XI

The Bubbling Cauldron

"I firmly believe that if the whole *materia medica* could be sunk to the bottom of the sea it would be all the better for mankind and all the worse for the fishes."
Oliver Wendell Holmes, *Harvard Medical School Lecture*

Not eye of newt, nor toe of frog, not even powered unicorn's horn nor mandrake root goes into the remedies doctors prescribe. Past is the era of nauseating mixtures when the worse the medicine tasted the more highly it was regarded. Pills now come in variegated hues, capsules in all the colors of the rainbow, and the liquids are fruit-flavored. Drugs are prescribed on a rational basis, no longer because they fit the phases of the moon or follow the traditions of the fathers.

It was not always so. Following the rise of scientific pharmacology and the discovery that most of the medications doctors were ordering were worthless for cure, came a period of therapeutic nihilism. Physicians still wrote prescriptions, it is true, but they were conscious of how little they helped the patient. The dialectic spiral continued; as chemistry progressed and animal and human experiment went on and more information was gathered, some old remedies regained their place and new ones were added to the list of useful drugs. Starting with the arsphenamines and the later sulfonamides, medicine entered the modern age of wonder drugs. Antibiotics, psychotropics, blood derivatives, anticancer drugs—every year sees more and more novel additions to the inventory of weapons the doctor uses in his fight against disease.

And every year sees more and more novel iatrogenic disorders brought on by those very weapons. (*Iatrogenic* comes from the Greek: *iatros = physician* and *genos = cause*; hence, iatrogenic = caused by physicians. This is a new word, not found in dictionaries published prior to 1953. In 1954 Stedman's *Medical Dictionary* defined it as meaning "caused by a physician's injudicious statement," indicating that the disease was all in the patient's head. By 1961 the current broader meaning, "caused by physicians in the course of treatment" was well established.) Iatrogenic disorders have reached the point where a prominent physician sadly says, "Unfortunately iatrogenic disease can now take its place almost as an equal alongside the bacteria as an important factor in the pathogenesis of human illness."[44] Another physician seriously recommended that departments of iatrogenic medicine be introduced into medical schools.

The drugs are *not* harmful in the sense that poisons like cyanide are. By no means. They accomplish what they're supposed to do—kill bacteria, prevent infection, suppress inflammation. But they do a little more because of their very potency and their effect on the total body organism. Bark tea and ground-up goats' testicles didn't do much of anything, but they didn't make the patient sicker, either.

Everyone knows about thalidomide, so let's forget that one. But let's not forget that pregnant women still ask for and take antihistamines for colds, antiemetics for nausea, and dozens of other medications prescribed during their pregnancies. "When will they ever learn?" Or their doctors. I know doctors who prescribe phenothiazines of various types for anxious or emotionally upset mothers-to-be; yet the manufacturers of those drugs warn that "the use of ..... is not recommended during pregnancy," and one tranquilizer (haloperidol) has been shown to be the cause of gross deformities in the newborn infant. A drug used for dizziness definitely causes monstrosities. Two drugs widely used in bladder and kidney infections are marked "contraindicated in pregnancy"; nevertheless, they are used during that time. I made an informal survey. I asked eight doctors

[44] Dr. David M. Spain, *Complications of Medical Practice*, New York, 1963. See also: Dr. David P. Baer, "Hazards of Modern Diagnosis and Treatment—The Price We Pay," *Journal of the American Medical Association, 159*:1452, 1955, and Dr. Elihu M. Schimmel, "The Hazards of Hospitalization," *Annals of Internal Medicine, 60*: 100, 1964.

whether they would use these two drugs during pregnancy. They were *all* surprised at my question. "Why not?" they asked. A very commonly used analgesic bears the warning: "The safe use of ———— during pregnancy has not been established." In my same survey my informants laughed at me when I asked whether they used ————. "What's the matter with you? Are you some kind of Ralph Nader nut?"

Let's start with the tried and true—penicillin and the other antibiotics, the use of which has been one of the major therapeutic advances of our time. (*Antibiotic* means, as you know, *against life*—by common consent, the lower forms of life. It is not meant to apply to humans.) Pneumonia has lost its terrors, subacute bacterial endocarditis (fatal when I went to school) has been conquered, septicemia (the *blood-poisoning* of folklore) is a rarity—all due to the naturally occurring and synthetically produced substances known as antibiotics. Other troubles have taken their place: severe asthma, violent skin reactions, an occasional death occurring when penicillin is given by mouth or injection in some individuals. To use pencillin routinely in the treatment of colds and other self-limited diseases is to kill a fly with a sledgehammer, or rather, to swing at the fly, because penicillin is seldom, if ever, of value in such conditions. What's accomplished is the sensitization of the hapless patient; he may become allergic to penicillin and then must be as careful to avoid it as the hay fever sufferer is careful not to pick ragweed. Unfortunately, penicillin is given to cattle, too, for their infections; it may be excreted in milk or stay in the tissues, so that a penicillin-sensitive individual may get allergic rhinitis or bronchitis or hives when he eats meat or drinks milk.

Another effect of penicillin and the other antibiotics is directly related to their effectiveness as destroyers of bacteria. What is known as *overgrowth* takes place. All the bacteria, noxious and innocent, having been destroyed, the fungi normally present in and on the body are kept from spreading by biologic competition with the bacteria are able to flourish luxuriantly. Monilial infections like the infantile *thrush* of preceding generations have become so common that some pharmaceutical companies have combined their antibacterials with an antifungal agent specific for the Monilia fungus. Other fungi also overgrow, but as yet no fungicide safe for ingestion has been developed to control them. The bacterial flora normally present in the intestinal tract can be so drastically reduced by antibiotics that their beneficial action may be lost. Diarrhea is not uncommon when antibiotics are given.

One of the most feared complications, a variant of overgrowth, is the development of infection by organisms resistant to the antibiotics. Staphylococci, particularly, are the most likely to develop such resistance. Epidemics of staphyloccal infection became a menace to surgical patients until semisynthetic penicillins effective against such germs were developed. That period of security lasted only a few years. Cases of resistance to the new methicillins are already being reported.[45] Now the biochemists will have to make another antibiotic to overcome the resistant staphylococci.

Warnings against the indiscriminate use of antibiotics seem to have little effect on doctors, especially the surgeons. The latter give antibiotics prophylactically; that is, they prescribe them for post-operative use to prevent wound infections. For example, 38% of patients were given antibiotics prophylactically after repair of simple inguinal hernias. I quote: "Since inguinal herniorraphy is one operation in which infection should not occur if proper selection and preparation of patients are observed, and if adequate surgical aseptic technique is followed, then this unnecessary prophylactic use is illogical, unscientific, and contrary to the welfare of the patient."[46] Survey after survey has shown that prophylcatic antibiotics have not conclusively reduced the incidence of post-operative infections, but they are still widely used despite the danger that the practice will favor and select organisms resistant to the antibiotics.[47]

Besides the general effects of the antibiotics, harmful changes occur when specific ones are used. Chloramphenicol is a highly efficient bacterial agent; it controls the growth of bacteria by inhibiting protein synthesis in them. It can do the same in humans—and result in a profound and fatal aplastic anemia. Testimony at the hearings of the subcommittee headed by Senator Gaylord Nelson disclosed that about 150 persons die each year from conditions attributable to the drug.

Less harmful but still distressing is the effect of tetracycline and its analogues on the permanent teeth when the drug is given to young children or pregnant women. A stable calcium compound is formed in bony

[45] Dr. Roger J. Bulger, "A Methicillin-Resistant Strain of Staphylococcus Aureus," *Annals of Internal Medicine*, 67:81, 1967.

[46] Dr. Robert S. Myers, "The Misuse of Antibacterials in Inguinal Herniorraphy," *Surgery, Gynecology, and Obstetrics, 108*:721–728, 1949.

[47] The latest survey (at Johns Hopkins Hospital) was reported in *Archives of Internal Medicine, 121*:1–10, 1949.

tissues. That's of no importance anywhere but in the teeth. The permanent teeth may take on a peculiar filthy gray or yellow-brown or even fluorescent orange appearance. You'd think then that no doctor would prescribe such drugs for children, wouldn't you? But they do, and the same pharmaceutical manufacturers who insert the legally-required warnings about tooth discoloration in the packages also supply a variety of forms of the tetracyclines made especially for children (flavored syrups, drops and so forth). If doctors wouldn't order them, the drug companies wouldn't make them. Not only do the doctors order them, but they object when the Food and Drug Administration takes them off the market. Over 3000 letters of protest came from physicians when pediatric drops containing tetracycline were banned.

Other antibiotics are harmful in their own way. Streptomycin can cause damage to the eighth cranial nerve, resulting in dizziness, noises in the head and deafness. Triacetylandomycin may lead to liver damage and jaundice. Polymyxin may be toxic to the kidneys.

Instead of whirling around his head magic beads to drive away disease, the doctor now brandishes an effective sword that damages more than bacteria. But he has to be aware that the sword is double-edged.

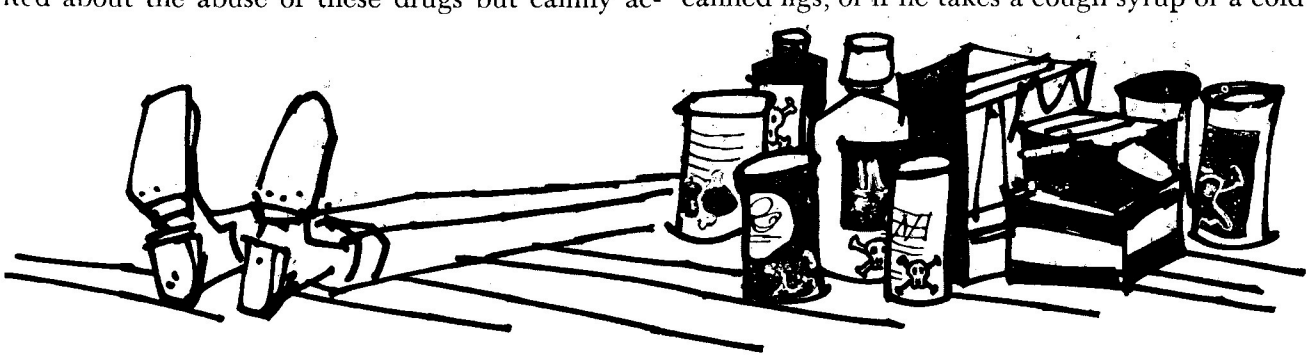
So does the patient. If you've got an infected hangnail or an annoying cough, don't ask the doctor for an antibiotic. Most times he'll be only too willing to oblige. You can also refuse to take any antibiotic unless it is clear to you that you have a serious illness and nothing else will do. That sounds as though you're pitting your judgment against that of the doctor's Why shouldn't you? It's your, not the doctor's, health that is at stake.

Fashion has much to do with drug therapy. If, confronted by any one of the varieties of psychic distress, the doctor didn't use the new psychotropic (having an effect on the psyche) drugs, his patients might regard him as an old fogey. The popular press is presently excited about the abuse of these drugs but calmly accepts their use. Indeed, the press shares responsibility for initially acclaiming the virtues of tranquilizers. (This word, formerly rarely used except as slang for a billy-club or a blackjack, came into the general vocabulary as the result of the influence of advertising agencies. *Tranquilizer* is supposed to mean a substance that makes people calm, as opposed to *sedative*, which quiets them. The distinction is nebulous.) Tranquilizers are prescribed in large quantities, as are the so-called psychic energizers. Effective medications? Certainly. And dangers from their use? Of course.

The phenothiazines, of great value in the treatment of some severe neuroses and psychoses, may cause changes in the retina of the eye, almost to blindness. More common, especially in children (where one of the phenothiazines is used to control vomiting) is rigidity of the neck and muscular twitchings approaching convulsive movements. Most common is the development of pseudo-Parkinsonism, the syndrome characterized by rigidity, tremors, head-nodding and short-stepped gait. Very recently, Dr. Carl S. Alexander reported at a meeting of the American Heart Association that long-term users of the phenothiazines face possible heart abnormalities (enlarged hearts, irregular heart beats and myocardial infarction). Discontinuance of the drugs, he said, may cause improvement in the condition, but cardiac damage and residual abnormal electrocardiographic changes may persist for months.

Meprobamate, sold under the registered trademarks of Miltown and Equanil, is effective—and habituating. After it is taken for a while and then stopped, withdrawal symptoms may occur: vomiting, incoordination, muscle twitching, even epileptiform seizures.

The most dramatic side effects occur with the group of psychic energizers known as monamine oxidase inhibitors. Useful in the treatment of mental depressions, they can cause acute high blood pressure reactions, sometimes fatal ones. They also are dangerous if the patient eats cheese, pickled herring, chicken livers, canned figs, or if he takes a cough syrup or a cold tablet



containing antihistamines. Sometimes I wonder if it's worthwhile to substitute for the depression the fear with which a patient approaches his table. Dr. Richard Hunter, a British psychiatrist, says, "As psychotropic drugs multiply and doctors prescribe them like aspirin, it becomes more important to take a thorough drug history than the time-honored sex history. Today sex, largely stripped of guilt, seems to be much less toxic or pathogenic than psychotropic drugs. . . ." *Verbum sap.*

Enlightened Americans who have no faith in the curative powers of relics are suckers for anything that smacks of a scientific short-cut to a *corpore sano.* The heck with the *mens sana*! Let a Boston lady find out that prayers did her more good than physicians when she was ill (undoubtedly true in her time and frequently in ours), and a new religion is born. Let a respected psychoanalyst announce the discovery of a new kind of energy and followers flock to him to be recharged in modified telephone booths. Let a science-fiction writer proclaim a physiologic basis for the merits of confession and he becomes the prophet of a new creed. (Dianoetics has now been elevated to scientology, a formal religion.) And let researchers discover a chemical compound that stops inflammation, and hosannas arise from the healing profession. Joy spreads that at last disease can have no victory. The universal panacea is here!

Cortisone and its modifications eliminate inflammatory changes in tissues. Acclaimed for its value in rheumatoid arthritis, its use was quickly extended to other morbid conditions. Doctors thought that was logical: inflammation anywhere is pathologic; do away with inflammation and the pathology disappears. They underestimate the self-righting powers of the body. By adding new steroids they upset the balance of the hormonal system. By the time the initial excitement had died down, the secondary effects of cortisone preparations were well known: fatness and floridity, exhaustion of the adrenal glands, susceptibility to infection, peptic ulcers, delayed healing of wounds, degenerative changes in the bones, stunting of growth and cataract formation in children, and a host of other damaging conditions.

Do you think that doctors then severely restricted the use of steroids? Do you think that if a witch doctor discovered a magic powder that eliminated what the patient complained of he wouldn't use it? That's too much to ask of him. There's enormous ego satisfaction to be derived when applause is won from an audience. The doctor continues to prescribe corticosteroids, telling himself he knows what he is doing and he'll stop if trouble develops. He extends the indications for their use until he no longer thinks twice about using it for such minor conditions as allergic rhinitis. That's not killing a fly with a sledge hammer; that's knocking it dead with a cannon.

When a doctor orders antibiotics, tranquilizers, or corticosteroids, he knows he is going to get results. That assurance causes cerebral atrophy in him—a side effect unmentioned in the package inserts. Why spend time on a painstaking diagnosis or why worry about clinical judgment when such fine remedies are at hand for whatever ails the patient?

Untoward effects occur with many drugs of lesser value. Some of the effects disappear when the drug is discontinued; others persist. Example: chloroquinone (used in arthritis and malaria) frequently causes permanent eye damage. Another example: Of 34 patients receiving indomethacin (used in arthritis), all had reduced visual acuity and all improved when the drug was stopped.[48] Chlorthalidone effectively used in the treatment of high blood pressure also effectively caused gout in ten per cent of the cases. Other antihypertensive drugs cause the surfacing of latent diabetes or actually bring on diabetes.

Doctors are as brainwashed as the general public when it comes to drugs. They believe the propaganda of the pharmaceutical manufacturers that specific brands have virtues. They prescribe by brand names. They argue that the first criterion in the selection of a drug should not be its cost; they value the reputation of the maker more than the cheapness of the same drug from another firm. Senator Gaylord Nelson stated in exasperation, "They [the Pharmaceutical Manufacturers Association] spend $4000 per year per physician to convince doctors all over the country they can't trust generic drugs. Yet every time I ask physicians about the wide price differences, why Schering sells its brand of prednisone at $17.90 retail and offers it on bid for $1.20 to the city of New York—the doctors just don't know. . . ." But they fight, just the same. They resent the intrusion of government agencies into their divine right of prescribing.

If they knew what happens in the body to the drugs they were prescribing, their anger would be justified.

[48] Dr. Charlotte A. Burns, *American Journal of Ophthalmology, 66*: 825, 1968.

But they don't. And now I'm not talking about side effects, but about pharmacology. Example: A doctor has a diabetic patient with heart disease, whose diabetes is controlled by tolbutamide; the patient develops swelling of the legs and is given ethacrynic acid to get rid of the fluid; he promptly goes into hypoglycemia, a condition resembling insulin shock; the diuretic intensified the action of the tolbutamide. Another diabetic is taking acetohexamide; his doctor prescribes phenylbutazone for his arthritis; again—hypoglycemia. Even the anesthetic given during an operation may cause kidney failure and death if the patient has taken tetracycline before surgery.[49] The combination of drugs may cure the disease but kill the patient. Years ago it was demonstrated that a patient in heart failure taking digitalis should not be given calcium intravenously because of the danger of sudden death from electrolytic changes in the heart muscle. Yet I have heard a doctor advise intravenous calcium to stop the leg cramps caused by a strong diuretic in a dropsical digitalized patient.

A note of caution. The drugs have value, but they cannot be used mindlessly. The doctor must take the time to read the medical data about them and to learn their potential for harm. He, equally with his patient, must not be on the lookout for something new merely because it's new. So—when the doctor says, "I'm going to try this new stuff on you that just came out," tell him, "No, thanks. Try it on the dog,"—if you don't like dogs.

2.

Let's leave the new drugs. What's old? Blood, for example, which carries with it overtones of cannibalistic rites. "In the blood is the life," says the Bible. Also death and illness. "Transfusions are still one of the most dangerous forms of medical therapy," states Dr. Aaron M. Josephson of the Michael Reese Research Foundation and Blood Center in Chicago. Transmission of hepatitis, syphilis and malaria are possible hazards of blood transfusions, but more important are sensitization to blood antigens, unpredictable shock-like reactions, and hemolytic changes. A significant alteration occurs in whole blood stored in blood banks; there is an increase of plasma potassium, plasma ammonia, inorganic phosphates and free plasma hemoglobin, besides a heightened alkalinity of the blood. The altered blood is often deleterious to patients with heart, liver and kidney ailments, to old people and to infants. And yet how many times have families expected and have their doctors ordered blood to be given to the unfortunate patient "just to make sure?"

3.

What else does the doctor do to help his patients get well? He uses instruments for diagnosis and treatment, not gourds or sand paintings, but ingeniously devised tubes and mirrors. Without them he'd be at a loss. Without them he could not photograph the arterial supply of the brain or map the chambers of the heart or supply air to damaged lungs and nutrition to unconscious patients. The doctor knows the hazards of such treatment, but in his zeal to do good he brushes that knowledge aside.

Tracheostomy is the making of an artificial opening in the windpipe so that oxygen may be more easily administered, under pressure, if need be. The operation has become almost routine in badly burned or severely injured patients. "The major fatal complication is no longer wound sepsis [infection] but pneumonia. The decline in wound infection is due to effective topical chemotherapy [local application of chemicals that kill germs], and the rise in fatal pneumonia is probably due to the effects of earlier and more prolonged ventilatory assistance and oxygen therapy . . . Tracheobronchitis is the most frequent finding in the lungs of burned patients. The focal ulcerative laryngeal and tracheal lesions seen are clearly related to tracheostomy rather than to inhalation therapy. . . .[50] In other words, in their zeal to help the severely burned patient, the doctors have overreached themselves and have ended up with harming him. Enough said.

Bladder catheterizations, often done to save bed linens and wear and tear on nurses, accounted for 40% of hospital-acquired infections in the Johns Hopkins survey previously quoted. That percentage does not include infections after diagnostic cystoscopies.

The routine use of intravenous infusions for support and nutrition, conveniently provided now by plastic indwelling tubes, has brought on almost an epidemic of septic phlebitis, inflammation of the vein in which the tube is lodged. The growth of bacteria in one part of the circulatory system then is frequently followed by septicemia. In burned patients especially, an eighteen-month study by the Army Surgical Research Unit at Fort Sam Houston, Texas, disclosed that post-phlebitic septicemia caused the death of 12% of those autopsied. A Harvard study in 1968 showed a 34.3% incidence of

[50] Capt. F. Daniel Foley, M.C., Col. John A. Moncrief, M.C., and Dr. Arthur D. Mason, Jr., "Pathology of the Lung in Fatally Burned Patients," *Annals of Surgery, 167*:251–264, 1968.

[49] Dr. E. Y. Kuzucku, in the *Journal of the American Medical Association, 211*:1162, 1970.

local infection from polyethylene catheters, 17.4% with pathogens, 16.9% with contaminants. Phlebitis occurred in 39% of the patients and bloodstream infection in three patients, two of whom died therefrom. The risk of infection and bacteremia was directly related to the duration of catheterization.

When the medicine man approaches with his paraphernalia, maybe the cringing patient should cry out, "Don't do me any favors!"

To put it bluntly, do not submit yourself to having instruments and devices pushed into natural or artificial orifices without good and sufficient reason. The doctors may call you uncooperative. So what? Names will never hurt you. The catheters may.

4.

That's for treatment. It's worse when sickness follows diagnostic procedures like angiograms, cardiac catheterizations or pyelograms. They are not entirely innocuous. Arteriography, the visualization of arterial circulation, one of modern medicine's most imaginative techniques, should not be used routinely in diagnosis, warns Dr. William Likoff, Professor of Medicine and Director of the Cardiovascular Institute at Hahnemann Medical College in Philadelphia. He says, "It is a sophisticated, expensive procedure fraught with danger and requiring hospitalization . . . The physician can inadvertently destroy the artery or cause the formation of a clot. . . ." When multiple angiograms using a contrast medium are used in infants, there is a grave risk of renal medullary necrosis, a fatal disorder.[51] Besides the dangers of infection and allergic reactions (often piously referred to as "an act of God," thereby removing the blame from the doctor and placing it on the Blameless One), the instrument that is being used may perforate the part being examined. Such accidents, although rare, happen often enough for patients to be wary of examinations "just for the record."

The antics of the witch doctor may be comical to behold and may not do much good, but at least he can't be held responsible if his patient gets sicker or dies. His jumping around didn't do that.

5.

"WE DID OUR BEST"

A young man had an acutely inflamed throat. He went to his doctor, who gave him an injection of penicillin. The sore throat quickly got better.

Three days later, the young man began to itch. The itching got worse and he developed hives all over his body. The doctor made the correct diagnosis of an allergic reaction to penicillin. He prescribed antihistamines. The hives disappeared.

The young man, a machine operator, got drowsy from the antihistamines and cut his hand at work. The nurse in the dispensary gave him first aid and put on an anti-bacterial ointment containing penicillin. The hives returned and now the young man had swelling of the eyes and lips. The doctor recognized that a potentially dangerous allergic reaction was present; he ordered a course of corticosteroid treatment. Result—the itchiness, the hives and the swellings disappeared and the patient was well again.

Except that now he had pain in his belly plus heartburn, and he began to show signs of blood in his stools. The correct diagnosis of a peptic ulcer (induced by the corticosteroid) was made. The young man did not do well on medical treatment; he continued to bleed from his ulcer. His doctor, therefore, had a surgeon in consultation. The two doctors agreed that partial gastrectomy was necessary, an operation to remove the ulcer-bearing portion of the stomach. The operation was successful.

But because of the previous bleeding and the unavoidable blood loss at the operation, a transfusion of 1000 milliliters (two pints) of blood was given. Hepatitis (inflammation of the liver) followed. The young man became intensely jaundiced; he vomited his food and had to be fed intravenously for a few days. His youth did him in good stead. He recovered from his hepatitis.

At the right ankle, where the intravenous needle and the plastic tube had been inserted into a vein exposed by cutting through the skin, a tender nodule appeared. It became red and inflamed, evidence of infection. Because of the bad experience the patient had had with penicillin, the doctor prescribed tetracycline. The inflammation promptly subsided.

Because of the antibiotic, diarrhea came on and the patient had severe colicky cramps. The doctor ordered a special diet and gave a new synthetic antispasmodic drug to control the cramps. Diarrhea stopped.

The new drug was in the belladonna class. It relaxed smooth muscle all over the body, and by its action on the iris, it caused dilatation of the pupil.

The young man's vision was impaired. He drove his car into a tree. Exitus young man.

This is a true story.

[51] Reported by Dr. Alan B. Gruskin, director of pediatric nephrology at St. Christopher's Hospital for Children, Philadelphia, basing his finding on histologic studies of 34 infants who died after diagnostic angiography to evaluate congenital heart disease.