IATROGENIC DISEASE IN CHILDHOOD*

AN ESSAY IN DEFINITION

BY

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Iatrogenic disease in childhood has been variously defined: on the one hand, as "disorder unwittingly induced in the patient and based on the physician's examination, manner, and discussion" (Ebaugh, 1950), and, on the other, as "illness caused by physicians" (Evans, 1956). The former, a psychiatrist's definition, openly admits harm done to the patient by an error of management, albeit an unwitting one, and limits the illness to emotional or psychoneurotic reactions to symptoms which generally have no organic basis. For the physician's purpose organic disease produced by his therapeutic or even his diagnostic activities must somehow be included. The second definition allows of this, but, discreetly silent about motive, includes physician-induced disease, designed as well as accidental and for better as well as for worse.

Paediatricians advise and perform Jennerian vaccination, giving their patients a disease which they would find it difficult to acquire by nature. Many advocate exposing healthy young girls to German measles to avoid infection during the first critical twelve weeks of some eventual pregnancy. That accidental measles has stimulated remissions in nephrosis and rheumatoid arthritis has tempted some to effective and beneficent action.

The word "unwittingly" must be added to Evans's definition and the word "harmful" to both. In this way the definition would not include cases where the doctor, having balanced possible harm against probable good, has judged the risk to be justified. Evans himself acknowledges his definition to be too broad, by specifically excluding from discussion "surgical accidents and errors in prescribing and dispensing." This restriction, which is wise, does not absolve the doctor from the responsibility when accidents do happen. The example should be shunned of the medical superintendent who cheerfully dismissed the mistaken notification to the family that a relative had died with these words: "In a place of this size there is a great turnover in deaths. One can only be glad that such a mistake does not happen oftener." In these days there is certainly a great turnover in operations, prescribing, and dispensing.

Errors in Prescribing

But what constitutes an error in prescribing? The dose of any drug, so runs the teaching, is that amount needed to produce the desired effect without causing toxic symptoms. A slip of the pen, the wrong drug or the wrong dose written down, or the wrong dose calculated or dispensed—these are gross preventable errors. What about the dose of aspirin given to the asthmatic child in good faith but with a fatal result, or old-fashioned mercury-containing teething powders repeated until the baby develops pink disease (Warkany and Hubbard, 1948)? What about daily use of vitamin D, leading to hypercalcaemic marasmus (Bonham-Carter *et al.*, 1955), or the prescription of an American dried milk which, unbeknown to the doctor,

lacked vitamin B₆ and produced convulsions (Molony and Parmelee, 1954)? Or the routine use of vitamin K and sulphafurazole, which lead to jaundice in the newborn, hyperbilirubinaemia, and perhaps kernicterus (Allison, 1955)? The doctor uses a drug to produce a desired effect. Often he does not know how the drug acts, nor all that it can do in the human body. Successful trial in general does not exclude individual idiosyncrasy.

The drug is still the main weapon with which the doctor attacks his patient's disease. Now that he has exchanged his catapult for a guided missile, he has increased his power for harm as well as for good. His therapeutic agnosticism of the turn of the century has given place to a sort of pantheism. He is enjoying a glorious therapeutic spree, and in the whirl of new drugs and refinements of old drugs he has more and more to rely on the data issued by the chemical industry, in which the profession properly places an immense though not an unquestioning faith. Disease may result from ignorance of the full action of a drug in general or of its full action on the particular patient. Such uncovenanted effects of treatment must be included in the definition, while pure accident is excluded.

One of the most difficult questions is when to use and when to withhold antibiotics. The family doctor pressed by the family and anxious to do good uses penicillin for a child with acute tonsillitis. The immediate result is excellent, the cure dramatic. Two weeks later the tonsillitis recurs. The process is repeated again and again. Is this iatrogenic disease, and would the child have avoided these recurrent attacks by taking longer to produce his own immunity without penicillin? More complex issues are raised by the following case.

A male infant aged 3 months was admitted to St. Bartholomew's Hospital moribund, with ulcers in the mouth, difficulty in swallowing and in breathing, skin sepsis, oedema of the skin, and diarrhoea. He had been completely well until aged 2 months. The mother complained that he had pain on micturition. He was referred to the local hospital and accepted for circumcision, although a history taken later revealed that the evidence for pain on micturition was no more than the crying before micturition so common in normal babies at this age. He had not been well since operation, developing symptomatic diarrhoea and vomiting, almost certainly due to pneumonia, probably staphylococcal. He was treated successively with succinylsulphathiazole, tetracycline, and erythromycin, blood transfusion, cortisone, prednisolone, further blood transfusion, chloramphenicol, and intravenous saline. The physician had ordered continuous tube feeding with a polyvinyl tube; the nurse had used a rubber catheter in error.

At the time of transfer to St. Bartholomew's one month after circumcision he had oral and nasal moniliasis, staphylococcal enteritis, superficial abscesses due to a different strain of staphylococci, sodium and chloride retention, hypokalaemia, and acidosis, with a combination of oedema and dehydration (Na 162, Cl 138, K 4.5, alkali reserve 21 mEq/litre).

Because of respiratory stridor and dyspnoea, a diagnosis of respiratory moniliasis was considered likely. Blood chemistry was corrected by suitable intravenous and oral therapy, the various infections responded to novobiocin and nystatin, and he recovered. The initial error was the circumcision, and the further mistakes depended on the use of potent drugs and ancillary treatments which could not be controlled by the complicated but necessary laboratory techniques. Although he might have died in the first round without the good effect of the drugs used, there is no doubt that his life was jeopardized and that some serious disorders were added to the clinical course by the actions of the physician.

Iatrogenic disorder must, then, be harmful, unwitting, and include organic disease resulting from the use of potent drugs, incompletely understood and inadequately controlled.

The physician planning his treatment must not only know his drug and his patient, but also know the best in contemporary practice. New forms of treatment have to establish themselves against initial scepticism. Their introduction, respectably sponsored, leads to their acceptance, though some through wantonness end disgraced. There is an aptness in timing the adoption of a treatment. When justifiable doubt becomes dangerous obstinacy, the error of omission is as culpable as an error of commission. Here is a true doctor's dilemma.

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A common and incompletely standardized biological fluid, human blood, used to save life, has slowly revealed its inherent dangers. The treatment of haemolytic disease of the newborn illustrates some of the dangers and the problem of timing in iatrogenic disorders.

Blood Transfusion

Thirty years ago blood transfusion was widely given in the treatment of acute infections in infancy, especially of gastro-enteritis. In this way little rhesus-negative girls were sensitized, because rhesus-positive blood is commoner than rhesus-negative and at that time no one knew of the rhesus antigen in human blood. When these little girls grew up, their own babies were liable to suffer severely from haemolytic disease. During the next few years babies with haemolytic disease were given simple transfusions, and it was not known that old blood or overheated blood might increase the risk of the most serious complication, hyperbilirubinaemia and kernicterus. With the discovery of the rhesus blood groups came routine antenatal blood-testing, and advice to the rhesus-negative mother to be delivered in hospital carried the unintended implication that something was certain to be wrong with the baby. The revealing of the rhesus blood group to the mother by a careless or hurried doctor or nurse induced an anxiety in the mother's mind that, by spoiling the happiness of her pregnancy and her confidence in her new baby, could lead to emotional and behaviour disturbance.

In the early days of exchange transfusion and with inexperienced operators the procedure was dangerous and sometimes fatal. The indications were not exactly known, and the paediatrician, sceptical and fearful, could withhold the treatment with good conscience. At some point in time the procedure has become safe, the indications more exact, the value in preventing kernicterus recognized. Now, and until some better method is found, the development of kernicterus in a known case of haemolytic disease of the newborn not treated by exchange transfusion has become in the opinion of some an iatrogenic disease, because it could and should have been prevented. And yet the physician must always be allowed freedom to exercise judgment, to run counter to current opinion and practice. There must be a clear distinction, a distinction that would stand up to cross-examination in the High Court, between iatrogenic activity and culpable negligence.

Dangers in Prophylaxis

While the bottle of medicine remains the symbol of medical treatment, the modern personal physician has an active part to play in community medicine, and in the control and prevention of epidemic disease, and prophylactic treatments, like drugs, may have harmful effects. The best-known examples are the occurrence of provocative anterior poliomyelitis following immunization against diphtheria and whooping-cough, of encephalitis following vaccinia, and of foetal disease and acquired "congenital" abnormality when a woman is vaccinated in the first three months of pregnancy (MacArthur, 1952). The use of antenatal x-ray pelvimetry to prevent obstetric difficulties has recently been blamed (by Stewart *et al.*, 1956, 1958) for some of the increase in childhood leukaemia.

Other physicians than the personal physician are involved in prevention and in the public health. It is a tragedy when the infant welfare service and the school medical service are in conflict with the personal physician and the consultant. One out of them all is bound to make a tactless remark or insist on a course of action which, to paraphrase Drake (1948), fixes in the patient's or the parents' mind the notion of organic disease or of inevitable invalidism, so that it can never be got out again, which, in other words, leads to iatrogenic disorder. The parents of a mildly bronchiectatic child were so terrified by the school doctor's heavy pronouncement that the child was bound to keep getting pneumonia and to die of it in adolescence—remarks of an

ignoramus—that they could not be persuaded to let her go to school again, and she became a complete and irrevocable invalid. A girl of 7 born after six boys to middle-aged parents began asthma at 2 years, and was treated as an animated doll, surrounded with restrictions. The school doctor later insisted on open-air school and encouraged frequent absences. With the greatest difficulty the medical officer was persuaded to allow her to return to the ordinary school, where she demonstrated to herself and to her parents that if treated normally and confidently she could live a normal life despite some asthmatic attacks.

Strains of Hospital Admission

Sometimes blame may attach, not to the doctor but to doctors, to some habit in the routine practice of medicine. In 1848 Semmelweis (Murphy, 1941) showed how doctors caused puerperal fever by transferring something from post-mortem room and from infected cases to the maternity patient. Hospital gastro-enteritis and cross-infections, encouraged by great open wards, little plumbing, and no isolation, are or should be largely of historical interest. Attention is now focused on the emotional strains arising out of the hospital admission, especially in the younger age groups (Spence, 1947). No longer does the ferocious ward sister snatch the beloved toy or piece of grubby shawl out of her new patient's hand or try to oppose the frequent and regular visiting by parents. In many hospitals attempts are made to explain by talk and booklet what hospital is all about. Even more important than words come deeds—the creation through staff attitude and methods of work of the knowledge that the place is friendly and good. The life of the ward is not home life, but it has its own programme of interests and occupation; it forms a community into which the child can appropriately fit. It is up to the paediatrician to remember to leave pomposity on his coat-peg and to conduct grand rounds and learned lectures out of earshot of his patients.

Because a bad experience of hospital, painful injections, horrible medicine, and lack of understanding of the needs of sick children can induce illness, break morale, and leave emotional scars, some advise home treatment. To others hospital life properly conducted seems to make a positive contribution to the cure of illness and indeed of emotional disturbance itself. To get such good results the whole ward personnel must co-operate. It is bad for the parents who have been with difficulty persuaded by the doctor that their newborn baby will live, to be asked by the night sister for the baby's names against emergency baptism; but at least she can learn. The gory, tragic surgical reminiscences with which the ward cleaner regales the patients do not often reach the doctor's ear.

Harmful Routine

Sometimes harm follows something advised for the patient not as a particular person but because he belongs to a special group. The prolonged use of high oxygen atmospheres in the routine care of premature babies, increasing the risk of retrolental fibroplasia, serves as an example. Is it possible to measure the harm in anxiety over tuberculosis induced by so useful a case-finding technique as mass radiography?

When the obstetricians advocate universal institutional midwifery they believe that they are reducing maternal mortality, and a maternal death nowadays shocks more than death in a motor accident. But the risk of infection to the baby is increased, and so is the chance of the use of some routine method which in due course is shown to be harmful. No one has yet decided the effect on breast-feeding or indeed on family life. Iatrogenic disorder may result from general treatment and management.

Diagnostic Dangers

To the dangers in drugs, in prophylactics, in hospital wards, and in clinics must be added the dangers in diagnosis; in the atmosphere engendered by a full-scale investi-

gation, as well as in the procedures themselves. The decline of clinical diagnosis and the rise in laboratory and radiological techniques have increased diagnostic accuracy, at enormous cost in money and personnel, in bed occupancy, and in the doctor's self-confidence. Who dares to say after inspection, palpation, percussion, and auscultation, after the full clinical examination laid down in the book, that any child is normal and healthy?

Because of the immense therapeutic power, medical and surgical, possessed by modern medicine, early diagnosis of organic disease is a desperate necessity; failure and delay may have disastrous results. For the paediatrician who relies for his history on the parents and usually expects negative physical examination, the problem of how far to investigate chronic symptoms is particularly difficult and always present. Let him remember that children may die of their investigations, of bronchograms, of sweat tests in infancy, of cardiac catheterization. Although patients are sometimes cured of symptoms by investigation, just as they are by relating the history, let him remember that repeated observations and painful tests may confirm in his patient's mind the idea of organic disease and so contribute to invalidism. To relax tension and relieve anxiety tests are often essential, but if the parents and the child know that the tests are made not to find disease but to rule it out the danger is reduced.

Basic Problems

When an organically sound child grows into an invalid, or mild disease devastates, the doctor need not take all the blame. His words and his attitude have the greatest power for harm when there are deep-felt fears, insecurity, and inadequacy already in the situation. Invalidism may feed on the family's fear of tuberculosis, of appendicitis, of sudden death in congenital heart disease, epilepsy, or asthma, and fear and insecurity play a large part in periodic disease. Or the basic problem may be the enjoyment that the patient finds in exaggerating symptoms, in dwelling on anxieties, in the special status assured by continued invalidism. The child may have learned to rule the household through its pain. These exasperating traits must not be allowed to flourish in children, however much their perpetuation is unconsciously desired by them or by their parents. They often lie behind the refusal of parents to be reassured, and their annoyance with the doctor who dismisses the complaints too lightly, just as they make patients unwilling to consult psychiatrists lest they be cured. It is to be hoped that someone can gently but firmly lead the child back to health. Unwise "examination, manner, and discussion," to quote Ebaugh, can certainly render cure extremely difficult. Impatience, apparent haste, or lack of sympathy on the physician's part may easily ruin the patient-doctor relationship.

The Doctor

And so at the end we come to the quality of the doctor himself. His personality is part of the cure, just as it can be the most direct cause in iatrogenic illness. One of the main functions of the paediatrician is to relieve anxiety. Parental anxiety is good if it leads to right action, and the dangers of under-anxiety are seen most commonly in the child with the perforated appendix. But the parents should carry their anxiety to the doctor and deposit it with him. They can do this only if they instinctively feel trust in his skill, his carefulness, his integrity, and his wisdom. If by his words, his demeanour, his actions he drops from this high standard, faith is destroyed and he cannot make amends with a show of dogmatism or expertise. The doctor may temporarily lose his nerve when a case that he has been treating for infected cervical lymph nodes suddenly reveals leukaemia, or when the vomiting baby treated by dietary change suddenly proves to be a case of meningitis. The doctor with a bowel neurosis may create this in a mother and baby when he is consulted because for the first time in its life the normal breast-fed baby has missed one day's motion.

Conclusion

So we see that all the powers mobilized for healing—the drug, the prophylactic, the apparatus of diagnosis, the hospital, the out-patient clinic, the ancillary personnel—all carry also the power to damage. And in the end of it all the doctor and the patient face each other, two human beings prone to error, both with mankind's portion of fantasy and fear, one trying to be scientific, the other to be brave, each trying to fathom the other by question and answer, but with the help of instinct and feeling as well as words. Small wonder that at times the patient is left the worse for the encounter with "a harmful disorder unwittingly induced in him by the inappropriate use of drugs or faulty management or treatment or because of the physician's examination, manner, and discussion" or with, in two words, iatrogenic disease.

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NAMING OF DRUGS

B.P. COMMISSION REPLIES TO CRITICISMS

The Committee on Cost of Prescribing (Hinchliffe Committee) criticized in its interim report¹ some of the British Pharmacopoeia Commission's actions in providing Approved Names for new drugs. The Commission last week replied in the following statement.

The Interim Report of the Committee on Cost of Prescribing contains various criticisms of the Approved Names which the General Medical Council publishes on the advice of the British Pharmacopoeia Commission. The Commission was not advised by the Committee that it proposed to discuss Approved Names, but had this intention been known the Commission would have wished to furnish evidence for the Committee's information, thereby avoiding the many inaccuracies which appear in the Report. The Commission regrets that they were not invited to appear before the Committee.

The Commission now offers the following observations on some of the statements which appear in the Report.

1. The Report states (para. 41): "There are for example just under 5,000 proprietary preparations available for prescribing. Economies would follow, we believe, if simple approved names for new products could be evolved quickly and given the widest possible publicity."

In the majority of cases the provision of an Approved Name has no effect on the price of preparations. The issue of the simple Approved Name primidone for the product "mysoline" has had no effect on the price of the drug, to quote only one of numerous possible examples.

2. The Committee states in para. 42 of the Report that "we are informed, for example, that the present rules of nomenclature require that the approved name should be based on a drug's chemical constitution."

This statement is erroneous. The guiding principles used in selecting or devising Approved Names do not impose an inflexible style and it will be seen that many names are not based on the drug's chemical constitution—e.g., most antibiotics, warfarin, azovan blue, gallamine, lignocaine, macrogol, mustine, sulpham blue. Among these guiding principles are the following:

"An attempt should first be made to form a name by the combination of letters or syllables from the systematic chemical name.

¹ *British Medical Journal Supplement*, 1958, 1, 382.