

Chechnya is currently witnessing a health and humanitarian crisis. Years of war have left medical services in chaos. Unable to cope, they are propped up by donations from the international aid community so that local medical staff can continue to treat patients. Available drugs and services are insufficient to treat key causes of morbidity and mortality: cardiovascular disease, cancer, and tuberculosis. Many medical staff have fled the country. Those who remain are frustrated at the lack of equipment and poor access to new and improved protocols.

Because of the repeated kidnapping of expatriate workers, Chechnya remains closed off to international scrutiny. Our colleague, Arjan Erkel, Médecins Sans Frontières' Head of Mission in Dagestan, was released by captors on April 11, 2004, after 20 months as a hostage. Arjan's long detention, and the abduction of more than 50 international humanitarian aid workers since 1995, has crippled the ability to provide aid to war affected civilians in this region.

It is almost impossible to deal effectively with medical emergencies because the risks involved in moving around prevent medical staff and patients from reaching the hospitals. Health centres are too dangerous for the war wounded and are consequently avoided. Many staff express fear for their own personal safety because they work in hospitals where guns and violence are commonplace.

Despite the violence and intimidation in their homeland, the forced return of thousands of Chechen refugees living in temporary camps and shelters in the neighbouring republic of Ingushetia continues. As part of the normalisation strategy, the authorities are attempting to close all tent camps by mid-2004. Such camps have provided refuge for more than 200 000 Chechens since the start of the second Chechen war in 1999. Measures include intimidation, deregistration of refugee status, and cutting off electricity and water supplies. Access to the camps for humanitarian aid workers has been severely restricted. Although many Chechens are living here in appalling and desolate conditions, most say they are too frightened to return to Chechnya.

The basic right of Chechens to take refuge in Ingushetia must be respected by the authorities until the situation in Chechnya is safe. For those living in Chechnya, the international community must ensure that medical and humanitarian aid reaches them, and

they must be reassured that they have not been forgotten.

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## Autoimmune disease and other potential side-effects of statins

Sir—According to the hypothesis of Bernd Moosmann and Christian Behl (March 13, p 892),<sup>1</sup> myopathy and some other side-effects of statins might be attributable to inhibition of selenoprotein synthesis. However, severe autoimmune diseases have been reported, suggesting that statins could have immunomodulator effects too.

An unexpected number of autoimmune diseases (more than 20 cases) have been reported in patients treated with statins in the past few years. Most of these patients had systemic lupus erythematosus (SLE) but dermatomyositis, autoimmune hepatitis, and pemphigoides have been reported,<sup>2</sup> and a lethal outcome has been recorded in one patient.<sup>3</sup> Unlike usual drug reactions, skin eruptions have been noted many months or even years after starting treatment. Side-effects generally improve after drug discontinuation, but not necessarily in serological disease. In many reported cases, antinuclear antibodies are still positive many months after interruption of drug treatment. The causal relation between drug intake and autoimmune disease can, therefore, be difficult to establish and many cases are probably not reported.

Several pathogenic mechanisms have been postulated in statin-induced SLE. Cellular apoptosis—which has an important role in SLE—might be exacerbated or triggered by second-generation statins, which are potent pro-apoptotic agents. Release of nuclear antigens into the circulation could cause production of pathogenic autoantibodies. The same mechanism has been implicated for other environmental factors such as ultraviolet light, which is a well known trigger in SLE. Likewise, the direct immunomodulator effect of statins on T cells is possibly involved. SLE is characterised by a shifting of T helper 1 to T helper 2 immune responses, causing B-cell reactivity and production of pathogenic autoantibodies. Statins and selenoprotein inhibition can aggravate this event.<sup>4</sup>

Epidemiological study and clinical trial findings suggest that selenoprotein inhibition might heighten the risk of prostate and colon cancer.<sup>5</sup> If Moosmann and Behl's hypothesis is confirmed, statins could not only trigger autoimmune diseases but also contribute to the development of some types of cancer. Further studies are, therefore, warranted to determine the long-term safety of these lipid-lowering agents.

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## Malaria intermittent preventive treatment and EPI coverage

Sir—I was interested to read the Rapid review on malaria intermittent preventive treatment (IPTi) in infants and childhood vaccinations by Jennifer Rosen and Joel Breman (April 24, p 1386).<sup>1</sup> Although I also see the great potential for this innovative approach towards malaria control in infants and young children, I would like to add some comments of caution.

According to the latest available figures, more than 90% of all deaths due to malaria in children younger than 5 years occur in sub-Saharan Africa (table).<sup>2,3</sup> Similarly, at our remote 400-bed hospital in a rural area in northern Tanzania, malaria is the leading cause for admissions and deaths in children younger than 5 years. Thus, preventive measures should focus on this age-group in Africa first.

Although combination of the IPTi approach with the existing Extended Programmes of Immunisation (EPI) is currently being planned,<sup>1,4,5</sup> immunisation coverage in these countries should be analysed carefully. For sub-Saharan Africa as a whole, EPI coverage rates (except for BCG) are not more than 58% (table).<sup>3</sup> There are also substantial

	Sub-Saharan Africa region	Western Pacific region	Southeast Asia region	Eastern Mediterranean region
<b>Under 5 mortality*</b>				
Total	4610	1368	3603	559
Malaria-attributable	1050 (22%)	14 (1%)	72 (2%)	23 (4%)
<b>EPI coverage</b>				
DPT3	55%	78%	71%	86%
Polio3	55%	79%	71%	86%
Measles	58%	80%	67%	87%

DPT=diphtheria, tetanus, pertussis. \*In thousands.

#### Mortality rates in children younger than 5 years and EPI coverage at 1 year in different WHO regions<sup>2,3</sup>

differences between countries such as Tanzania or The Gambia, which achieve coverage rates of more than 85%, and Niger or the Central African Republic, for which coverage is less than 55%. Within countries there are disparities between rural and urban areas and between wealthier and poorer families. Thus, in general, EPI also needs to be scaled-up massively if the aim to achieve a major decrease in malaria morbidity and mortality (the latter not having been shown yet)<sup>4,5</sup> in the infant population through a combined EPI-IPTi approach is to be realised.

Other factors such as the choice of antimalarial drug, the effect of the EPI-IPTi approach on development of immunity against malaria and on drug resistance rates, and the interaction with the immune response to the concurrent vaccinations will have to be analysed carefully in large-scale, high-quality field studies before this promising approach can be implemented throughout sub-Saharan Africa and elsewhere.<sup>1,5</sup> Meanwhile, other preventive measures such as the use of insecticide-treated nets should not be neglected.

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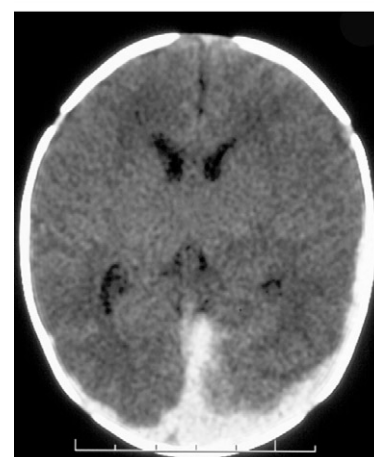
### Spontaneous subdural haemorrhage in newborn babies

Sir—In their study of the frequency and natural history of subdural haemorrhages in term newborn babies, E H Whitby and colleagues (March 13, p 846)<sup>1</sup> conclude that the presence of subdural haemorrhage is not necessarily indicative of excessive birth trauma, and that subdural haemorrhages that completely resolve by age 4 weeks are mostly benign, clinically asymptomatic, and of no long-term importance. Although we agree with their conclusions, one should be alert to possible underlying causes, including coagulation abnormalities, that might contribute to the development of subdural haemorrhage in uneventful perinatal courses.

A term baby girl was born by non-instrumented, vaginal delivery. Her mother (gravida 2, para 1) had an unremarkable pregnancy apart from a previous early miscarriage. The girl's birthweight was 2585 g (3rd percentile), length 49 cm (50th percentile), and head circumference 33 cm (25–50th percentile). The placenta was small but unremarkable otherwise. Striking sutural diastasis (1.7 cm) with full, opened anterior and posterior fontanelles were noted. She was neurologically normal and clinically asymptomatic.

Cranial ultrasonography and subsequent CT scans diagnosed subdural haemorrhage (figure). Preliminary investigations revealed a low haemoglobin concentration (111 g/L), normal platelet counts, normal international normalised ratio, but a slightly long partial thromboplastin time (51 s). Subsequent coagulopathy work-up showed that both the baby girl and her mother were heterozygous for the prothrombin 20210 mutation. Congenital infections were excluded. The subdural haemorrhage resolved completely, and she had normal neurodevelopment at 18 months of age.

The pathogenic mechanism for intracranial haemorrhage in neonates is complicated, but thrombophilia with



**Cranial ultrasonography (top) and subsequent CT examination (bottom) of neonate**

Ultrasonography shows 6-mm thick subdural collection along left outer cortex associated with mild shifting of midline structures to right and smaller left lateral ventricle. CT shows subdural haemorrhage.

coagulation abnormalities including factor V Leiden and prothrombin 20210 mutations are not uncommon in those with haemostatic and thromboembolic complications.<sup>2</sup> Petaja and colleagues<sup>3</sup> suggested intraventricular haemorrhage as one of the disease states triggered by thrombophilic coagulation abnormalities. The G20210A polymorphism in the prothrombin gene is not rare in white populations (1–2%)<sup>4</sup> and has been associated with recurrent miscarriages and lower birthweight in newborn babies of heterozygous mothers.<sup>5</sup>

In our case, several factors, including maternal obstetric history, small but unremarkable placenta, low birthweight, and a slightly long partial thromboplastin time raised the possibility of this mutation. The presence of thrombophilic risk factors in this uneventful delivery might have been coincidental or a real predisposition for the development of idiopathic subdural haemorrhage. Nonetheless, our case illustrates the importance of identifying potential causes of subdural haemorrhage in newborn babies. Furthermore, it shows that cranial ultrasonography in