

unrecognized hazard might exist or because the reaction appeared to be of an unusual or even bizarre type or because the subcommittee was seeking to establish that a certain clinical sequence was, in fact, due to a particular drug. In such cases the probability that the reported events are drug-related may be either more or less than was found in this sample.

As might be expected the proportion of serious or fatal reactions was higher in hospital reports (60%) than in those sent by general practitioners (32%). The preliminary assessment of causal relationship was modified as a result of follow-up in 14 cases (see Table VI). "Probable" assessments before follow-up were changed to "possible" in five cases and "unlikely" in one. "Possible" assessments were changed to "probable" in two cases and "unlikely" in six. It is the usual practice of the committee to record all reports in the register of adverse reactions so that no event, however improbable it may be that a drug has caused it, will be overlooked permanently. This practice may have influenced the assessment of some of the more doubtful cases before follow-up, and it is likely that this accounted for the fact that six of the seven cases assessed as "unlikely" after follow-up were rated "possible" initially. Useful information was obtained in 41 out of 57 interviews (72%) compared with 15 out of 25 investigations completed by correspondence (60%). But the advantages of interview were even more apparent in both the quality and quantity of the additional data obtained than these proportions suggest.

The following general conclusions can be reached as a result of this analysis. (1) Valuable information can be obtained by

follow-up whether by correspondence or interview, but the second approach is more rewarding and is preferable if deductions are to be made which may affect the future use of a drug. (2) Causal relationship does not appear to be related to the severity of the reported reactions. (3) Of the 82 reactions 64 (78%) were considered to be probably drug related, 11 (13%) possibly related, and only 7 (9%) unrelated to the use of the suspect drug. Since the sample is believed to be fairly representative of the total input of reports, and because a high proportion of drug-related reactions were confirmed by follow-up, many of the reports to the committee are likely to be true examples of drug reactions. (4) The present system of reporting is valuable and should be encouraged because it forms the basis for more detailed investigations which may yield new knowledge.

We wish to thank Professor Eric Scowen, Sir Richard Doll, and Dr. David Mansel-Jones for their helpful comments, and the Committee on Safety of Medicines for permission to make use of these data.

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References

- ¹ Witts, L. J., *British Medical Journal*, 1965, 2, 1081.
- ² Doll, R., *British Medical Journal*, 1969, 2, 69.
- ³ Inman, W. H. W., and Vessey, M. P., *British Medical Journal*, 1968, 2, 193.
- ⁴ Inman, W. H. W., *British Medical Bulletin*, 1970, 26, 248.

European Counterparts

Variations in Pharmaceutical and Medical Practice in Europe

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The statement that medicine is international and knows no frontiers has become almost a platitude. It is true, of course, that throughout the world our profession has roughly the same ideals and speaks to some extent the same clinical and scientific lingua franca. The diagnosis and treatment of most diseases, too, such as appendicitis, pneumonia, and rheumatism are similar in different countries and therapeutic success depends on the skill of the physician or surgeon and the resistance of the patient. Nevertheless, the advent of more rapid communications and the tendency to form wider groupings like the Common Market have made it clear that it is a gross oversimplification to assume that the practice of medicine is at all homogeneous, even in the western world. There is, however, a universal search for higher standards and there are great advantages in submitting our long established national conventions, institutions, and attitudes for criticism by our colleagues in other countries. It is also salutary for us in the United Kingdom to remember that in Europe fairly comprehensive health services exist in various ways with good hospital facilities which in some inst-

ances are superior to our own. In this paper an attempt has been made to portray some of the odd divergencies which occur in different parts of Europe in pharmaceutical and medical practice.

Pharmaceutical Industry

The multitude of controls imposed on the pharmaceutical industry varies enormously in different countries, and even within the Common Market there are still many regulations preventing the free movement of medicines from one country to another. Thus pharmaceutical products manufactured in Britain or France can be imported freely into Germany, Switzerland, and the Scandinavian countries, provided they are manufactured so as to comply with certain specifications, but not into Belgium, where all products must be packed under the supervisory control of a Belgian pharmacist. Although there is close co-operation in Benelux countries it is easier for Holland to import Belgian-packed medicines than for Belgium to import Dutch. France has such stringent rules that it is virtually impossible to import medicines except on a small scale by a Government agency. It is extremely difficult to find a colouring agent which will be at once acceptable in the U.S., U.K., and continental countries. There are wide variations in different

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countries in the availability or otherwise of cyclamates. These are only a few illustrations of the differences which operate.

These discrepancies are not surprising when consideration is given to the rapidly changing conditions which exist and the variety of circumstances under which in this century legislation on drugs has been enacted in different parts of the world. In consequence, however, international pharmaceutical companies encounter many frustrations and difficulties as they strive to prune their production and marketing policies to conform to the widely diverse national controls that exist. It would be highly desirable that general rules could be framed for good practices in the manufacture and quality control of medicines which would be acceptable for reciprocal agreements between nations and made eventually a basis for international legislation.

The signing in October 1971 of E.F.T.A.'s Convention for the Mutual Recognition of Inspections in respect of the Manufacture of Pharmacological Products constituted a small advance in this connexion. Though the standards were not uniform they were sufficiently similar to render them mutually acceptable and to obviate the need for authorities in importing countries to make their own inspections. It is to be hoped that during the next 10 to 20 years we will see the free circulation between the various countries of the world of high-standard medicines with a general uniformity of quality control.

Doctors

On the average doctors on the Continent enjoy a higher status financially (and perhaps socially) than those in the U.K. (Fig. 1). In all other Western European countries doctors and lawyers

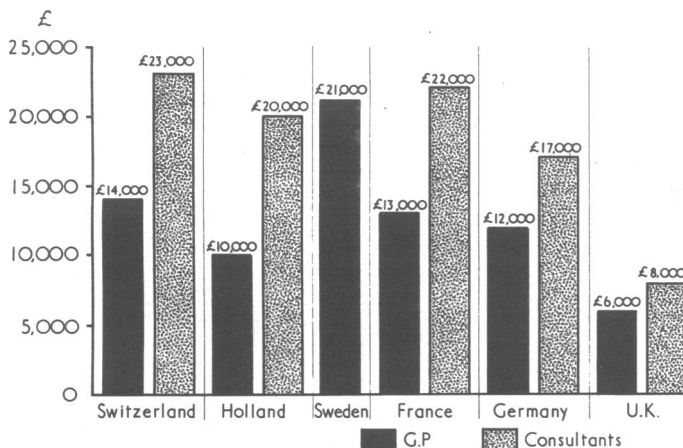


FIG. 1—Average earnings of general practitioners and consultants in various European countries.

have defended their financial and professional position more strongly than they have in the United Kingdom, and they are among the wealthiest group of citizens. With few exceptions health services on the Continent, though often efficient and effective, have not been nationalized, as they have been here for 23 years. In considering these figures, however, the comparatively lower cost of living in the United Kingdom must be taken into account, though this is now rising more rapidly than in the countries under discussion.

It is surprising (see Table) that the number of qualified medical men per head of population should be so much greater in Austria and Germany than in the U.K., Sweden and Finland.

Number of Doctors per 100,000 Population

Finland	77	France	121	Switzerland	141
Sweden	110	Norway	127	W. Germany	157
England and Wales ..	115	Iceland	135	Austria	158
Netherlands	117	Denmark	135		
Scotland & N. Ireland	119	Belgium	140		

Source: World Health Organisation.

To a slight extent this may be because many doctors qualify in Austria and Germany who do not continue to practice. For many years, however, far more doctors have qualified in Austria than were required there, and Austria in consequence exported large numbers to North Africa and other European countries—particularly Sweden. In Britain we export nearly 400 doctors a year, chiefly to English-speaking areas in North America, Australia, New Zealand, and South Africa, but the numbers of non-British doctors required to staff our National Health Service reached the amazingly high figure of 10,809 in 1970 according to the annual report of the Department of Health and Social Security for that year. The medical resources of developing countries suffer because of the failure to return to their own countries of non-British doctors trained here. English is widely spoken throughout the world, which facilitates the free movement of British doctors, but language difficulties apart, it will be a long time before a French doctor is able to practise freely in Germany or vice versa. It is not only, however, for these reasons that Russian or Chinese doctors are unlikely to travel freely in the future.

In North America average middle-class families tend to have their own paediatricians, obstetricians, surgeons, psychiatrists, and so forth and consult whichever one they think appropriate when they are ill. It is of course unfortunate when they get into the wrong queue. In the United Kingdom some 57% of doctors are in general practice compared with 24% of Sweden's doctors, all of whom practise only privately. Thus a Swedish patient has the alternative of going to a polyclinic between 9 a.m. and 5 p.m.—domiciliary visits are paid only if the patient is in extremis—or of consulting a private practitioner at a not inconsiderable fee for his visit. The patient can also telephone the doctor and describe his symptoms. After two or three minutes of such consultation the doctor may say that the patient's sore throat merits treatment with an antibiotic and that if he calls round in half an hour to such and such a pharmacy he will get the antibiotic prescribed and instructions on how to use it. At the pharmacy he pays for the medicine and in addition some 20 kr., roughly £1.60, which is about the usual fee to the doctor for such a consultation.

Prescribing of Medicines

Prescribing, of course, varies greatly in different countries even when they are neighbouring like France and Belgium or Denmark and Sweden. This is particularly the case in regard to the use of medicines. No matter how desirable it may be to establish universal standards for the good manufacture and quality control of medicines, any attempt to exercise national or international bureaucratic control over the freedom of the doctor to prescribe as he thinks best would be most undesirable. There is no safe depository of ultimate power in this respect save the medical profession, and should we be thought insufficiently enlightened to exercise that power with a wholesome discretion, the remedy is not to take it away from us but to improve our discretion by education rather than by legal edict.

Many of the discrepancies which exist are due to the varying incidence and severity of diseases in different countries—bronchitis, for instance, is known as the English disease, and in its chronic form is far more prevalent in Britain than in many countries in Western Europe. It is well recognized, too, how difficult it is to extrapolate to man the effect of drugs on animals, but to a lesser extent the same applies to different human ethnic groups, even perhaps in European countries. Thus amidopyrine, which was used widely throughout Europe as an effective analgesic, is now virtually unobtainable in the U.K., is on prescription only in Scandinavia, is available in small quantities without prescription in Switzerland, but is freely available to the general public in Germany. Is this disparity due to the fact that the British doctors detected more readily the potential hazard of agranulocytosis resulting from its use, that Scandinavian doctors though well aware of the danger regarded it less

seriously, while German doctors do not consider it of much significance? Or may there be a genetic difference in response to the drug in different ethnic groups? We are well aware, after all, of the remarkable variations which exist in response to drugs between African and non-negroid populations.

Nevertheless, it would be foolish to pretend that there are not widely varying fashions in medical practice which change from time to time just like styles in men's hairdressing. Variations in prescribing practice seem most obvious when we contrast our own with those of other countries, yet the fashions vary widely even in different districts of our own country, depending on the local influence exerted by predominating characters among consultants and professors and the activity of promotion by the pharmaceutical industry.

A great many fantastic diversities in prescribing could be quoted between different European countries; only a few examples are given here. The understandable French delight in the pleasures of their cuisine and wine is reflected in the concern of Frenchmen with their livers. Cholagogues are bought by them to the extent of about £8½ m. a year, whereas our yearly expenditure on these medicines does not reach even a quarter of a million pounds. We seldom give medicines by suppositories, whereas this is a commonplace in France, and perhaps we should profit from this example of their more fundamental administration of medicines, especially in the case of those likely to irritate the stomach. French doctors firmly believe that when broad-spectrum antibiotics like the tetracyclines are given they should always be accompanied by a prescription for lactobacillus to counteract the effect of the antibiotic on the intestinal flora and so to prevent some of the side effects of antibiotic therapy—particularly the orogenital syndrome. They may be right, but their expenditure of over £7m. a year on the lactobacillus, in comparison with ours of a very few thousand pounds, is surprising in a nation where the consumption of cheese and yoghurt is also so high. Further, the figure of £2,400,000 for calcium supplements in France in comparison with the £300,000 in the U.K. can hardly be attributed entirely to the large amount of fresh milk consumed in this country.

In our welfare state the consumption of vitamin supplements is probably excessive, but in comparison with Sweden it is minute (Fig. 2). It might be thought that the high standard of

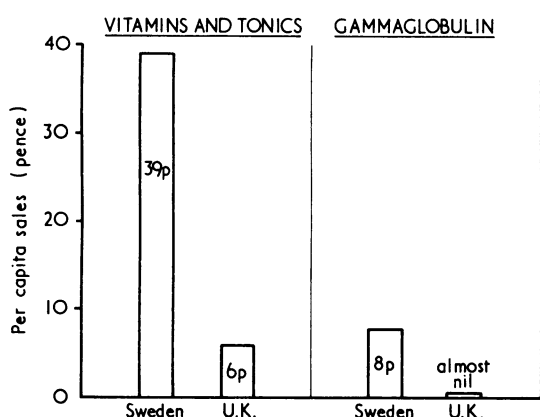


FIG. 2—Sales per head of vitamins, tonics, and gamma-globulin in Sweden and the U.K. in 1971. (Intercontinental Medical Statistics and Läkemedelsstatistik.)

living in Sweden compensated in this respect for their cold, dark winters. Nor does there seem to be any good reason, other than medical fashion, why the use of gammaglobulin should be so high in Sweden and so low in the U.K.

Lastly, although phenylbutazone is a valuable drug it should not be prescribed indiscriminately for aches and pains when less formidable agents will suffice. Extraordinary contrasts in its use exist between Switzerland, Germany, the U.K., and France (Fig. 3).

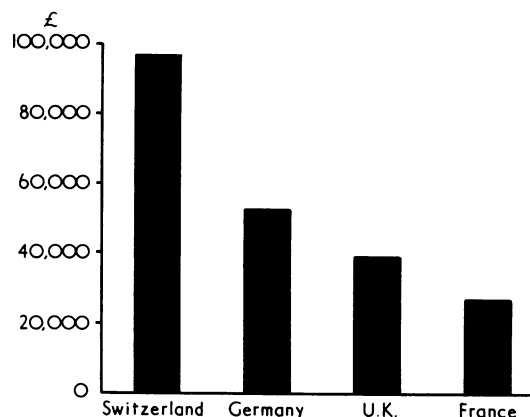


FIG. 3—Estimated sales of phenylbutazone (and derivatives) per million population 1971. (Intercontinental Medical Statistics and I.H.A. Institut für Markt-Analysen.)

To end this discussion on medical fashion the erstwhile supremely fashionable subject of spa treatment should be mentioned. In Britain until the first part of this century a sojourn in a spa was an accepted practice at some time in the year for the privileged classes, but it is very unusual now. Nevertheless, in France, Germany, Switzerland, Czechoslovakia, and Russia spa treatment is still commonplace, and patients are often sent to such resorts at the expense of the health service. Perhaps the excellent physiotherapeutic and dietetic services available at these centres are more beneficial than the actual hydrotherapy.

Certification of Death

It might be expected that death certificates would give some indication of morbidity. Were this so, remarkable variations must exist in the incidence of disease in European countries though the expectation of life among them does not differ very greatly. We all know, of course, that certification of the cause of death is a crude statistical tool, for it is often difficult even with the help of necropsy to certify the exact cause of death in some cases. Variations in terminology may also account for some of the differences which exist. Yet when taking all this into consideration it is hard to explain why death certificates should indicate such a striking difference in malignant disease between Finland and Austria (Fig. 4). It might be argued that a number of patients in Finland suffer from malignant disease without it being diagnosed because of their distance from medical care, but if the same argument is used it is hard to explain the divergencies in certified death from malignant disease between Holland and Belgium.

It is also impossible to explain the extraordinary differences in certification of death from degenerative heart disease between

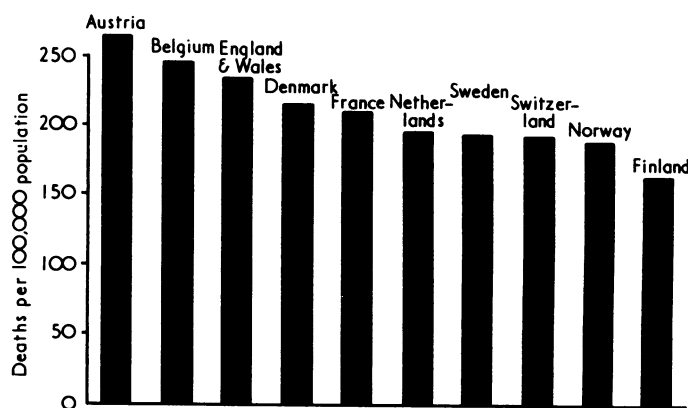


FIG. 4—Deaths from malignant neoplasm in 1968 per 100,000 population. (World Health Statistics Annual, 1968.)

France on the one hand and Sweden on the other, save on terminological grounds (Fig. 5). Lastly, it is incomprehensible why death from vascular lesions affecting the central nervous system should be nearly twice as common in Austria as in the Netherlands. The diagnosis of "strokes" should not be difficult however complex the exact classification of a stroke may be (Fig. 6).

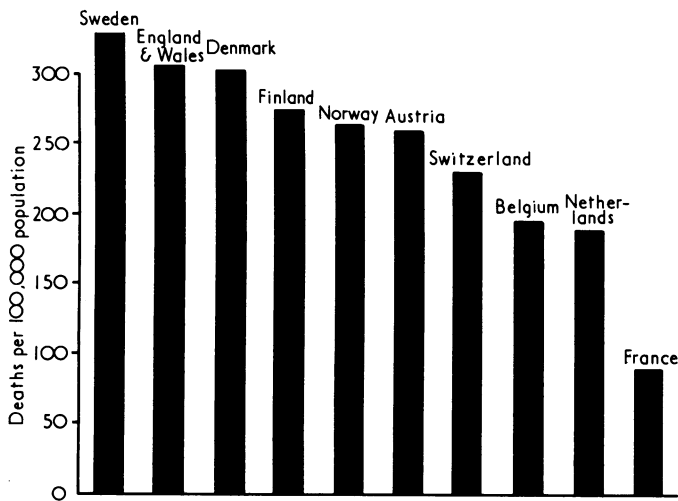


FIG. 5—Deaths from degenerative heart disease in 1968 per 100,000 population. (*World Health Statistics Annual*, 1968.)

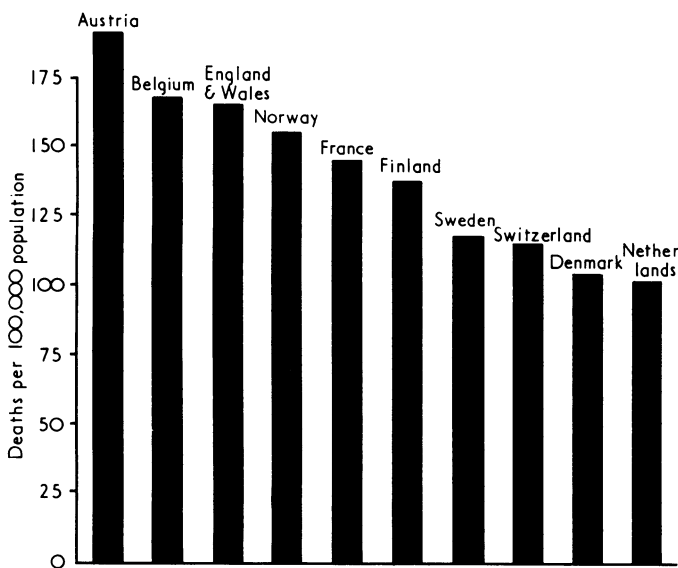


FIG. 6—Deaths from vascular lesions affecting central nervous system in 1968 per 100,000 population. (*World Health Statistics Annual*, 1968.)

Expenditure on Health

The British National Health Service constitutes one of the larger areas of national expenditure. The hospital sector accounts for more than 60% of the National Health Service budget. It comprises some 434,000 beds through which pass some five million patients a year, involving vast amounts of food, drugs, surgical and other appliances, nurses, technical and administrative staff, and other unskilled or semiskilled workers. Each of the 10,000 consultants in the National Health Service hospitals controls an average of about £120,000 a year. The rest of the

Service is not quite so expensive, though the average general practitioner prescribes over £8,000 worth of medicines a year as well as sending patients for radiological and biochemical examinations.

Over the past decade our expenditure on health has increased by a third, but this is modest compared with that in Canada, the U.S., and Sweden, even though these countries initially spent a higher proportion of their income on health than did Britain. The appetite for medical care and treatment is infinite. In the provision of hospital beds the United Kingdom occupies a middle position in the European league, but who would have guessed that the expenditure per capita on health in Sweden is probably three times that of ours?—£118 per head compared with £36 (figures from the annual report of the Department of Health and Social Security and the National Swedish Social Welfare Board). The cost of almost everything is of course much higher in Sweden than in the U.K., and Swedish incomes are adjusted accordingly.

Pharmacies

The differing number of pharmacies per head of population is interesting and surprising. Fig. 7 shows particularly that in Holland, Denmark, Norway, and Sweden there are fewer than

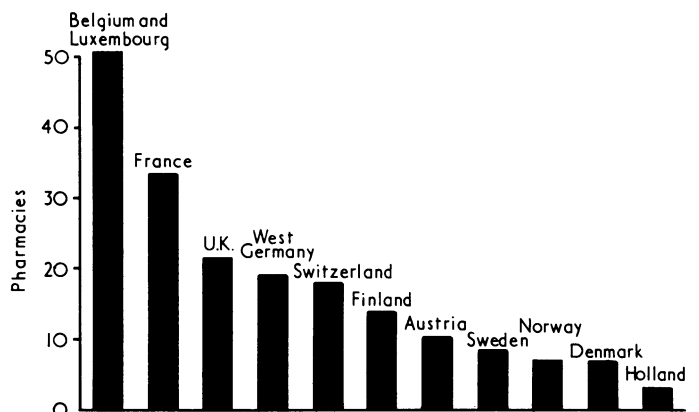


FIG. 7—Approximate number of pharmacies in 1971 per 100,000 population. (Official Government statistics.)

eight pharmacies per 100,000 inhabitants compared with over 50 in Belgium and Luxembourg. In Holland the small number of pharmacies is largely due to the manner in which Dutch pharmacists have operated a closed-shop policy, as in the old days of the guilds. Thus pharmacists in Holland are usually very prosperous citizens indeed, generally remunerated above all but the most successful doctors. In Denmark and Sweden pharmacies are closely controlled by Royal Patent—in Sweden they are now actually state controlled in the same way as in Finland, and in this respect resemble in varying degrees a British post office. The commercial atmosphere varies from none at all in Finland to some in Sweden and a good deal in Denmark.

We are living in a period of intellectual ferment and of great flux and change. We will have to learn to live more with other peoples of different culture and language. The study and practice of medicine, which at the beginning of this paper was said to be to some extent international and to know no frontiers, should help us to understand these problems and to find solutions to them.

P.S. As a corollary you can prove almost anything from international statistics.