Commentary on Iatrogenic Disease

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The definition of iatrogenic disease supplied by O. H. Perry Pepper makes use of the Greek *iatros* (physician) and *genesis*, signifying origin. Initially referring to a disease induced by a physician, the term is frequently used in relation to imagined ailments. Even the most conscientious physician administering the most proper of treatments may produce devastating effects. A comprehensive review of the literature of iatrogenic diseases reveals that they are, indeed, chiefly generated by ignorance, error, carelessness, greed, or in extreme instances, even malice on the part of people in the medical field. Kent, in *Deadly Medicine*, makes us aware that greed and malice have been charged to our colleagues and that in previous centuries poisoners had a free rein. Peddlers "blithely and without fear" dispensed their wares of "Spouse-remover and Inheritance-powder by the wholesale ton"—while in early anatomic dissection, the growing demand for fresh cadavers by the pupils of Dr. Robert Knox were met by Burke and Hare and led to the humorous observation:

"Up the close and down the stair
Around the house with Burke
and Hare,
Burke’s the butcher, Hare’s the thief,
Knox the boy who buys the beef."

An updated—and always growing—list of iatrogenic diseases takes us into nearly every specialty and is replete with tumors, poisonings, intracranial hemorrhages, drug interactions and surgical injuries, to name only a few.

Iatrogenic disease has not gone unobserved over the world. Mulroy in Britain and Hurwitz in the United States see most iatrogenic disease today as a result of commonly used and often potent drugs. Cortico-steroids, digoxin, antibiotics, anticoagulants, analgesics and tranquilizers were deemed the most common offenders responsible for patients being hospitalized for adverse drug reactions. In a year’s survey of iatrogenic disease in general practice, Mulroy has found one consultation in 40 to be the result of iatrogenic disease. Mulroy has also discussed the doctor/patient relationship in cases of iatrogenic disease and suggested in his survey that a patient who suffered one iatrogenic incident was more likely to suffer another one.

A careful history of what drugs the patient is receiving is of obvious importance. As reported in *The Medical Letter on Drugs and Therapeutics*, unexpected reactions will still occur, and the mechanisms of interactions are not always understood. Drug metabolism can be affected by alcohol interaction and also by genetic differences. Physicians are advised to prescribe as few drugs as possible for concurrent use and to be mindful that overdose or misuse is always
a potential risk. Another potential iatrogenic problem with drugs is “drug fever” or “malignant hyperthermia”. Generally this mechanism is difficult to recognize, but some of the many therapeutic agents reported to cause fever include blood components, vaccines, antineoplastic drugs and antimicrobial agents. Antibiotics have even been suggested as a possible cause of matrix renal stones.

Iatrogenic drug reaction becomes even more complex when considered with rheumatoid arthritis, peptic ulceration and the anti-inflammatory agents associated with rheumatoid arthritis. Rooney et al found elevated gastrin levels in patients with rheumatoid arthritis and suggest that anti-inflammatory therapeutic agents are potentially iatrogenic.

Perhaps the most tragic of all iatrogenic diseases are those occurring in the very young; unfortunately, these are not unique. Careless errors in the newborn nursery have caused accidental boric acid poisoning of children, and Wong et al have presented such cases in which five infants died. Simpson has suggested probable poisoning from using copious quantities of borated talc on small infants.

In another newborn nursery, Finberg et al has reported a mass accidental salt poisoning disaster in which 14 infants were fed formula that had been mistakenly prepared with salt instead of sugar; six of these infants died. In these, as in the boric acid poisoned infants, the classical symptoms of diarrhea, vomiting, skin changes and central nervous system irritation, were present. The removal of boric acid from the nursery is strongly urged and formula ingredients should be segregated and labelled.

Hypernatremia, according to Simmons et al, has occasioned the deaths from intracranial hemorrhage in 11 of 24 neonates treated for respiratory distress syndrome with excessive amounts of sodium bicarbonate. Volpe has cautioned against vigorous therapy of neonatal acidosis with sodium bicarbonate.

Infants and small children may, on occasion, be victims of other potential iatrogenic diseases. Proteus mirabilis osteomyelitis occurred in two neonates following puncture for the purpose of obtaining blood specimens. In infants with congenital dislocation of the hip, there is also the risk that avascular necrosis of the femoral head may be imposed by the various regimens of conservative treatment.

Shaywitz has discussed the danger of using the unoccluded needle in performing lumbar puncture in children. Unlike the standard needle with stylet, it carries the very real hazard of cutting free some epidermal tissue and depositing it in the subarachnoid space where it may give rise to a tumor.

Newton and Abell have suggested iatrogenic implants of another type. Five women who had dilatation and curettage, usually for what was thought to be incomplete abortion, had complaints afterwards of persistant heavy bleeding or polypoid lesions. At histologic examination there were findings of such heterotopic tissues as bone, cartilage and neuroglia in the endometrium and/or endocervix. Chronic inflammation, an altered metabolic state, metaplasia and neoplasia could not account for the lesions in these patients, but the instrumental implantation of fetal tissues during curettage does provide an explanation.

Iatrogenic disease is not uncommon after other surgery or diagnostic study. Wolloch et al report nine cases of perforation of the esophagus (two of which died) after surgical instrumentation. The morbidity associated with tubal instruments is stressed by Wolff and Kessler.
in their investigation of 62 patients who had specific lesions of the hypopharynx and cervical esophagus which could be directly related to instrumentation. In this study, the nasogastric tube was found to be the common cause of chronic ulcers, and a 48 hour period was enough to produce a chronic ulcer.

Livstone et al have reported iatrogenic perforation and hemorrhage after colonoscopy, and iatrogenic injuries to the spleen have also been documented. Roy and Geller have stressed the morbidity of splenectomy and have discussed the implications of blood dyscrasias, infection and misdiagnosis. Mearns has cited trauma to the spleen after pleural biopsy and aspiration.

The literature is also well documented with an increasing number of iatrogenic complications during those diagnostic and therapeutic procedures involving exposure or entrance of vessels. Rich et al have reported vascular trauma such as arteriovenous fistula and vascular injuries associated with urologic and gynecologic procedures occurring with radical lymphadenectomy for cancer. Barabas et al studied 25 cases of brachial artery injury following left cardiac catheterization. The human heart, in fact, seems to have particular potential for iatrogenic disease. Complications such as atrial septal defects (Timmis et al and Ibarra-Perez) dissecting aneurysm (Bulkely and Roberts) and coronary ostial stenosis (Yates et al) occurring iatrogenically after valvular heart surgery have all been reported. Air embolism following subclavian vein catheterization has been revealed by Paskin et al while Farhat et al have discussed arteriovenous fistula after this procedure.

In a report of 206 patients undergoing 209 thyroid resections, there were five instances of permanent hypoparathyroidism and three cases of permanent recurrent laryngeal nerve injury. In four of these patients, the diagnosis of cancer was missing during nodulectomy. Haff has advised avoiding nodulectomies if possible, refraining from excessive resection, and being certain of good visualization of the recurrent laryngeal nerve.

Iatrogenic renal hypertension is reported by Julian et al as a rare complication of excision of pheochromocytoma. McCormack et al however, have presented detailed physiological studies and have observed that delayed development of renal vascular hypertension occurs secondary to surgical ligation of a major branch of the renal artery.

Other iatrogenic complications include surgically induced urethroperineal fistula following abdominal perineal resection, and hypercapnia secondary to physician-induced metabolic alkalosis. Acute pancreatitis and hypercalcemia were apparently iatrogenically induced in a patient receiving hyperalimentation. Sugarbaker et al discuss glove starch granulomatous disease as an iatrogenic problem in the operative field.

Eye surgeons, too, are advised of iatrogenic disease potential. Scherz and Dohlman warn that any surgical procedure totally eliminating the main lacrimal gland is potentially dangerous for keratoconjunctivitis sicca.

Dentists may cause iatrogenic fracture of the coronid process when removing maxillary third molars. As pointed out, iatrogenic disease is not an isolated problem. However, in a report of an interview between Senator Edward M. Kennedy and American Medical Association President Malcolm C. Todd, Ferber has shown that “good doctors” are apparently being accused—by such persons as the Senator—of protecting “bad ones”, and that much physician induced disease probably goes unproached.

In partial rebuttal, there is the belief that many patients are themselves re-
sponsible for their own ill health produced by such “errors of omission or commission” as smoker’s cancer, alcoholism, obesity, improper diet, etc. In lieu of today’s sensationalized publicized malpractice claims, Bartlett et al have felt that a “recognized term should emphasize that maintenance of health is a dual responsibility for both doctor and patient” and the term “egogenic disease” is suggested as applicable for patient-induced problems.

A philosophical appraisal of the problem of iatrogenic disease inevitably brings us to Illich’s recently published “Medical Nemesis”,14 which is discussed by many, but perhaps most lucidly by Paton. Illich, concluded Paton, would doubtless advocate closing half the world’s medical schools and allowing Man—instead of Technology—to deal with pain, disease and death in dignity. Discombe5 has agreed that not everything is—or should be—curable, and Vaisrub43 has stated that Illich believes iatrogenic diseases “cause more suffering than all accidents from traffic or industry”. If this is true, today’s physician has much to contemplate before he operates, prescribes a drug, orders an advanced study or hospitalizes a patient for any kind of treatment. The “cure”, the problem, perhaps the definition, of iatrogenic disease remains obscure, but it may be that prevention and philosophy together will one day reduce its all too frequent occurrence in the modern world.

References

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