



**Figure 1 | Experimental manipulation of the respiratory system.** **a**, Basic anatomy of the intact respiratory system. BS, brainstem; SC, spinal cord; C, cervical level; PMN, phrenic motor nucleus; PN, phrenic nerve. **b**, After a partial spinal-cord injury at C2, innervation to the left PMN is interrupted and the diaphragm is paralysed on the left. **c**, Alilain *et al.*<sup>1</sup> show that 12 weeks after peripheral-nerve grafting and injection of chondroitinase ABC (chABC), activity is restored in the paralysed side of the diaphragm.

abolished the regained respiratory function.

Intriguingly, when the graft was cut, the residual electrical activity of the paralysed half of the diaphragm muscle was significantly, albeit transiently, increased compared with residual activity after the initial SCI. This suggests that spinal-cord circuits were also rewired to some extent in this experimental setting: descending regenerating axons may have connected with different targets, and denervated neurons may also have found new synaptic partners before regenerating axons could reach them<sup>7</sup>. It is encouraging that, despite the havoc such rewiring could wreak, the system could still adapt to the changes — perhaps through a type of learning process — to restore proper firing patterns to the motor neurons innervating the diaphragm.

Such adaptability might be a special property of the respiratory circuit: it has long been known<sup>8</sup> that there are latent connections in the respiratory system that can be activated after injury. Alternatively, it may be a common property of all spinal-cord circuits that can be unleashed by the degradation of CSPGs, as well as by extensive rehabilitation. At an axon's target site, such as the PMN, CSPGs are thought to stabilize circuits after development is complete<sup>9</sup>. Degradation of CSPGs after injury may therefore give circuits the flexibility they need to make new connections and adapt to changes. The built-in rehabilitation regimen that the paralysed diaphragm receives — by virtue of the fact that the animal must continue to breathe if it is to remain alive — probably also plays a part in shaping the new circuit. In support of this, chABC treatment together with physical rehabilitation promotes recovery of manual dexterity after cervical SCI in rats<sup>10</sup>.

Overall, Alilain and colleagues' results<sup>1</sup>

suggest that combinatorial strategies that promote both long-distance axon regeneration and local circuit reorganization may be universally useful for enabling functional recovery after SCI. Because not all axons of the central nervous system have the same ability to regrow into permissive grafts<sup>11,12</sup>, it may be necessary to use other methods to stimulate axon regeneration<sup>13</sup>. Future studies should investigate how best to facilitate integration of regenerated axons into local circuits and to harness the potential of anatomical plasticity to restore multiple functions after SCI. ■

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## 50 Years Ago

*Mathematical Methods in the Theory of Queueing.* By A. Y. Khintchine — This beautiful little book breathes reason and modesty from cover to cover ... A particularly pleasing feature is the way in which the results are developed; the mathematics is 'done', not merely indicated, and nowhere does the author state a result and refer the reader elsewhere for the details. Thus there is a satisfying aspect of completion about the exposition ... The theory of queues has undergone considerable development in recent years. Some mathematicians think the development has gone too far. Whether this is so or not the book under review will serve to show that the phenomenon of queueing represents another human experience which has bowed to the forces of applied mathematics; the concepts that have been built around this experience have proved to be of the right kind, and sufficient in number, for the mathematical development to go 'with a bang'.  
**From Nature 15 July 1961**

## 100 Years Ago

We published recently (June 29) a short article on the progress of radiography in medical diagnosis, and alluded in particular to the work of the staff at Guy's Hospital in their investigation of pathological conditions of the intestine. In this connection we note the appearance of a new paper ... by Dr. A. C. Jordan, medical radiographer to Guy's Hospital ... in which he shows that it is often possible to detect duodenal obstruction by the X-ray method after giving the patient a bismuth meal. Diseases of the duodenum are often extremely obscure, and this new method of diagnosing the condition will be welcomed both by the medical profession and the sufferers from such complaints.  
**From Nature 13 July 1911**