shows gross dilatation of the colon leading to a narrow funnel in the aganglionic rectum.

Constipation in the elderly may be due to diminished motor activity of the bowel, and this also may be prominent in patients with hypothyroidism. Other, rarer causes include organic nervous diseases affecting the sacral nerve roots or the cauda equina—including spinal tumour, transverse myelitis, and multiple sclerosis. Almost always, however, there will be urinary symptoms and obviously abnormal neurological signs on examination. Finally, the doctor should make a careful inquiry about the use of medicines and tablets since many drugs have a constipating effect: codeine, morphine, ganglion-blocking agents, and antacids such as aluminium hydroxide are common examples.

Having excluded all possibilities in this check list of organic or mechanical causes of constipation, the medical practitioner now has one of his most common yet most challenging and difficult problems. He has to re-educate his patient away from a lifetime of preconceived ideas of the physiology of his large intestine, wean him from his ritual purgatives (which often themselves are responsible for many of the patient's symptoms), and convert him to a regimen in which the bowel actions are controlled by a sensible bulk diet.

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**Drug lag bad: drug lack worse**

The delay in introducing new drugs in the United States compared with similar countries has become known as the "drug lag." Despite official claims to the contrary, valuable drugs have been partially or wholly denied to the American people for long periods. Critics have argued that the United States Food and Drug Administration has been depriving rather than protecting the public or even cynically avoiding risk by waiting to see what happens elsewhere.

The countries against which America is compared have also experienced increasingly stringent and bureaucratic regulation of drugs, and in the past the decade in which pharmaceutical research is conducted has steadily deteriorated. Britain is often used as the baseline for estimating the drug lag. Here people are particularly concerned over the difficulty and delay in starting early small-scale clinical trials—contrary to scientific logic and despite their remarkable record of safety.

America is of overriding importance to the pharmaceutical industry. It represents 18% of the world drug market and no international manufacturer can afford to ignore it. Yet the Centre for the Study of Drug Development has reported that between 1974 and 1976 the number of new chemical entities reaching clinical study in the United States fell by nearly half. The few that survive now take about nine more years to reach the market. The nominal life of a US patent is 17 years but the delays imposed by regulatory agencies made the average patent life 13-8 years in 1966 and only 8-9 years in 1977. By 1976 the average cost of marketing a new product had risen to over 50 million dollars. Not only have research costs increased rapidly, but the proportion devoted to innovation has been reduced, as has the amount of support for basic research from both industrial and non-industrial sources. The implications for future therapeutic progress are plain to see.

Drug regulation is the most important determinant of the climate of research but other factors include economic, political, ethical, and legal restraints. The introduction of strict product liability could pose a huge additional burden and one that cannot yet be estimated. These restraints limit research options to such an extent that the problem has ceased to be simply a drug lag, which is relative: it has become an absolute lack of many types of new products. For some years the development of drugs for rare diseases or for diseases that are common in poor countries has been economically profitless even when technically possible. Manufacturers are driven to concentrate their efforts in progressively fewer and often the same areas, which are not always where the need is greatest. Some have already learned the hard way that it is unrewarding to develop the nth beta-blocker or non-steroidal anti-inflammatory agent.

If present trends continue the pharmaceutical industry, which depends heavily on research for its prosperity, seems certain to run down in the coming decade, with serious direct and indirect consequences. Increasing diversification by the big companies already shows their lack of confidence in the future. The trends will be difficult to counteract. Many of the contributory factors are themselves socially desirable, but a growing body of informed opinion holds that the pendulum has swung too far and that the problem must be tackled, whatever the difficulties.

The Council for International Organisations of Medical Sciences (set up by WHO and UNESCO in 1949 as a federation of national and international biomedical organisations: address care of World Health Organisation, CH-1211 Geneva 27) recently adopted a special programme with the title "Drug Development and Use—Medical, Social, and Economic Implications." It has the support of WHO, of the International Union of Pharmacology, and of a broadly based international advisory board. The start of the new decade is a very suitable time for a reappraisal.

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