have made claims for the value of measuring D-dimer concentrations in patients suspected of having venous thromboembolism.[7,8]

One issue has been clarified: raised concentrations of D-dimer should not be interpreted as supporting the diagnosis of deep vein thrombosis or pulmonary embolism. The test is non-specific; raised values can be found in many other conditions and, indeed, in the postoperative period, a high risk time for thromboembolism. On the other hand, measurements of the concentration of D-dimer may be used to exclude the diagnosis—that is, the absence of a raised concentration implies that there is no fresh thromboembolic material undergoing dissolution in the deep veins or in the pulmonary arterial tree. Such a (nearly) exclusionary test would be valuable, especially when combined with other well studied non- invasive tests for deep vein thrombosis (impedance plethysmography, ultrasonography) and pulmonary embolism (lung scanning).

Will this promise be fulfilled? It is still too early to tell; indeed, we are some distance from knowing. Too many assays have been used in different studies—at least four enzyme linked immunosorbent assays (ELISAs) and four latex assays. Normal values differ for each: as Bounameaux *et al* recently said, standardisation and calibration are urgently needed.[9] Furthermore, any test born in the tightly controlled incubator of research tends to slide a bit in performance when it comes into general use.

Other issues need to be addressed. Normal values tend to vary with age. How long does it take for a deep vein thrombosis or pulmonary embolism to become sufficiently organised that it no longer releases D-dimer? How severely will the value of the test be reduced by all of the competing causes for a raised D-dimer concentration in patients in hospital?

Venous thromboembolism is potentially lethal, so the margin of tolerable error is not wide. D-dimer has not yet been put to the ultimate test—a trial in which treatment is withheld from patients suspected of having deep vein thrombosis or a pulmonary embolism with D-dimer concentrations below a specified cut off value. Such trials of outcome should take account of the existing diagnostic approaches that have already gone through such trials—impedance plethysmography and ultrasonography[10] for detection of deep vein thrombosis and perfusion ventilation scanning[11,12] and pulmonary angiography for exclusion of pulmonary embolism. In these instances, the available data indicate that treatment may be withheld without adverse outcomes.

What is the way ahead? After standardisation and calibration, assays for D-dimer must be subjected to the definitive study: they should be combined with other established tests to support decisions not to treat. Let us hope that D-dimer will not descend the parabola of other diagnostic blood tests, but only time and further investigations will tell.

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Botulinum toxin in the cerebral palsies

Grounds for cautious optimism

Botulinum toxin is now routinely used in adult focal dystonias,[1] including blepharospasm,[2] spasmodic torticollis,[3] and hemifacial spasm, and also in squint and some types of tremor.[4] When injected close to the main area of nerve arborisation within a muscle, the toxin is selectively taken up by cholinergic nerve terminals and blocks neuromuscular transmission for between two and four months until new terminals grow. Recent reports of its use in the cerebral palsies are encouraging but need to be placed in context.

The cerebral palsies are motor disorders arising from static brain abnormalities that may result from early embryological defects or damage in utero or early extrauterine life. Cerebral palsy phenotypes often include primary cognitive, psychiatric, sensory, and seizure disorders and a wide range of secondary skeletal and general medical illnesses. The motor disorders vary greatly in severity and neurological signs. Each pathology may therefore cause a range of types of cerebral palsy without any necessary concordance between pathological and clinical categories.[5]

The process of progressive developmental revelation with age, the cascade of disabilities in the first two to three decades, and the propensity of the developing nervous system to compensate for early damage (albeit by its own efforts[6] rather than those of doctors and therapists) have prompted a drive for early intervention. Very early definition of motor disorders and even of the population at risk may result in many babies with transient abnormalities being treated, who may then feature as "cured." Until now, however, no solid evidence of the medical cure of a cerebral palsy syndrome has been published, and the problems of running good randomised studies in such a heterogeneous population are clear.

As we move from global treatments (early management[7]) through regional approaches (such as dorsal rhizotomy[8]) to selective interventions in which one or two muscle groups have their tone reduced, we can more easily define problems in objective terms and conduct trials likely to yield statistically valid conclusions. That does not preclude benefit from less selective approaches; it merely means

that we may never have good evidence of their efficacy.

The cerebral palsies are very different from focal dystonias, particularly in their involvement of a large number of muscle groups. Hypertonus is often not the main problem, and botulinum toxin could exacerbate the loss of motor control and weakness that often occur unless the problem of motor control is focal hypertonus. Recent publications by a group in Belfast have begun to clarify some of the basic science and clinical issues. The group used a developmental model of a hereditary spastic mouse and in a randomised controlled study injected gastrocnemius before symptoms occurred.[9] This produced obvious transient weakness for up to 10 days, and at maturity the muscle length had been sustained in the treated group but the expected shortening of the muscle belly (contracture) had occurred in the control group.

The group's paediatric study was an open, uncontrolled study of 26 children aged 2 to 17: eight with hemiplegia, seven with diplegia, and 11 with appreciable involvement of both arms and legs ("quadriplegia").[10] The study was confined to the calf (32 muscles) and hamstring (21 muscles) in children without "obvious" fixed contractures in whom "an abnormal increase in muscular activity was interfering with function." Within a few days of injection with botulinum toxin A all but one injected muscle had developed decreased tone, which persisted for between six and 16 weeks. The parents of 14 of the 26 children reported considerable functional improvement with an appreciable shift in ambulatory status; only one child showed deterioration. In the group who received injections into the calf muscles the range of passive and active dorsiflection at the ankle improved mainly in those under 7.

Of those who received hamstring injections (all but five of whom also received injections of gastrocnemius), the range of passive and active movement at the knee increased and the improvements did not depend on age. In two children with appreciable foot inversion and dystonic features injection into the tibialis posterior resulted in substantial improvement. Although many patients relapsed as expected after two to four months, some showed persisting gains and evidence of strengthening of antagonist muscles. No systemic side effects or spread of weakness to surrounding muscles was seen.

A group from North Carolina recently reported the results of a small randomised double blind trial in which botulinum toxin was injected into the calf muscles of children with cerebral palsy.[11] Improvement occurred in five of the six children given active compound compared with two of the six children given saline.

Larger randomised controlled trials are obviously needed. If these confirm benefit then botulinum toxin could find several uses in the treatment of the cerebral palsies. These include the modification of early patterns of axial asymmetry that may influence later development of the spine and hips. It could be used early to modify the effects of spasticity on soft tissue and bone, thereby reducing the extent of later surgery.[12] It could also be used to mimic the effects of possible surgical procedures. It could provide a time window for physical, including orthotic, interventions—for example, in thumb adduction in hemiplegia[13] and unilateral hip adduction in early wind sweeping of the lower limbs in severely affected non-ambulant children. And it could be used to treat focal dystonias within the cerebral palsies, for which surgery has gained such a bad reputation.

Regular injections of toxins over years are unlikely to be acceptable to children despite the toxin's obvious advantages over phenol and alcohol as a local agent, and their effect may not be sustained. Botulinum toxin is expensive and requires further studies combining careful clinical and biomechanical delineation of specific problems and methodological rigour. The subject also demands the cautious style of reporting that the Belfast group has used in an attempt to curb the media impression that this is yet another "cure" for cerebral palsy. Botulinum toxin may become one modality in the integrated management of the cerebral palsies.

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Follow up by telephone

It may be just as good to talk on the telephone as in a clinic

Health service workers seem to regard the telephone as intrusive. For patients and staff alike, mention of the telephone conjures up images of haughty, unhelpful receptionists and tardy, impolite switchboard operators. Its insistent ring demands immediate attention, interrupting the ward round and disturbing consultations. For patients a call from the hospital is often bad news, and they are expected to call the hospital only when absolutely necessary. Even in the newly consumer conscious NHS the interaction between staff and patients over the telephone can hardly be described as convivial.

And yet, with a little imagination, the much maligned telephone could be used to improve patients' care. Take several examples from the United States. Jones *et al* have shown that telephone follow up of patients attending an emergency room can be beneficial.[1] In one month 281 patients (15% of the total) were selected for such contact. Two fifths of the patients needed clarification of instruc-