Recent advances

Paediatrics—I: Infancy and early childhood

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Children born in the last decade of the 20th century have been healthier, and will be longer lived, than ever before.¹ Recent advances in paediatrics have seen national infant mortality rates fall below 5.0 per 1000 live births. The countries in which this has been achieved—Hong Kong, Taiwan, and Japan—have thus set benchmarks for the century ahead. In the context of world medicine, all who care for children rejoice in the momentum of advanced technology, which is saving hitherto unsavable individual children^{2,3}; yet we are seeing the failings of delivery of health systems whose principles have been proved for decades. The major killers of the 13 million children who die annually before their fifth birthday⁴ remain pneumonia,⁵ gastroenteritis,⁴ malaria,⁶ measles,⁷ and trauma.⁸ The potentiating effects of malnutrition contribute to more than 80% of child deaths from infectious disease.⁹

One of the signal advances in paediatrics is the recognition that children's safety⁸ and health, indeed the very existence of whole races of children¹⁰ is a responsibility for all who practise in a contracting world.

Neonates and infants

Mortality

Current best paediatric practice uses neonatal mortality rates specific to birth weight as a combined index of antenatal care and obstetric and paediatric care. In affluent countries these rates continue to fall and show no evidence of plateauing.¹ The current United Kingdom neonatal death rate (deaths per 1000 live births in the first 28 days of life) for infants above the median birth weight of 3500 g is 0.9. The international benchmark for all infants who are not premature (those born weighing more than 2500 g) is a rate below 2.0 per 1000 live births.

The new treatments that have made this possible include the use of exogenous surfactant, high frequency ventilation, extracorporeal membrane oxygenation (ECMO),^{11,12} with the promise of nitric oxide and partial liquid ventilation of otherwise unsavable preterm infants.¹³ Extracorporeal membrane oxygenation has been an accepted rescue treatment for otherwise fatal neonatal and infantile respiratory failure for the past five years,¹¹ and its provision in selected high technology centres has enabled survival of an increasing number of infants with acute, catastrophic myocardial or respiratory failure.¹²

Such splendid results have a downside: over 30% of survivors who weighed less than 1000 g at birth will manifest severe significant neurological disabilities such as cerebral palsy, intellectual impairment, and deafness or blindness.¹⁴ Best practice policy is not to intervene below 22 weeks of gestation but to do so at 25–26 weeks.² Such treatment, and the allocation of resources to achieve such survival statistics, remains a source of tension among doctors, parents, judges, and policymakers. Analysis of resource use indices show that most tiny premature babies who die do so quickly; and the medical resources allocated to non-survivors are relatively small and independent of birth weight.¹⁵

Follow up of children conceived by in vitro fertilisation has shown that they do not have increased rates of minor or major malformations¹⁶ and do not differ in mean percentiles for weight or head circumference from their peers conceived in the usual way.

Placental blood banks

Placental blood banking is now an exciting reality in paediatrics. Cord blood, unlike adult blood, contains immunogenetically naive B lymphocytes. Transfusion of such leucocytes, and of stem cells, engenders a lower incidence of graft versus host disease in recipients, irrespective of age. This fact allows a broader range of recipients, who need be only partially matched on standard tissue markers¹⁷ and thus offers rescue to a

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Fig 1 New treatments have made it possible to save preterm infants who previously would have died

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Recent advances in paediatrics

Child mortality

- Infant mortality rates are the lowest they have ever been, falling below 5.0/1000 live births in Japan and in Hong Kong
- The major killers of children remain pneumonia, gastroenteritis, malaria, measles, and trauma
- 13 million children a year die before their fifth birthday; malnutrition contributes to 80% of such deaths

Neonatal care

- Birthweight specific neonatal mortality rates are the lowest ever in affluent countries; the international benchmark of best practice is a neonatal death rate below 2.0 for infants above 2500 g at birth
- Exogenous surfactant, high frequency ventilation, and extracorporeal membrane oxygenation (ECMO) enables premature infants with otherwise fatal respiratory and myocardial failure to be saved
- Best current neonatal policy attempts to save premature infants of 25-26 weeks' gestation but not those of 22 weeks' gestation.

Transplantation

- Placental blood banking is now in place on four continents; these banks are a potential lifelong rescue source for neonate donors who later develop cancer or require a transplant during childhood or in later life
- Selected centres now offer children transplants of livers, hearts, heart-lungs, liver-intestines, and small intestines; child liver transplant recipients now have a median 10 years of good quality life

Genetics and gene therapy

- Genes for cystic fibrosis, Duchenne muscular dystrophy, fragile X syndrome, spinal muscular atrophy, and phenylketonuria are now defined
- Gene therapy is now the central tenet of medical science in paediatrics

Immunisation

- Less than 60% of children are fully immunised in parts of the United States, Australia, Africa, and Europe
- Protection by herd immunity against disease preventable by vaccination varies with individual diseases
- Parents are refusing to have their children immunised not because of cost, any difficulty with access, or the presence of intercurrent illness at the scheduled time for immunisation, but because of a lack of perceived risk, concern about side effects, and the inadequacy of tracking or reminder systems

wider range of marrow-ablated, non-related donors.¹⁸ Such banked blood is a potential source of premutational stem cells for the donor children themselves when they grow to adult life and develop neoplasms. Special precautions are needed—the neonate donor must be screened for genetic and infectious diseases (including HIV), and relatively large amounts of blood are required, with the potential danger of neonatal anaemia.¹⁹ Several companies now exist to harvest and store such stem cells—in the United States, the United Kingdom, and Germany.²⁰

As one third of us will die from neoplasia, the possibility of citizens of the future having their own, neonatally collected, pluripotential stem cells which are stored and banked for postablative rescue and hopefully for engraftment and cure is an exciting development. It is the ultimate form of gene therapy for acquired mutational disorders. By mid-1996, the Australian Cord Blood Bank (based at the Royal Hospital for Women in Sydney) was publicly advertising for neonatal blood donations.²¹

Gastrostomy feeding

Gastrostomy (enteral) feeding has been used increasingly in the past two years.²²⁻²³ It avoids the need for of recurrent nasogastric tube feeding for long periods. Children with many life threatening diseases²⁴ and congenital abnormalities²⁵⁻²⁶ are subject to malnutrition—which raises the risk of death or morbidity from the primary disease. Gastrostomy feeding arrests this deteriorating vicious spiral and allows catch up growth.²² After the surgical operation to create a gastrostomy port,²³⁻²⁷ enteral feeding is used in children gravely ill from generalised disease²⁴; children with conditions such as corrosive injury to the oesophagus,²⁸ severe gastro-oesophageal reflux with chronic, destructive acid and enzymatic pneumonitis (the "pickled lungs" of severe gastro-oesophageal reflux),²⁹ or dysmorphogenetic conditions with congenital airway obstruction²⁵; and in selected children with severe neurological impairment.²⁶⁻²⁹

The principal complications of prolonged gastrostomy nutrition include perigastrostomy infection,²⁷ diarrhoea, bloating, and reflux.²³ Gastro-oesophageal fundoplication has become one of the most common major operations performed on infants and children by paediatric surgeons.²⁹

Preventing childhood illness

The past decade has seen a shift in focus away from the central role of hospital in the care of ill children. Throughout much of the affluent world, the momentum in children's health care is encapsulated in such phrases as "partnerships with parents," "child friendly hospitals," and "day hospital admission only" and an emphasis on primary care for children. The median duration of hospital inpatient stay is now less than 48 hours in most major children's hospitals.

Child abuse

Deaths from child abuse have been reduced in some centres, but the overall rate of reporting of suspected child abuse continues to rise in all centres where better surveillance systems have been incorporated, recognising the different syndromes of unlawful child killing.³⁰

Hundreds of cases of child abuse deaths have appeared in the literature of the past two years from Europe, Asia, Australasia, and the United States.³¹⁻³³ Research into prevention is notoriously difficult, both clinically and methodologically.³⁰ Most child homicide victims in Europe, Asia, and Australasia die as a result of blunt injury,³⁴ the "shaken baby syndrome," or drowning. Recent research has highlighted two unmet needs in the domain of child abuse. The first is the better identification of the child victim who is subject to prolonged crescendo assaults, about whom society still does not seem to be able to offer protection.³⁰ The second is the unmet need of siblings of identified abused children, who are also at major and sometimes fatal risk.³⁴

Genetics and gene therapy

The human genome organisation has, using semi-industrial techniques concentrated in a few large genomic centres, produced a human transcript map. The human genome is now known to harbour between 50 000 and 100 000 genes, of which half have been sampled to date in the form of expressed sequence tags. Some 16 000 human genes have been mapped relative to a framework map that contains 1000 polymorphic genetic markers.³⁵

Some 80% of children in hospital have diseases which have genetic or familial implications. In recent years the genes for the most common genetic diseases have been defined, including those for cystic fibrosis,³⁶ phenylketonuria,³⁷ the fragile X syndrome,³⁸ Duchenne muscular dystrophy,³⁹ and spinal muscular atrophy. Molecular diagnosis, especially molecular prenatal diagnosis, has begun to supplant biochemical and cytogenetic diagnosis for many inherited diseases. One holy grail of prenatal diagnosis—the selective harvesting and diagnosis of fetal cells from the maternal circulation (from blood taken by simple venepuncture at the first antenatal visit)—remains an unrealised hope.

In spite of many setbacks,⁴⁰⁻⁴¹ more than 500 patients are currently being treated by insertional gene therapy.⁴¹ And, of course, a more crude form of gene therapy, using whole tissue or whole organ transplants, has seen signal success. Transplants of hearts, heart-lung complexes, livers, liver and intestines, and intestines are now options in a variety of centres.⁴² Median survival after childhood liver transplants now exceeds 10 years. Allogenic bone marrow transplantation remains the most effective treatment for patients with inherited metabolic diseases.

Gene therapy has become one of the central tenets of medical science. The first human trial was begun in September 1990 at the US National Institutes of Health when a 4 year old girl was treated for adenosine deaminase deficiency. For patients with homozygous familial hypercholesterolaemia it has been shown that liver derived, autologous, ex vivo gene therapy (using recombinant, retrovirus encoded gene inserts) produces no harm, at least in the short term. Gene transfer agents have included retroviruses, adenoviruses, liposomes, cationic lipids, and even naked DNA.

Two types of childhood diseases in particular are candidates for gene therapy—immunodeficiency diseases and diseases in which epithelial cells carry metabolic deficits which might be selectively targeted by corrective viruses carrying DNA. Genetically corrected

cells of patients with primary immunodeficiency diseases have a selective survival advantage, thus making these diseases a principal focus of the current clinical attempts at human gene therapy.⁴³

In the past two years research trials of gene therapy have been accepted as a treatment of last resort for life threatening conditions; current limitations are scarce resources on the one hand and biological problems such as host rejection of the inserted gene product on the other.⁴⁰ To date, human gene therapy treatment for severe combined immune deficiency, hypercholesterolaemia, Duchenne dystrophy,³⁹ and cystic fibrosis³⁶ have all indicated some degree of gene transfer and even prolonged gene expression. At least one child with adenosine deaminase deficiency, treated by gene transfer, has been disease free for three years. However, no published evidence has yet been presented of a long term therapeutic effect.

Immunisation

Compliance rates

Two hundred years after Jenner's discovery of practical and safe immunisation compliance rates remain unacceptably low. Protective immune status in the early childhood years ranges from less than 20% in war torn countries¹⁰ to 50-70% in the United States,⁴⁴ 60-77% in Australia,⁴⁵ 80-90% in Switzerland,⁴⁶ and over 90% in Italy, where vaccination is compulsory.⁴⁷ Immunisation rates exceed 90% in the United Kingdom for the tetanus-diphtheria-pertussis (TPD) triad and for *Haemophilus influenzae* type b (Hib) vaccine.⁴⁸⁻⁴⁹

The immunisation rate needed for herd immunity is disease specific. A seroconversion rate of 60% is adequate to confer herd immunity to diphtheria,⁵⁰ but a rate of 95% is needed against measles.⁷

All nations, particularly affluent ones, have been concerned by the suboptimal levels of childhood immunisation evident by 1997. In Australia pertussis has been epidemic since 1994, with 9890 new cases notified in the two years 1994 and 1995. In 1993, 6335 new cases of pertussis were reported in the United States.⁵¹ Urgent rescue programmes have been mounted in many countries, one of the most high pro-

Fig 2 In the United Kingdom, over 90% of children are immunised with TDP and Hib vaccines

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file ones being President Clinton's Vaccine for Children programme.⁵² In several countries the responsible authorities now ensure that children admitted to government preschool classes have evidence of current immunisation or an exemption by a medical practitioner. The United Kingdom, Australia, New Zealand, and the United States have undertaken public health campaigns in the past year.

Parents are refusing to have their children immunised, not because of cost, access, or intercurrent illness but because they see no risk to their children in an otherwise healthy society; because of concerns about side effects⁵³; and because of lack of tracking and reminder systems.⁵⁴ Influential antimicrobial, anti-immunisation lobby groups have evolved in all affluent countries, and anti-immunisation beliefs are receiving much publicity. The fact that some vaccines, particularly those against pertussis, are only 70% effective⁵⁵ is often used by groups in their campaigns against immunisation programmes. Countering this disturbing trend remains an unmet challenge for all health professionals.

A recent nationwide case-control study has shown unequivocally that immunisation of infants is not linked with any increased risk of the sudden infant death syndrome.⁵⁶

New vaccines

Acellular pertussis vaccines, introduced in the past two years, are efficient and have reduced the number of reactions by over 50% compared with whole cell vaccine.^{51 57} The complications with these new vaccines are fever (4%), persistent severe crying (5%), and local swelling at the injection site (24%); the risk of convulsions is less than 0.1%.⁵⁷

Immunisation against hepatitis B has been progressively introduced in all countries since universal immunisation was adopted as national policy in the United States in November 1991.⁵⁸ Infants in Asia and Africa and the indigenous populations of Australia, New Zealand, Papua New Guinea, and the Americas are at high risk. In the United States the three dose compliance rate at 12 months increased from 1% in 1989 to 50% by 1993.⁵⁸ In low risk countries (such as the Netherlands, where only 0.44% of the population is positive for hepatitis B surface antigen⁵⁹) current practice is routine antenatal screening for hepatitis B, with selective immunisation of infants born to positive mothers. Early and urgent immunisation of infants of such mothers will protect 70% of these high risk children from contracting the infection.⁶⁰

H influenzae type b immunisation rates of 40-70% have been achieved in most Western countries.⁴⁵ The incidence of invasive haemophilus disease has decreased by 80% since 1992, when the vaccine became available,⁴⁶ and in some countries (particularly in Japan and Scandinavia) invasive haemophilus disease has all but disappeared.

In 1988, the 41st World Health Assembly committed the World Health Organisation to the global eradication of poliomyelitis by the year 2000.⁶¹ The technical feasibility of this goal is supported by the availability of easily administered, inexpensive oral vaccines and by the epidemiological characteristics of poliomyelitis and the successful experience in the Americas⁶² and in Australasia, where wild poliomyelitis infection has been completely eradicated. Infants and children from

developed countries travelling to endemic areas in Africa, Europe, and Asia also remain at risk.

Immunisation generally is one of the four most cost effective stratagems for reducing mortality in childhood. This, together with better acute management of sick children, improved preterm and delivery care, and better family planning,⁶³ remains the responsibility of all who wish to see not just equality of opportunity for the world's children, but life itself.

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Focal myositis mimicking acute psoas abscess

An unusual presentation of systemic lupus erythematosus

We describe an unusual presentation of severe focal muscle inflammation in a young woman in whom the clinical and radiological findings were suggestive of a psoas abscess. Eighteen months after the onset of her illness, systemic lupus erythematosus was diagnosed.

Case history

A previously healthy 20 year old woman presented to her general practitioner with a two week history of severe pain in the lower back and thighs. Five weeks earlier she had developed neck pain followed by pain in her upper limbs, but these symptoms had resolved. She was treated initially for one week with erythromycin, failed to improve, and was then given aspirin. The development of abdominal pain, vomiting, and a swollen right knee prompted urgent referral to the rheumatology department. Her only other treatment was the contraceptive pill. She had been on holiday in Spain three months previously.

On examination she was pale, had a fever (38°C), and was systemically unwell. There was a pronounced lumbar lordosis, and both hips were flexed, any attempt at extension causing excruciating pain. There was tenderness and swelling of both thighs with an area of erythema overlying the tender muscles of the right thigh extending from the groin to the knee joint. A moderately sized effusion was present in the right knee.

Sepsis was suspected clinically, and empirical treatment with flucloxacillin 1 g four times a day and cefuroxime 1.5 g three times a day was started.

Haemoglobin concentration was 96 g/l (normochromic normocytic pattern), white cell count $11.3 \times 10^9/l$, platelet count $467 \times 10^9/l$, erythrocyte sedimentation rate 58 mm in the first hour, aspartate aminotransferase 223 IU/l (normal 5-45 IU/l), and creatine kinase 946 IU/l (0-170 IU/l). Midstream urine specimens and four blood cultures were sterile. Synovial fluid from the right knee was clear with a few mononuclear cells and was sterile on aerobic and anaerobic culture.

x Rays of the chest and lumbar spine were normal apart from a pronounced lumbar lordosis. A pathological process involving the psoas muscle was suspected and computed tomography of the abdomen showed the typical radiological features of a left psoas abscess (fig 1(top)). Laparotomy was performed after an unsuccessful attempt at ultrasound guided drainage. At operation, the left psoas muscle was swollen, but there was no evidence of suppuration. Biopsies were taken, some of which showed normal individual muscle fibres with a few inflammatory cells surrounding blood vessels and a localised mononuclear leucocyte infiltrate between individual fibres. Other sections showed severe disruption and muscle necrosis with areas of haemorrhage, but no evidence of vasculitis. Occasional lymphocytes were

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Fig 1 Top: Computed tomogram shortly after admission showing swollen left psoas muscle with hypodense areas within muscle. Bottom: Follow up tomogram four weeks later showing complete resolution of previous changes

seen, but neutrophils and eosinophils were absent and there were no granulomata. Culture of the sample was negative for acid fast bacilli.

Viral screen and complement fixation tests for Q fever, *Mycoplasma pneumoniae*, brucella, salmonella, toxoplasma and gonococcus were all negative. The antinuclear factor IgG was weakly positive with a homogeneous staining pattern, but other autoantibodies were negative. CH₅₀, C3, C4, and immunoglobulin values were also normal. An electromyogram of the left quadriceps, left tibialis muscles, and the right deltoid showed myopathic changes. T2 weighted magnetic resonance images of the thighs showed multiple abnormal high signal areas in the quadriceps muscles consistent with myositis (fig 2). Over the following four weeks, symptoms and signs resolved spontaneously on no specific treatment, and all biochemical and haematological parameters returned to normal. A repeat abdominal computed tomogram done four weeks after the first showed almost complete resolution of the previous abnormalities (fig 1(bottom)).

After five weeks in hospital the patient was discharged home taking no treatment but was readmitted six weeks later with pain in the buttocks, abdominal muscles, and left upper arm (the latter

being swollen, tender, and erythematous). Her haemoglobin concentration was 98 g/l, erythrocyte sedimentation rate 70 mm in the first hour, C reactive protein concentration 100 mg/l, and creatine kinase 5070 IU/l; antinuclear factor was weakly positive. No other autoantibodies were detected, and the CH₅₀, C3, and C4 values were normal. A biopsy of the triceps muscle at a time when pain in this muscle was decreasing showed normal fibres with occasional lymphocytes interspersed between individual muscle fibres. There was no evidence of muscle fibre necrosis. Subsequent immunohistochemistry showed the lymphocytes to be CD4 positive T cells. Electron microscopy showed no evidence of necrosis, inclusion bodies, or mitochondrial abnormalities. Portions of the specimens were sent for in vitro hybridisation studies, but no enterovirus RNA was detected.

Because of the severity of her symptoms oral prednisolone 60 mg daily was prescribed. Symptoms and signs resolved, and creatine kinase concentration, erythrocyte sedimentation rate, and C reactive protein all normalised within three days. She was discharged home; the steroids were gradually reduced and finally discontinued after six months. During one follow up visit she had a mild leucopenia (white cell count $3.3 \times 10^9/l$), but this did not persist. Several months after discontinuation of steroids, another relapse occurred with myositis affecting the right upper arm (fig 3) and right thigh. Once again symptoms responded rapidly to steroid treatment, which was continued for a further 10 weeks.

She remained well on no treatment until 1 year after initial presentation, when she developed an erythematous rash around the eyes, neck, and upper chest, but this resolved completely before a biopsy could be arranged. At this point she was lost to follow up, although she remained well for a further six months before she returned with recurrence of the facial rash and polyarthralgia. A biopsy was performed, and histological examination showed hyperkeratosis, mild follicular plugging, and epidermal atrophy with loss of a defined basal layer and vacuolation of basal cells with dyskeratotic cells. There was a mild lymphocytic periadnexal infiltrate in the superficial dermis. Direct immunofluorescence showed a granular

Fig 2 T2 weighted magnetic resonance images of thighs showing abnormal signal (white) from vastus intermedius and lateralis muscles particularly on left

band at the dermoepidermal junction consisting of IgG, IgA, and C3.

The antinuclear factor was now positive at a titre of 320 with homogeneous staining pattern and anti-double strand DNA (crithidia immunofluorescence assay), and anti-SS-A antibodies were also present. Haemoglobin concentration was 114 g/l, white cell count 3.69×10^9 /l, platelet count 230×10^9 /l, erythrocyte sedimentation rate 48 mm in the first hour, and C reactive protein concentration 1 mg/l. Urea, creatinine, electrolytes, liver function tests, creatine kinase, and urine analysis were normal. CH₅₀ was 46% (60-140%), C3 0.56 g/l (0.97-2.00 g/l), and C4 0.10 g/l (0.14-0.45 g/l).

Systemic lupus erythematosus was diagnosed and treatment with hydroxychloroquine started. Symptomatic control remained satisfactory for six months until readmission was necessary because of a worsening rash, breathlessness, and swelling of the face and legs. On examination the blood pressure was 180/110 mm Hg, and she had extensive facial erythema and pitting oedema to above the knees. Haemoglobin was 90 g/l; white cell count 8.7×10^9 /l; platelet count 376×10^9 /l; CH₅₀ 17%; C3 and C4 concentrations 0.35 g/l and 0.09 g/l respectively; erythrocyte sedimentation rate 76 mm in the first hour; concentrations of C reactive protein 3 mg/l, urea 9.5 mmol/l, and creatinine 78 μ mol/l; 24 hour urine protein excretion 13.7 g; serum albumin concentration 25 g; and creatinine clearance 56 ml/min. The nephrotic syndrome secondary to lupus nephritis was diagnosed. Renal biopsy showed diffuse proliferative glomerulonephritis (World Health Organisation class IV) with strongly positive granular staining around glomerular basement membranes with IgG, IgA, IgM, C3, C4, and Clq on immunofluorescence. Pulse intravenous cyclophosphamide 750 mg was administered monthly and 40 mg oral prednisolone daily. Proteinuria has reduced to 0.1 g/24 h, and renal function is normal. The patient remains well on 10 mg prednisolone daily and has not had any further episodes of myositis.

Comment

In patients with an established diagnosis of systemic lupus erythematosus, clinical symptoms suggesting muscle disease are often present, with myalgia and weakness being the commonest.¹ Previous studies suggest that 5-11% of cases of systemic lupus erythematosus also have evidence of an inflammatory myopathy,^{2,3} although non-specific abnormalities on muscle biopsy may be more frequent.^{1,4} Myositis is rarely the presenting feature, however, and when it does occur in patients with systemic lupus erythematosus it is usually mild, and creatine kinase concentrations tend to be normal even though aldolase concentrations may be raised in more than 60% of cases.⁵ In most cases of myositis in systemic lupus erythematosus, the muscle inflammation develops at the time of diagnosis and occasionally the clinical findings are those typically associated with polymyositis¹—namely, proximal muscle weakness developing slowly and progressing steadily over weeks to months.⁶ The response to treatment with steroids is good and the prognosis more favourable than that seen in patients with polymyositis associated with rheumatoid arthritis or scleroderma.⁷

Fig 3 Painful, swollen right upper arm with erythema of overlying skin

We have described an unusual case in which the development of repeated episodes of severe focal muscle inflammation was the initial presenting feature of systemic lupus erythematosus. The patient's muscle disease would fulfil the criteria for "probable polymyositis" as defined initially by Bohan and Peter⁸ and later by Dalakas,⁶ but the acute multifocal, asymmetrical onset with spontaneous remission and subsequent relapses is very atypical. A few cases of polymyositis have been described in which the initial presenting features were those of focal muscle inflammation,⁹⁻¹¹ although none of these patients to our knowledge subsequently developed systemic lupus erythematosus. Focal myositis usually presents as a solitary, painful, rapidly enlarging muscle mass with no associated systemic features or laboratory abnormalities.^{12,13} It can occasionally mimic deep vein thrombosis¹⁴ or have an infective aetiology.^{14,15} The diagnosis of idiopathic focal myositis and polymyositis is therefore made after excluding the many toxic, neurological, metabolic, and infectious causes of muscle pain and weakness.

This case illustrates the heterogeneous nature and the potential difficulties involved in the diagnosis of the inflammatory myopathies and highlights their association with other connective tissue disorders. The initial clinical presentation of focal muscle inflammation and necrosis strongly suggested a psoas abscess; the subsequent spontaneous resolution and evolution of the disorder into a recognised connective tissue disorder is extremely unusual. Follow up of patients with such a presentation is therefore indicated.

Discussion

MHP: Do you think that the initial presentation was infective but that prior treatment with antibiotics made isolation of the bacteria difficult?

JJ: Although the initial clinical presentation strongly suggested sepsis, there was no evidence of suppuration in the psoas muscle at laparotomy and the

histological findings were those of myositis and not bacterial infection. This is very unusual, however; the commonest cause of this radiological appearance is bacterial infection, although metastatic tumour may occasionally be responsible.¹⁵ Indirect evidence implicates virus infection, in particular picornaviruses, as a possible triggering factor in the inflammatory myopathies. Viruses have been isolated from the muscle of patients with polymyositis only in a few cases.¹⁶⁻¹⁷ However, an extensive study of 44 patients with an inflammatory myopathy failed to detect the presence of nucleic acid sequences from Coxsackie virus, mumps virus, encephalomyocarditis virus, adenovirus, human T lymphotropic virus types I and II, and HIV in affected muscle by means of a polymerase chain reaction based method.¹⁸

JPC: There have been no features of muscle disease in this patient since systemic lupus erythematosus was diagnosed. Is it possible that they were unrelated conditions?

JDJ: In considering the relation between the focal muscle inflammation and the subsequent appearance of systemic lupus erythematosus, we cannot exclude the possibility that the two were different conditions that appeared by chance in this patient. However, as some serological and haematological abnormalities were present at the time of her initial presentation, we consider it more likely that early treatment with corticosteroids may have delayed the onset of the more typical clinical and serological features associated with systemic lupus erythematosus. It is not surprising that she has had no recent attacks of myositis as the immunosuppressive drugs prescribed for treating the lupus nephritis would prevent this.

LKB: Is the psoas muscle commonly involved in inflammatory muscle disease?

BDW: We have reported one other case—a young man in whom the initial clinical and radiological features indicated a psoas abscess. The symptoms and signs resolved spontaneously, and again the diagnosis was idiopathic focal myositis.¹⁹ As the young man returned to India we do not know whether he subsequently developed any features of a connective tissue disorder. Inflammation in the iliopsoas muscle is more common in inclusion body myositis than polymyositis,⁶⁻²⁰ but this condition occurs in the older age groups, responds poorly to immunosuppression, and has histological features that are different from those noted in this case.

JPC: This patient's myositis resolved spontaneously, although she subsequently relapsed. Have you seen this in any other cases of inflammatory muscle disease?

BDW: The course of the illness in this case is very unusual. The inflammatory myopathies tend to run a steadily progressive course until immunosuppressive treatment is introduced. Spontaneous resolution of a case of focal myositis in which the presentation resembled deep vein thrombosis has previously been reported, although subsequent relapse with involvement of the opposite calf required treatment.¹⁴ Tsokos *et al* reported that 18/228 patients with systemic lupus erythematosus had myositis confirmed on biopsy, but only one had a raised creatine kinase concentration.⁵ That patient's condition resolved spontaneously with no immunosuppression, whereas all the other patients

responded rapidly to low doses of steroids and did not need additional cytotoxic treatment.

LKB: This patient has clearly responded well to pulse cyclophosphamide and steroids with improvement in renal function. Given the potential problems associated with cyclophosphamide, particularly in young women, how long will you continue with the pulse cyclophosphamide?

JDJ: Pulse intravenous cyclophosphamide in conjunction with steroids is considered the optimal treatment for patients with systemic lupus erythematosus who have diffuse proliferative glomerulonephritis (WHO class IV) who need more aggressive and prolonged treatment. The most frequently used regimen consists of monthly pulses of intravenous cyclophosphamide (0.5-1 g/m² body surface) for six months followed by quarterly (three monthly) boluses for two years. Addition of a quarterly maintenance regimen to monthly pulse cyclophosphamide reduces the rate of exacerbations of nephritis and other disease manifestations.²¹ Intravenous cyclophosphamide is at least as effective as oral cyclophosphamide but is less toxic, although the risk of premature ovarian failure remains similar at 20-40% and increases with the age of the patient.²² Patients clearly need to be warned about the potential risks before treatment.

The *BMJ* welcomes grand rounds from other hospitals.

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