The taking of adequate Papanicolaou smears

To the Editor: In an article[1] published in the *SAMJ* 4 years ago, I emphasised the need for taking adequate Papanicolaou smears during routine screening. An adequately taken smear should contain both squamous and columnar endocervical cells as an indication that it has been taken from the squamocolumnar junction, the common site for the development of carcinoma of the cervix. In order to ensure that the spatula reaches the squamocolumnar junction, it should have a long arm that enters well into the cervical canal and a broad base to cover the ectocervix. In postmenopausal women and other patients in whom the squamocolumnar junction may not be visible, a brush should be used in conjunction with the spatula.

I recently conducted a limited survey in the western Cape to assess whether there has been any improvement in the taking of smears for cervical cytological screening. The results are as follows:

Adequate smears	*1994*		*1990*
General practitioners	65,3%		54,0%
Gynaecologists	84,7%	85,4%	58,6%
4-partner specialist practice (Aylesbury spatula)	86,3%		
Solo specialist screening mainly postmenopausal patients with Aylesbury spatula and Cervibrush	96,0%		98,3%

It is gratifying to report an improvement in the quality of the smears taken by both gynaecologists and general practitioners over the past 4 years. Further improvement can be expected if the Aylesbury spatula is consistently used and in addition the Cervibrush is used in all postmenopausal women and women in whom the squamocolumnar junction is not visible.

Cervicography as a screening tool is very accurate in the hands of experts, but as yet the specific cameras and trained interpreters are not available in South Africa. It is therefore important that all who take cervical smears should do so in an adequate manner using the best tools.

Thanks to Drs Judith Whittaker and Pauline Close for supplying some of the figures.

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1. Craig CJT. The taking of adequate cervical smears. *S Afr Med J* 1990; **77:** 237-240.

Cost-benefit of medicines — indapamide compared with other thiazide diuretics

To the Editor: With close to R1 billion spent annually on the promotion of medicines by the pharmaceutical industry, a responsible and balanced perspective on cost-effectiveness of medicines is like the proverbial flatus in a thunderstorm; it is just not noticeable unless because of the odour. This letter serves the latter function.

The *SAMJ* recently published a supplement[1] on the diuretic-induced dysmetabolism in the long-term management of hypertension.[1] Although this supplement was published for Servier Laboratories it was nowhere stated whether it had been excluded from any peer review.

For the sake of optimal patient care, which, especially in South Africa, should take into consideration an optimal cost-benefit ratio, the facts about the cost and efficacy of indapamide (the medicine promoted in this paper) compared with other thiazide diuretics should be brought to the attention of the prescribing doctor.

1. Indapamide (Natrilix) is an idole derivative of chlorosulphonamide and is as such indeed classified as a thiazide diuretic.[2]

2. Indapamide has been available on the South African market for more than 20 years as a diuretic. In the early 1980s the package insert was changed to omit the indication of oedema, which was replaced by the indication of hypertension.

3. The efficacy of the antihypertensive effect of indapamide is well established, but so is the efficacy in hypertension of other thiazide diuretics, even in low dosage, e.g. hydrochlorothiazide 12,5 mg and chlorthalidone 15 mg.[3]

4. Low-dose chlorthalidone and hydrochlorothiazide do not have any undesirable side-effects on either lipid or glucose metabolism, although uric acid values may be slightly raised in patients taking chlorthalidone.[4]

5. Despite several requests to Servier over many years there still is no clinical study available to compare directly the efficacy and toxicity of indapamide 2,5 mg with low-dose hydrochlorothiazide or chlorthalidone. All studies sponsored by Servier compare indapamide 2,5 mg with hydrochlorothiazide in doses of 25 mg to 100 mg, which, of course, show metabolic effects of the hydrochlorothiazide. Academia cannot finance such a study, and because the results would probably not be in the commercial interests of Servier, the company would predictably not be interested in doing so.

6. The MIMS price of Natrilix 2,5 mg/day is R57,33 for 30 days, and that of Dichlotride (hydrochlorothiazide) is R41,07 for 100 tablets of 25 mg or R6,16 for 30 days.[5]

7. In South Africa, where the cost of medication has become a major concern in both the private and the public sector, this tenfold price difference (which is even more pronounced in the public sector) in the absence of any proven clincial superiority with regard to either efficacy or safety surely needs to be brought to the attention of medical practitioners (and the public?).

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2. Reynolds JEF, ed. *Martindale: The Extra Pharmacopoeia*. 29th ed. London: Pharmaceutical Press, 1989: 933-934.
3. The Treatment of Mild Hypertension Research Group. A randomized placebo-controlled trial of a nutritional-hygienic regimen along with various drug monotherapies. *Arch Intern Med* 1991; **151:** 1413-1423.
4. Neaton JD, Grimm RH, Prineas RJ, *et al*. The treatment of mild hypertension study. *JAMA* 1993; **240:** 713-724.
5. *MIMS* 1994; **34** (2): 152-153.

Professor Mokhobo replies: Dr Van de Wal compares indapamide (Servier) with other diuretics such as hydrochlorothiazide 12,5 mg and chlorthalidone 15 mg. Much lower doses of thiazides are now used, with the aim of reducing their adverse electrolyte effects. However, no

convincing evidence exists to support antihypertensive efficacy of thiazides at low and very low dose; findings are at best equivocal. Studies investigating thiazides at low dosage, in particular hydrochlorothiazide 12,5 mg, have failed to establish effectiveness in lowering blood pressure.[1-3] In addition, it is worth while noting that hydrochlorothiazide 12,5 mg is not available in South Africa.

Dr Van de Wal states that low-dose chlorthalidone and hydrochlorothiazide have no undesirable side-effects on either lipid or glucose metabolism. But once again the antihypertensive efficacy of the drugs at these doses is not entirely convincing. In addition, at the dose for which antihypertensive efficacy has been established, thiazide diuretics increase total cholesterol, low-density lipoprotein (LDL) and triglycerides and cause slight reduction of high-density lipoprotein. The Veterans Administration Mild Hypertension Trial reported that patients treated with chlorthalidone experienced increases in total serum cholesterol, LDL and very-low-density lipoprotein.[4] Grimm[5] confirmed these findings in a thiazide-lipid study which showed that thiazide diuretics increase total serum cholesterol by 6 - 8%.

In contrast, the antihypertensive properties of indapamide 2,5 mg are established worldwide. Clinical studies show that with indapamide, total cholesterol is not modified but LDL cholesterol tends to increase. All studies show that at the recommended dose of 2,5 mg/d blood pressure control is achieved without inducing adverse lipid changes. The long-term lipid neutrality of indapamide is in contrast to the lipid-lipoprotein elevating properties of the commonly used thiazide diuretics.[6]

The introduction of the thiazides was rapidly followed by spontaneous and widespread reporting of induction or worsening of glucose intolerance. In contrast, the effect of indapamide on glucose has been widely and extensively studied. Clinical studies with indapamide in more than 4 000 patients showed that blood pressure control is achieved with no significant change in fasting blood glucose levels.[7,8]

As pointed out by Dr Van de Wal, the cost of medication and public health in South Africa has become a major concern in both the public and the private sector, and the prescriber has to make a wise drug selection. But behind the cost of the medication, the cost to the community is at stake: the cost of mortality from a stroke in patients whose blood pressure is uncontrolled by a low-dose thiazide and not yet controlled by the addition of a second drug would far exceed the cost of prescribing indapamide as first-line therapy.

The introduction of indapamide offered prescribers a timely alternative to the new costly agents. Although costing rather more than the thiazide diuretics, indapamide has the advantage of a therapeutic profile similar to the newer class of antihypertensive agents but at a lower cost.

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2. Magee PFA, Freis ED. Is low-dose hydrochlorothiazide effective? *Hypertension* 1986; **8:** suppl II, 135-139.
3. McKenney JM, Goodman RP, Wright JT, Rifal N, Aycock DG, King ME. The effect of low-dose hydrochlorothiazide on blood pressure, serum potassium, and lipoproteins. *Pharmacotherapy* 1986; **6:** 179-184.
4. Goldman AL, Steele BW, Schnaper HW, *et al*. Serum lipoprotein levels during chlorthalidone therapy. *JAMA* 1980; **224:** 1691-1695.
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6. Amos RP. The effects of antihypertensive drugs on serum lipids and lipoproteins: I. Diuretics II: non diuretic drugs. *Drugs* 1986; **32:** 260-278, 335-357.
7. Demanet JC, Degaute JP, Hubert C. Safety and therapeutic efficacy in a long-term study of indapamide in the treatment of essential hypertension. *Curr Med Res Opin* 1977; **5:** suppl 1, 129-136.
8. Colo G, Gevaro G, Lombardo F, Moratti P, Cicuttini L, Rotolo V. Indapamide in the treatment of essential hypertension in the elderly: influence upon carbohydrate and lipid metabolism. *Boll Soc Ital Cardiol* 1981; **26:** 1527-1530.

Zero population growth — and national unity

To the Editor: In October 1993[1] a summit meeting of the world's scientific academics took place in New Delhi. There 56 institutions endorsed a 15-page statement drafted by the Royal Society of London and others, calling for 'zero population growth within the lifetime of our children'. This echoes the 'Club of Rome' sentiments of 1972,[2] and was seen as the only realistic step for dealing with humanity's social, economic and environmental problems.

Notable exceptions to the signatories were the scientists of Africa, Ireland and the Vatican. (Maybe the Vatican will recall the case of Galileo!)

Delegates from Africa stated that overpopulation was not a problem in Africa! Perhaps not, but we in the RSA appear to be heading for a ceiling of 80 million — any figure above that may be catastrophic.

With the advent of a Government of National Unity, and all citizens experiencing a new orientation of ownership of the RSA, has not the time come for us to take a lead in this important matter in Africa?

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2. Meadows D, *et al*. *The Limits to Growth: The Club of Rome's Report on the Predicament of Mankind*. New York: Universe Books, 1972.

Erratum

The following abstract was inadvertently omitted from the SAGES abstracts published in the July *SAMJ*.

HEPATITIS B MARKERS IN SCHISTOSOMIASIS

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A study was undertaken to clarify the incidence and influence of Hepatitis B markers on clinical presentation and selection of management options in schistosomal variceal bleeding.

METHODS

HBs ag, HBe ag, HBs Ab, and HBc Ab were identified serologically in 70 patients referred for treatment of schistosomal variceal bleeding over an 8 year period. Patients were investigated with endoscopy, Bilharzia CFT, liver biopsy, angiography and Galactose elimination capacity (GEC). The Wilcoxon test was used to compare pre and postoperative Albumin, Bilirubin and GEC.

RESULTS

The mean age and F : M ratio were 34 years and 1 : 1.2 respectively. The incidence of no evidence of previous infection, immunity to Hepatitis B and HBs ag carrier state was 17%, 62% and 14% respectively. Although some HBs ag positive patients were jaundiced on presentation, all patients were in the child's A category after recovery from variceal bleeding. In 9 HBs ag positive patients treated with distal spenorenal shunt the pre vs postoperative results respectively were:
Albumin 35 vs 30 g/l ($p = 0.08$); Bilirubin 24 vs 64 umol/l ($p = 0.002$) and GEC 298 vs 234 mg/min ($p = 0.05$).
There was no difference in the duration of admission and mortality in 22 patients treated with sclerotherapy as compared to 42 treated with distal splenorenal shunt.

CONCLUSION

1. Postoperative hyperbilirubinaemia in HBs ag positive schistosomiasis patients is associated with a deterioration of hepatic function.
2. Schistosomiasis patients with variceal bleeding can be treated with either sclerotherapy or distal splenorenal shunting irrespective of Hepatitis B markers.