetes. The effect seems to be related to a delay in the introduction of cow's milk to the infant's diet. It is thought that bovine albumen can mimic islet cell antigens and encourage an autoimmune islet cell attack. Breastfeeding is generally more prolonged in tropical areas than northern more 'developed' countries, which would fit in with this theory. However, a trial is in progress comparing formula (non-bovine) milk with cow's milk in infants at high genetic risk for type 1 diabetes. So far, a difference in future development of type 1 disease has not been demonstrated.
- The 'accelerator hypothesis'. There is evidence that children are currently growing faster and bigger compared with previous generations. This is likely to 'strain' beta cell reserves, inducing relative insulin resistance, which will augment other factors (eg auto-immune) predisposing to type 1 diabetes. Northern areas of the world are clearly more 'obesogenic' than in the tropics, so this hypothesis would fit in with the global variation in type 1 incidence. However,

though there is some evidence to support the 'accelerator hypothesis', it remains a controversial idea.

All of those four theories are interesting, and could play a part in the low type 1 diabetes incidence in the tropics. More research is vital so that the high-risk northern areas of the world can learn from the tropical environment.

Hyponatraemia and mortality

One of the commonest blood tests requested in hospitals is the 'renal profile' or 'urea and electrolytes' (U&Es). A common abnormality detected by this test is a low-level of plasma sodium (Na). In fact, hyponatraemia is probably the commonest biochemical abnormality with a hospital prevalence of about 15%. Traditionally, hyponatraemia is often categorised as mild (plasma Na above 130 mmol/l, but below the lower limit of the reference range), moderate (125-129 mmol/l), and severe (below 125 mmol/l).

There are many causes of hyponatraemia, of which drugs are probably the commonest. Of these, thiazide diuretics are the most frequent cause, but there are many others including loop diuretics, anticonvulsants, antipsychotics and omeprazole. Hypoadrenalism is an important treatable cause - either Addison's Disease or hypopituitarism. Syndrome of inappropriate antidiuretic hormone (SIADH) is common, and may be due to a variety of malignancies, drugs, chest and neurological problems. Finally, in hospital there are iatrogenic causes - usually due to the overuse of hypotonic infusion fluids (eg 5% dextrose).

Whatever the cause, there is evidence that hyponatraemia is associated with excess mortality - both in hospital and after admission. A number of early mortality studies were small and uncontrolled, but there have been much better designed recent studies confirming a significant association between hyponatraemia and mortality. Perhaps the biggest and most convincing of these was a USA report of 98 411 adults hospitalised between 2000 and 2003 in Boston, Massachusetts.² There was an increased mortality risk for those with all degrees of hyponatraemia both in hospital (Odds Ratio 1.47), at 1 year post admission (OR 1.38), and at 5 years (OR 1.25). It was noted that reduction of the degree of hyponatraemia in hospital also reduced mortality risk.

A more recent study from London, UK recorded a case-control study of 139 hospital patients with a plasma Na level <128 mmol/l compared with a matched control group of 254 normonatraemic patients.³ The hospital mortality in the hyponatraemic patients was 17.3% - almost 12 times that of the control group (OR 11.89). Careful group matching and univariate analysis showed clearly that hyponatraemia was an independent risk factor for mortality.

There is therefore convincing evidence that hyponatraemia is a significant and independent mortality risk factor amongst hospital patients. Two important questions however remain. Firstly, what is the actual cause of the mortality - is it a direct effect of low plasma Na levels in the extra-cellular fluid, or is it related more to the underlying causal condition? Secondly, will therapeutic elevation of low plasma Na levels reduce or abolish the mortality risk? The answers to these important questions are not known, and clearly

further research is needed.

For the present, it is important for hospital doctors to recognise the importance of hyponatraemia, and to take the problem seriously. Attempts should be made to find the cause of the abnormality, and if possible correct the underlying problem. Sometimes this may be difficult, but it may also be simple - for example, stopping a thiazide diuretic in a hypertensive patient and substituting an alternative drug.

Neurocystercosis - a new WHO initiative

The syndrome of neurocystercosis is well-known to tropical doctors. It is due to the pig tapeworm *Taenia solium*, and specifically not to the beef tapeworm *Taenia saginatum*. If the segments of *T. solium* disrupt in the upper human bowel, cysts are released and can be absorbed into the circulation. They can then travel to distant organs, and enter a 'blind alley' of the life cycle. After some initial growth they die and calcify, forming typical 'torpedo-shaped' cysticerci. These give a characteristic radiological appearance - particularly on plain X-rays of the muscles of the limbs (especially the thigh), and on CT scans of the brain. It is the central nervous system cysticerci which cause the real clinical problems, and in many countries neurocystercosis is the commonest cause of epilepsy.

The World Health Organisation (WHO) has recently decided to 'prepare battle on cystercosis'.⁴ Standard measures of control are not easy, and include multiple approaches to break the life cycle. This may include control of pig movement, improving meat inspection and sanitation in slaughterhouses and, and possibly mass anthelmintic treatment of pigs and humans in endemic areas.

However, these strategies have so far not been greatly effective in achieving significant reductions in cases of neurocystercosis. New strategies are however now becoming available. One is a pig vaccine to eliminate porcine *T. solium* infection. Preliminary trials in Cameroon have been encouraging, but wider and more definitive studies are needed. It is conceivable that the vaccine could in the future be used in high-risk human populations. A further possible control strategy is the drug oxfendazole, which can be 100% effective in clearing *T. solium* cysts from pigs. Again, there is a possibility of future use of this drug in humans.

There are clearly now a variety of ways in which neurocystercosis may be either eradicated or significantly controlled. To achieve this, however, there will need to be political support, adequate funding, and investment from the pharmaceutical industry. Nevertheless, it is to be hoped that the current WHO initiative will be at least a start to bringing neurocystercosis under control.

Professor Geoff Gill, Liverpool School of Tropical Medicine and University Hospital Aintree, UK

References:

1. Kennedy E. Type 1 diabetes. *Diabetes Update* 2014 (Autumn), 29-33
2. Waikar SS, Mount DB, Curhan GC. Mortality after hospitalisation with mild, moderate and severe hyponatraemia. *Amer J Med* 2009; 122; 857-865
3. Tzoulis P, Bagkeris E, Bouloux P-M. A case-control study of hyponatraemia as an independent risk factor for inpatient mortality. *Clin Endocrinol* 2014; 81: 401-407
4. Maurice J. Of pigs and people - WHO proposes to battle cystercosis. *Lancet* 2014; 384: 571-572

R-Biopharm AG 

The New Standard for Economic Allergy Diagnostics

RIDA qLine® Allergy

- **Quantitative**
real standard curve on each strip
- **Reliable**
calibrated against "1st WHO IRP 67/86" for human IgE
- **Accurate**
high reproducibility



R-Biopharm AG • An der neuen Bergstraße 17, 64297 Darmstadt, Germany
E-mail: clinical.sales@r-biopharm.de • www.r-biopharm.com



AJRM

The African Journal of Respiratory Medicine

THE JOURNAL OF THE PAN AFRICAN THORACIC SOCIETY

www.africanjournalofrespiratorymedicine.com

Includes review articles, original articles, short reports, and up-to-date diabetes medicine news items.

Authors wishing to publish in the AJRM should write to editor@fsg.co.uk for more information.



visit www.africa-health.com today!

History | Subscription | Advertising | Testimonials

Home | Latest Issues | Back Issues | Info centre | Meetings | Staff | Our Publishing Partners | Register for Updates | Contact us

Info centre

Links >>

Register for email updates >>

Opportunities

Meetings >>

Contribute to Africa Health >>

Welcome to the Africa Health web site, the home of practical and relevant information for the busy health professional.

Latest editorial

Can Ebola deliver a legacy?

No apologies, but this issue is Ebola heavy. The extraordinary outbreak in West Africa, the worst in the four decades since the disease was first recorded, caught everyone unawares. In reality, given the foothold it established after going unrecognised for several months within an extremely rural and poor region, it is remarkable that only one case was carried (to Nigeria) beyond the immediate epicenter of Liberia, Guinea and Sierra Leone.

Latest issues

To read the issue click on a cover



Back issues >>

Other titles

 The African Journal of