Recent advances in paediatrics

II—Childhood and Adolescence

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Infants die from prematurity, congenital malformations, and infectious diseases; over 90% of those who succumb do so in the less affluent countries of the world. Infection with HIV and malaria are afflicting an increasing number of children and teenagers in tropical countries, and everywhere children who survive infancy become exposed to trauma and neoplasms. Prevention of child trauma,¹⁻² drug resistant malaria,³ and violence to and exploitation of children⁴⁻⁶ remain the topics central to the professional life of all doctors, irrespective of their nationality.

Child trauma

Child trauma continues to rank fourth after infections, prematurity, and genetic disease as a major cause of child mortality. After the first year of life, trauma is the leading cause of death until early adulthood.⁷ The professional world has been slow to accept a medical model for the prevention of child trauma.⁸

Reduction in child mortality resulting from injury has been one of the success stories of the past decade. In affluent countries the rate of injury and violent death in children and adolescents has decreased by 20%, and child deaths from accidental poisoning are now rare. In all Western countries the rank of causes of traumatic death remains road trauma, drowning, non-accidental injury, and burns (particularly in children living in relative or absolute poverty).⁷⁻⁹⁻¹⁰ Strategies for preventing road deaths include controlling speeds near schools and compulsory seat restraints and bicycle helmets.¹¹ In all studies of violent child death and injury, male sex, poverty, and underprivilege are risk factors. Rural children are particularly vulnerable to trauma.¹²

Such deaths are prevented by increased public awareness of risk, improved safety hardware, and legislation. Most children who die violently do so before reaching hospital; once injury has occurred, death may be prevented by improving resuscitation and first aid.¹³ Better retrieval systems and algorithms for trauma management and the rise of paediatric intensive care are preventing deaths in hospital; 12% of post-traumatic deaths in hospital remain preventable.¹⁴

In both the richest and the poorest countries, a major problem is deaths of children from firearms. In the United States, almost 10 000 children and adolescents die annually of gunshot wounds, an increase of 60% in the past decade.⁹ In affluent countries poverty is a more important factor in homi-

cide and infant mortality than in fatal malignant neoplasms and cerebrovascular disease.¹⁵ Mass killings by firearms at Dunblane, Scotland, and Port Arthur, Australia, have produced dramatic action in several countries to limit accessibility and use of firearms.¹⁶ Such political vigour establishes benchmarks for reducing firearm deaths in the international arena.

Neoplasms

The most common childhood neoplasms are leukaemia (30-35%); paediatric brain tumours, especially astrocytoma and medulloblastoma (20%); neuroblastoma (6-7%); Wilm's tumour (5-7%); and non-Hodgkin's lymphoma (4-7%).¹⁷⁻²⁰ The rate of childhood malignancies is increasing in all countries where detailed national surveillance data are collected, and this increase is not simply due to better ascertainment.¹⁷ The 10 year survival rate for all childhood malignancies is about 65%, and in the United States,²¹ Japan,²² Germany,¹⁸ and Australia is increasing by about 10% each decade. Specific five year survival rates, illustrating best practice, are shown in table 1.

Most childhood cancers result from specific genetic mutations. Current management includes:

- Extensive biochemical, immunological, cytogenetic, and ultrastructural categorisation of each new case, especially in planning the management of acute lymphoblastic leukaemia;

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Bicycle helmets have been shown to reduce road deaths and injuries

ALEXIS WALLERSTEIN/IMPACT

Table 1 Five year survival for common childhood neoplasms, following best practice, protocol based treatment coordinated in centres in the United Kingdom,^{19 20} United States,^{21 25} Japan,^{28 47} Germany,¹⁸ and Australia¹⁷

Neoplasm	Five year survival (%)
Acute lymphoblastic leukaemia	70-75
Acute myeloid leukaemia	25-40
Malignant lymphoma	70-80
Astrocytoma	70
Medulloblastoma	40
Neuroblastoma	
Onset in infancy	85
Later onset (eg, p53 positive)	35
Wilm's tumour	85
Hepatoblastoma	80
Retinoblastoma	90-95

- Accurate staging of solid tumours at diagnosis;
- Specific planning of stratified treatment specific to the multiple diagnostic staging and genetic markers identified in each new case;
- Managing child cancer victims in specialised paediatric oncology centres using protocol based therapy^{18 21}; and
- Including each newly diagnosed child in surveillance studies.

Currently, centres such as the UK Children's Cancer Study Group (founded in 1977) treat 75% of childhood malignancies.²¹ In Australia 90% of new malignancies are managed in centres forming the Australia and New Zealand Cancer Study Group. International linking of such paediatric oncology groups (including the US Children's Cancer Study Group) is a feature of best practice in paediatric oncology.

Accurate staging and marker profiling of newly presenting tumours saves many children from unpleasant treatment and is critical for an accurate prognosis.²³ In neuroblastoma, for example, linking N-myc status (single copy versus amplification) with age at presentation (infants usually carry a single copy of this gene) gives a better idea of the prognosis.²⁴ When surface antigen p53 is found in newly presenting children with neuroblastoma a median survival of one year can be expected, compared with 12 years when it is not present.²⁵

A major development in the management of children in remission from acute lymphoblastic leukaemia is the use of the polymerase chain reaction to detect residual leukaemia cells. A review of 20 studies indicates that a consistent pattern of such cells is an important indicator of bone marrow relapse.²⁶

For parents, improvement in prognostic skills is a major advance in the overall management of childhood malignancy. Older children presenting with solid malignancies (such as Wilm's tumour or medulloblastoma) tend to obey Collins' Law—the period of risk for recurrence of such tumours is approximately the age of the patient plus nine months.²⁷ Survival curves for children with cancer plateau five years after presentation, approximating anticipated rates of true "cure," but the late effects of treatment and of the underlying cancer diathesis are becoming increasingly important. A second neoplasm may appear, and problems of infertility, cardiomyopathy, intellectual deterioration, and deleterious effects on growth are inescapable in many

treatments needed to achieve the dramatic increases in survival currently reported.¹⁸⁻²⁹

A major unmet challenge is "an obsession with cure of advanced [adult] disease rather than the prevention of early disease."³⁰ This is particularly relevant to the prevention of skin cancer in white people. In Queensland, Australia (population 3.8 million), more than 1000 new cases of skin cancer are diagnosed each week. Ninety per cent of lifetime ultraviolet exposure occurs before age 20.

Malaria

Malaria remains the world's most important parasitic infection³ and is a resurgent problem. Mortality from severe *Plasmodium falciparum* malaria remains 10-20%, despite current treatments, resulting in the death of 3000000 children each year. The problem of malaria is increasing because of declining drug sensitivity of *P. falciparum* and the emergence of multiple drug resistant strains of other species. In East Africa, 70% of children have malaria resistant to chloroquine; and randomised, controlled trials have shown that organisms resistant to chloroquine, halofantrine, fansidar, and amodiaquine³¹ are now present in the tropical regions of four continents.

The past two years have seen important field trials of malaria vaccines, which have shown seroconversion in Thai children³² and in the Gambia³³ but no practical effects on the reduction of *P. falciparum* malaria. Treating bednets and clothes with permethrin remains the best form of individual protection for infants; treating nets reduces the prevalence of anaemia in young children in malarious regions by at least 50%.³⁴

Children with potentially fatal *P. falciparum* malaria present with fever and either acute neurological syndromes or with respiratory distress due to metabolic acidosis.³⁵ My experience in treating children in Papua New Guinea and in Rwanda is that, because of the problem of drug resistance, intravenous quinine together with oral or parenteral clindamycin or erythromycin is required in severe cases. Special care, including electrocardiographic monitoring, is required, especially if the children have been receiving fansidar or halofantrine as (failed) prophylaxis. Infants and young children are particularly susceptible to quinine toxicity.³⁶ Artemether, which clears malarial parasites more rapidly than quinine, is undergoing comparative trials.

In many chloroquine resistant areas, clindamycin, erythromycin, or sulfadoxine and pyrimethamine are now routinely used. Doxycycline alone, very effective as a prophylactic in adults, cannot be used in children because of dental damage. Considerable morbidity continues to occur in children returning from malarious areas who have not received a curative course of primaquine to eradicate the exoerythrocytic forms of the parasite.

Landmines

Antipersonnel landmines are an inhuman,^{37 38} escalating, and uncounted threat to children in some 26 countries, and more mines continue to be laid than cleared.³⁹ The 2000-3000 victims killed or maimed each month⁴⁰ include many children. Mines made of plastic float on the runoff of annual floodwaters and so

kill or injure civilian farmers and children far from the site of primary implantation or dispersal.

The medical consequences of landmines include avulsion of one or both feet and shrapnel wounds to the pelvis, abdomen, and face. Blinding in one or both eyes is common and some degree of conductive deafness is inevitable.³⁷ When children are playing together or collecting firewood or farming, whole sibships can be engulfed in the blast.⁴¹ Refugee children are killed when they return home to their villages,^{37 38 41 42} when collecting scrap metal for subsistence survival, or when simply using found objects to make toys.⁴³

Medical journals, international agencies, and governments have called for a total ban on the sale and use of antipersonnel landmines. Even if such a ban³⁷ were enacted this year, it would take many decades for many countries to be rendered safe for children. The unanswered threat of antipersonnel landmines, like resurgent drug resistant malaria, is one of the urgent themes in preventive paediatric medicine.

Child victims in society

Against the falling mortality from prematurity, infections, neoplasms, and trauma, the identified rate of child exploitation is increasing. Paedophilia is currently the subject of high profile court actions in the United States, Britain, Belgium, and Australia. Several countries, including the Philippines and Thailand, which have had extensive international tourist paedophilia industries, have responded to international advocacy to enforce existing protective legislation. Other countries have made it a national offence for their citizens to exploit children offshore, but much remains to be done to bring this world problem under control.

Child victims of war include not only those wounded and killed but also those surviving with post-traumatic stress.⁴¹ Other child victims are those who become acclimatised to resolving conflicts by using explosives, guns, or machetes.³⁸ Child and adolescent soldiers, used as combatants in more than 20 countries in the past decade, are exposed "to militaristic socialisation characterised by the unlearning of humaneness."⁴⁴ The past decade has seen increasing advocacy to limit the use of children as armed combatants in civil and international conflicts.⁴⁴

AIDS

In the remaining years of this century millions of children will die from AIDS. Currently 1.5 million children are infected with HIV through mother to child transmission. The overall risk to infants of HIV positive mothers is 22%. The disease depends on maternal viral burden, and risks to children of mothers with high viral loads not treated with zidovudine exceed 40%.⁴⁵ Some 15% of infants of HIV infected mothers become infected by breast feeding.⁴⁶ African children who are seropositive rapidly develop clinical AIDS and die, usually before the age of 5 years; median survival times are longer for seropositive children in Europe and the United States. Zidovudine treatment of HIV positive mothers during pregnancy will reduce the risks of their children being infected to less than 8%.⁴⁵ This treatment is effective regardless of the viral burden or CD4 count at the first antenatal visit.

TRYGVE BÅLSTAD/PANOS

Many of the 2000-3000 people killed or maimed each year by landmines are children

In the next two decades HIV infection—particularly in Africa, but increasingly elsewhere—will particularly strike young heterosexual couples, leaving their children as orphans. The international world will be increasingly responsible, ethically and morally, for the care of millions of such orphans who cannot be accommodated in their surviving extended family groups.

Paediatrics and specialisation

The past five years have seen an acceleration in the trends towards superspecialisation in paediatrics. The major advances in many specialties are so specific that a generalist paediatrician can no longer manage all cases if he or she is practising in an area where referral is easy and appropriate. Many generalist paediatricians in affluent cities no longer manage sick neonates (especially those requiring neonatal intensive care), new cases of malignancy, diabetes, complex renal disease, and gastroenterological conditions.

In paediatric and adolescent psychiatry, the "new morbidities" include apparent epidemics of attention deficit-hyperactivity disorder, behaviour and conduct disorders (particularly those involving vandalism and aggression), and the consequences of bullying at school. Adolescent conduct disorders are challenging general practitioners and paediatricians; physical risk to others from psychotic⁴⁷ and bullying adolescents is being recognised as a "recent problem" rather than a "recent advance." The increasing independence of teenagers in the Western world has led to the concept of a "new inverse care law"—whereby teenagers with low self esteem and little hope for their future are more likely to be exposed to lifestyles which put them at risk.⁴⁸

One challenge of adolescent health is the acceptance of safe sex practices amid increasing risks of contracting HIV infection from heterosexual encounters. Though teaching about safe sex practices has been widely implemented in schools in America, Australia and New Zealand, and Europe, it is conspicuously absent in many populations at highest risk. The cost effectiveness of clinical interventions for various health risk behaviours among adolescents is unknown⁴⁹; unresolved adolescent health problems tend to persist into adulthood⁵⁰ and the costs of treatment to increase.

Conclusion

1996 was not only the bicentenary of Jenner's invention of inoculation⁵¹ but also the centenary of the first pedestrian death from a motor vehicle. These two events, the one ushering in the era of immunology and ultimately the concept of genetic individuality, the other the era of high energy destruction and death, have their echoes in the daily practice of all who deal with children. Recent years have seen the unprec-

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Child trauma

- In affluent countries the rate of injury and violent death has decreased by 20% in the past decade
- The rank order of traumatic child death remains road trauma, drowning, non-accidental injury, and burns
- Firearm injuries to children are increasing; in the United States deaths of children by firearms have increased by 60% over the past decade

Cancers in childhood

- The 10 year survival for all childhood malignancies is 65%; it has increased by 10% per decade over the past generation
- Best five year survival percentages are achieved in paediatric oncology cancer centres with active international participation programmes
- Late effects, after primary "cure", include second neoplasms, infertility, cardiomyopathy, effects on growth and intellectual deterioration

Malaria

- Multiple drug-resistant strains of malaria are now present in the tropical regions of four continents, and chloroquine resistance exceeds 70% in parts of Africa
- Trials of malaria vaccines for children in Africa and in Asia have not yet shown any practical effect
- Treating infants' bednets with permethrin will reduce anaemia in malarious regions by 50%

Landmines

- Landmines are a threat to children in 26 countries, and more mines continue to be laid than are cleared
- All responsible medical bodies, the major international medical journals, the Red Cross, Oxfam and the governments of several countries now support the total ban on the sale and use of anti-personnel landmines

Child victims of society

- The known rate of paedophilia is increasing
- Children used as soldiers, who survive, become conditioned to militaristic socialisation "characterised by the unlearning of humaneness" and the philosophy that conflict can be resolved by gun or machete
- Current WHO projections are of 40 million HIV infected persons by the year 2000; the burden on children is twofold—mother to child transmission of HIV and being left orphans after parents' premature death

Child health in perspective

- General paediatrics as a specialty is contracting because of referral or shared care with superspecialty units, but there are not enough generalist paediatricians in many parts of the developing world
- Unmet challenges include the need for improved selection for drug treatment for children with the attention deficit—hyperactivity disorder; bullying by preadolescents and adolescents of both sexes; and education about safe sex practices among adolescents in communities at highest risk

edented saving of children privileged to be born into a world where such technologies can be exploited for good. The challenge persists for all doctors to bring these benefits to all children in a contracting world.

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