POINT OF VIEW

ENVIRONMENTAL CANCER

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Nineteen Hundred and Seventy-Five will mark the bicentennial of Percivall Pott's report on environmental cancer.[1] Much of the developing program of the National Cancer Plan provides evidence of the pertinence of his observation, and will be a fitting commemoration of his wisdom.

The Irish physician's perceptive characterization of an association between cancer of the scrotum in adult male patients and their exposure to soot decades before, while employed as chimney sweeps in childhood and adolescence, solved no pressing clinical problem. The disease was not common then, nor is it now (although its setting has changed from the chimneys of 18th century Britain to, for example, the oil-splashed facilities of tool and machine shops).[2] Rather, the clear demonstration that a cause of a well-defined human cancer existed in our environment, and could affect many of those in contact with it, was important.

The past twenty years have made Pott's hint and direction much more exciting and potentially rewarding. The demonstration by Hammond, Doll, Wynder, Dorn and others that the most common cancer in males—cancer of the lung—was not due to misprogrammed genes in our pulmonary chromosomes, but to something in our personal environment, has marked a turning point in our thinking about cancer. The fault, dear God, lies *not* within us (unless we so judge our capacity to react to carcinogenic agents!) but without.

Recently, Richard Doll reviewed known causes of human cancer associated with immunological disorders, and had to limit genetic varieties to four or five rare conditions; ataxia-telangiectasia, Wiskott-Aldrich syndrome, Chediak-Higashi syndrome, congenital agammaglobulinemia (and perhaps Sjögren's syndrome).[3] At the same time, the list of exogenous agents grows: bladder cancer with B-napthalamine, lung cancer of uranium miners, skin cancer among pitch workers, pleural and peritoneal mesothelioma with asbestos exposure. Leukemia with benzene (and radiation) joins the lip cancer of some pipe smokers. Those lung cancers (a minority) not due to cigarette smoking can be due to hematite ore dust, or chromate work, talc mining and milling or perhaps even arsenic. When two ethmoid sinus cancers were seen, months apart, by a general practitioner in South Wales 50 years ago,

continued on page 30

letters to the editor

THE SCIENCES welcomes comments from its readers. We suggest that correspondents limit their letters to 200 words or less.

Some aspects of "Feathered Reptiles" (Nov., 1971) puzzled me and perhaps further clarification is needed. If I have understood Dr. Jensen's contention correctly, he is suggesting that the ostrich and its modern ratite relatives are possible descendants of reptiles that developed feathers as thermal insulators—which did not also evolve as part of the flight mechanism. Whether this is true or not, the inescapable fact is that modern ratites *are* warm blooded creatures, thereby defying their inclusion under a reptilian classification *as it is now designated.* This would suggest one of the following possibilities: 1) that modern ratites are indeed "flightless birds"; 2) that they are mammals, a farfetched idea; 3) that they represent an extant line of ancient, possibly warm blooded reptiles, an astonishing notion that would necessitate a complete redefinition of all vertebrate classes; or 4) that they are none of the above and constitute a hitherto unnamed class of animals, certainly a major taxonomic discovery.

Marc Krauss
Former Editor-in-Chief
NYAS

Dr. Jensen replies:

I welcome the attitude of Mr. Krauss. My ideas are

continued on page 31

 continued from page 4

the astute observation that the men both worked in a nickel smelter led to investigation of the plant and successful definition of the prevalent risk of lung and nasal cancer. Consideration of their family tree would hardly have been as fruitful. At about the same time (1921), a layman made the practical suggestion to Dr. Margarete Uhlig that the continued occurrence of pulmonary neoplasms among the miners of Schneeberg might be due to the radioactivity in the mines. Not long afterward, the riddle of Schneeberg and Erzeberg was solved and their mines could perhaps be safe for the first time in more than 400 years.[4]

Some of these discoveries were late in coming, for nature scattered the pieces of the puzzle. The long-lapsed period between onset of exposure—twenty, thirty, forty or more years—and evident clinical disease tends to blur and diffuse the cause-and-effect relationships. Youngsters begin smoking at 14 or 19 or 12, but don't die of lung cancer at 20 or even 25; deaths tend to occur at 50, 60 or 70. Similarly, apprentices join the Asbestos Workers Union at 17 or 18. Lung cancer takes twenty per cent of its members, but not until 30 years or more have passed. Three months of contact with B-napthalamine can produce bladder cancer, but not at once. Decades usually pass—and then, with enough exposure, 50% of the men in some workrooms will be so afflicted.[5]

Epidemiological methods can sort out the difficulties, though the investigations must often be extensive and cover many years. Perhaps the best examples have been the extraordinary prospective study of the American Cancer Society, headed by Dr. E. Cuyler Hammond, which has maintained observation of more than 1,000,000 Americans throughout the country, analyzing their experiences according to their recorded smoking habits,[6] and the careful investigation of British physicians by Sir Richard Doll, documenting the falling incidence of lung cancer among those who stopped smoking while recording the continued high risk of those who did not.[7]

Now that we know how far back to look, some remarkable discoveries can be made. Dr. Herbst and his colleagues, for example, recently saw 8 cases of clear cell adenocarcinoma of the vagina (1966-1969) in Boston. This tumor is uncommon enough, but even more striking was that, unlike the usual case (in older women), these were in young patients, from 14 to 21. Such an occurrence was perplexing, because this cancer had not been seen in a young woman in more than 100 years at the Massachusetts General Hospital. A hint was available. All had been born from 1946 to 1951—and 1946 was about the time that a synthetic estrogen, diethylstilbestrol, was introduced for the treatment of threatened abortion. Questioning soon revealed that in seven of the eight cases, the *mothers* of the patients had been treated with this medication in the first trimester of their pregnancies.[8]

There are exceptions to the twenty-forty year rule; leukemia in children peaks at about age 4 and this fits well with observations concerning leukemia among those exposed to radiation from the atomic explosion in Hiroshima. Nevertheless, most human cancers fit the usual pattern; perhaps this speaks for continued or intermittent exposure to environmental cancer agents generally.

Epidemiology made many important contributions to the solution of problems of the infectious diseases; at one time, the two areas seemed co-limited. This relevance is still acknowledged, and defined in the added phrase "infectious disease epidemiology." As it is now applied to chronic disease problems, however, its versatility and power become even more evident. A recent example was the demonstration that multiple factors may operate in the etiology of human cancers. Considerable experimental data had shown that this could occur in animals. We now know it to be the case in some human cancers. Thus asbestos is fibrogenic and carcinogenic in workers who may die of scarred lungs or mesothelioma. If they do not smoke cigarettes, however, they do not have a great risk of lung cancer; on the other hand, if they *do* smoke, then their risk is much greater than that of cigarette smokers in general.[9]

The combination of the two gives a much greater risk than their sum. Similarly, uranium miners seem to get lung cancer in great excess only if they also smoke; again a multiplying effect.[10]

It is likely that for some human cancers there may be three, four or more etiological factors, links in a chain that tie a cause to the neoplastic effect. While it may be tedious and difficult to identify each link, it will also be rewarding. Even if we cannot break them all, we can anticipate that *some* of these links can be eliminated or altered. Among them, there will be some weaker links, some amenable to change. This offers great promise for the future. While we may not yet be able to change our genes, we can do much about our environment. Identification of agents, their specific effects, their interactions, will point to solutions of the cancer problem. Should breast cancer be found associated with an oncogenic virus, a major breakthrough will have occurred. Leads are being sought for cancer of colon and rectum, for cancer of pancreas, ovary, kidney, brain. We may some-

times be naive in seeking single agents; we can look for two or more factors in our rich and varied environments.

Expansion of cancer research thus comes at a promising time. Important breakthroughs have been made, and can now be exploited. Governmental agencies have recruited skilled and capable staffs; the American Cancer Society provides unique statistical and epidemiological resources and its wide research support concentrates on suppleness and originality. The National Cancer Plan can attract many highly competent and well trained scientists, fresh from current triumphs in molecular biology and immunochemistry.

Lewis Mumford tells of his teacher, Patrick Geddes, and his pleasure when others advanced his ideas to successful completion, likening it to the good fortune of the cuckoo bird, which lays its eggs in other birds' nests, and gives them the trouble of hatching and caring for the offspring. Perhaps Percivall Pott is chuckling now.

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Reports of studies in environmental epidemiology begin on page six.

worthless if they cannot withstand a few good kicks.

Mr. Krauss seems to be under the impression that an animal's metabolic rate is important in classifying it as a reptile or a bird. This is not true. Vertebrate taxonomy is not based upon soft tissue function but only upon the bony structure, the skull and skeleton.

A false significance attaches to metabolic rate simply because modern birds are very warm blooded while their reptilian neighbors are cold. I of course contend that there are warm blooded reptiles, the ratites. . . . At one time, the earth was populated *only* by cold blooded vertebrates, the amphibians and reptiles. . . . According to the fossil record, warm blooded birds and mammals emerged in modern form after having undergone millions of generations of a slow process of adaptive evolution. Birds as well as mammals evolved from reptiles. . . . There were considerable lineages of mammal-like reptiles before there were dinosaurs. Feathered reptiles also preceded dinosaurs.

Many workers in the past have agreed that feathers appeared long before any creature could even glide much less fly. They originated as a thermal device allowing their reptilian bearers to develop and maintain a higher rate of metabolism. Thus warm blooded reptiles were present long before any pro-avian developed. . . . Flight was the result of a secondary adaptation of existing structures which first served as insulation.

The result of reptiles trying to fly is the flying reptile, the Pterosaur. These creatures were extremely highly specialized and were terminal forms not in the line of bird evolution.

Archeopteryx, the famous feathered reptile from the European Jurassic period . . . displays a very bird-like plumage yet its frail, unfused skeleton was totally incapable of withstanding the tremendous pressure of flying muscles. The fact that it could not fly is well established by the total absence of a "flying" keel on the breastbone. It didn't even have a breastbone as we know it in birds. This keel serves as the attachment for some of the most powerful sets of flying muscles used in free flight. *Archeopteryx* could only glide at best for although it had flying-type feathers it lacked the muscles and supporting bone structure to operate its forelimbs in free flight.

Self preservation put the small feathered reptiles in the air while their larger contemporaries simply ran away from their dull-witted reptilian enemies which probably did not even have the advantage of a high metabolic rate sustained by a feather blanket. The ostrich today successfully preserves himself from a great variety of considerably more intelligent, warm blooded mammals, including man, during his total evolutionary history.

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Press coverage of my AAAS talk garbled the point. ["Science & Man," Jan-Feb] . . . Biological factors represent a significant variable in human behavior. The very limited evidence suggests only that women . . . would be less violence-prone. But not all women are alike, either biologically or in terms of their experience. I also emphasized that politics involves a cultural selection process which tends to favor more competitive and aggressive individuals . . . We must, finally, eschew both simple explanations of the causes of human violence and equally simple solutions to the problem. . . . Men (and women) also go to war deliberately for "rational" reasons. Thus, political solutions to problems and conflicts are also an important part of any remedy for violence.

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IN THIS ISSUE

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