Sexual development: What's the difference

"Is it a boy or a girl?" That is probably the question new parents most often hear. Gender is a key factor in shaping a person's life. Yet for the first two months of embryonic life, there are no sex differences — anatomically or physiologically — just the appropriate chromosomes and genes. The cascade of events that leads to sexual differentiation starts with a difference in activities of just one or two enzymes at the crucial time in the embryonic sex organs, Jean D. Wilson explained in New York last week at the Endocrine Society's Seminar for Science Writers. Wilson outlined the three-step scheme that currently is considered the basis for both normal and abnormal sexual development. "I think the simplicity is particularly impressive," he says.

The basic scheme, first proposed thirty years ago by Alfred Jost, is that genetic sex directs the differentiation of the sex organs, which in turn direct the development of other sexual characteristics.

In the very early stages, each embryo has two separate duct systems — one that can become the basis for the female internal reproductive tract and the other the male. Recent work has established that three hormones are responsible for converting the sexually "indifferent" embryo into a male. A protein hormone called the "mullerian regression factor" causes the female duct systems to degenerate. Testosterone produced by the testis initiates development of the male internal reproductive tract from the other duct system. And a derivative of testosterone called dihydrotestosterone produces the masculine external genitalia. If these hormones are not present a female will develop.

The crucial difference in the sex organs that sets the fetus on its sexual path is just a matter of one or two enzymes. Wilson says that in the male fetal gonad at about eight weeks of gestation the rate at which testosterone is produced is 100 times greater than in the female. In addition the female fetus, but not the male, contains an enzyme that converts testosterone to another hormone, estradiol. Together, those enzymes ensure that the male will have much more testosterone.

Insight into how testosterone acts in the fetus to control further sexual development comes from studies of three groups of patients — genetic males that have normal testes but for some reason do not respond to testosterone.

One group of patients is missing the enzyme that converts testosterone into dihydrotestosterone. Although no one knows why the two related hormones have different actions, each is responsible for a distinct portion of development. Therefore, in these patients the internal genital tract conforms to normal male anatomy but terminates in a vagina. "Half the anatomical development is male and half is female," Wilson says. The condition is inherited and more than seven families passing on the trait have been described. In some families there is an enzyme defect where it binds testosterone, and in others there is an abnormality where the enzyme binds a required cofactor.

In the second group, patients have a defect in the receptor that binds testosterone or dihydrotestosterone in cells. These patients do not respond to the hormones internally or externally supplied. Because the defect prevents action of both hormones, the effect is more extensive than the absence of just dihydrotestosterone. These patients develop normal female genitalia. Wilson suggests that less complete defects in the receptor may be responsible for males born with incomplete penis development, and that in 15 to 20 percent of infertile men a subtle abnormality of the receptors is the cause.

In the last group of patients, the hormone binds to the receptor and moves into the cell nucleus, but the complex is not active there. Again the effect is to prevent masculinization of the genital tract, and at birth the child appears to be female.

So far 19 different genes have been implicated in human sexual development, Wilson says. "The involvement of such a large number of genes does not imply a greater complexity for sexual differentiation than for other developmental processes but rather reflects the comparative ease with which mutant genes affecting the normal process of sexual development can be identified," he says. "Individuals with even the most profound abnormalities of sexual development survive, usually come to the attention of physicians and have been the subject of many detailed pathophysiological studies."

Four to eight live male births out of every thousand show some extent of abnormal sexual development, Wilson estimates. The problems range from minor deformities of the penis to the extreme example of genetic males who have the genitalia of females. Wilson and other researchers are studying sexual abnormality in order to develop treatments.

In terms of patient care, physicians are using the accumulated knowledge to make more rapid decisions on a course of action when a child is born with abnormal sexual development. Wilson says a "gender crisis group" at the University of Texas Southwestern Medical School helps make the decision in consultation with the baby's family. Such prompt action allows the physicians to perform surgery and begin hormone treatments early. Although the importance of the early hormone treatments has not been proved, Wilson believes such treatment is beneficial. If nothing else, he says, the parents are relieved to have a baby who looks normal and to have a definite answer to the question "Is it a boy or a girl?" □

Birth pangs of a climate program

The National Climate Program is taking on an adjective that often becomes attached to nascent bureaucratic efforts — beleaguered. But, as observers at the first meeting of the program's advisory committee noted last week, once the program gets through its infancy, it will be a model of intragovernmental effort.

The National Climate Program was created by Congress in 1978 "to understand and respond to natural and man-induced climate processes and their implications," with the emphasis on implications (SN: 10/7/78, p. 246). What makes the program both unique and difficult is that it tries to coax a little teamwork from players long used to individual sports. It attempts to coordinate the nearly $120 million worth of climate research now spread among seven federal departments and agencies — the Departments of Agriculture, Defense, Energy and the Interior, NASA, the National Oceanic and Atmospheric Administration and the National Science Foundation — most of which have years-old climate-related programs. Moreover, as one member of the advisory committee pointed out, the program office, which is part of NOAA, has no budgetary strings to pull or other direct means to coerce the agencies into playing a coordinated game.

The problem is illustrated by the attempts to develop an acceptable game plan. As directed by the 1978 act, a preliminary five-year plan was drafted last July (SN: 9/8/79, p. 173). Since then, however, the plan has undergone five revisions and, as presented to the advisory committee last week, has yet to win final approval from the Office of Management and Budget or from the federal agencies and departments. Program office director Edward S. Epstein told the advisory committee that the preliminary plan "didn't define priorities, had a lack of specificity, a paucity of information on costs and direction... and little attention to program management." The revised plan presented remedies those problems, he said.

It consists of three major divisions of activities, each including two high priority projects and several lower priority areas:

- Climate services. The two high priority items are climate prediction and the supply of climate information to users such as state climate offices, federal agencies and independent climate experts. The lead agency for both is NOAA.
- Climate impacts and policy implications. The program of primary importance is a DOE-coordinated investigation into the timing, magnitude and effects of a carbon dioxide-induced climate change. Also included is an expansion of current research by the USDA on the effects of climate changes on national and world food production.

• Understanding climate. Included in this area is a NASA-led study of solar and earth radiation in order to understand how the climate system gains and loses energy and an NSF-coordinated study of the ocean's role in climate.

The 13-member advisory committee, chaired by Werner Baum of Florida State University in Tallahassee, is expected to review the plan and make recommendations. According to one committee member, the plan "is short on impacts" and clout. But despite its inadequacies, he said it represents an important step toward other much-needed interagency programs. □

Acid rain clouds gather

President Jimmy Carter's recently announced plan to encourage utilities to convert to coal has split the administration camp over the issue of acid rain. Testifying before a Senate subcommittee March 19, Environmental Protection Agency administrator Douglas Costle made public what had been an internal dispute, questioning the adequacy of pollution controls provided in the plan and saying that coal conversion would worsen acid rain if sufficient controls were not added.

The first phase of Carter's proposal, outlined March 6, would give 107 northeastern and mid-Atlantic oil-burning power plants $3.6 billion to aid their conversion to coal or some other energy source. The second phase, to begin in 1985, would give $6 billion to other oil-burning power plants that volunteer to convert. An additional $400 million would be provided in phase one to help finance voluntary air pollution controls.

And there's the rub. Current air quality standards allow larger emissions of sulfur dioxide and nitrogen oxides — which can combine with water vapor to form environmentally damaging acid rain — from coal-burning plants than from oil-burning plants. The EPA had pressed for allowing conversions only if more pollution controls were added to the plants so that total emissions would not increase. But the Department of Energy and coal interests prevailed, saying that tight controls would jeopardize passage of the measure and discourage utilities from converting.

Saying that the plan does not include sufficient pollution controls, Costle told the subcommittee that conversion would increase sulfur emissions by 25 percent and acid rain by 10 to 15 percent. "I would clearly prefer a bill that prevents acid rain from getting worse," he said. "And I have my doubts that this measure will do that." To offset the lack of controls in the plan, Costle called for earlier retirement of older, more polluting power plants and washing of coal prior to burning. □

Proxmire shorn by defamed 'fleecer'

Five years ago Sen. William Proxmire (D-Wis.) voted Ronald Hutchinson one of his infamous "golden fleece" awards for allegedly bilking the public of more than $500,000 "to determine under what conditions rats, monkeys and humans bite and clench their jaws." Complained the thrift-conscious senator, "funding of this nonsense makes me almost angry enough to scream and kick and clench my jaw."

But Proxmire's characterization of Hutchinson's work made the behavioral scientist mad enough to sue — for libel. And the lawmaker's defense against the $8 million suit — reputed to have cost the taxpayers more than $120,000 — didn't cut the mutton. The Supreme Court ruled that Proxmire's immunity from libel did not extend off the Senate floor; the golden fleece award was issued as a press release. This week Proxmire announced he had settled out of court for $10,000, court costs and a press release retracting defamatory and inaccurate charges in the original fleece award. □

Nuclear advertising for objectivity?

Advertising Age

Sticker from winning campaign: "Phase out nuclear energy, but in a sensible way."

How can the federal government ensure objectivity when attempting to inform the public about issues as contentious as the safety of nuclear power? Sweden tried competitive advertising.

Over the past three months, the Swedish government has channeled some $12.5 million into three competing advertising campaigns to inform its citizens on issues relating to the nation's fourth national referendum, a vote on nuclear power stemming from public concern over the Three Mile Island accident one year ago. Handled by separate agencies or groups, each agency advocated and justified one of the three proposals offered on the March 23 ballot: to support nuclear power by building at least six new power plants; to build just six more plants — but only under public ownership and only with the proviso that they be shut down after 25 years; to not support nuclear power, just stick with the six existing plants, which would be phased out within the next 10 years.

The result? Winning with 39.4 percent of the vote was the conditional option, number two. Another 38.6 favored the third — and antinuclear — choice; 18 percent voted for number one. Although the vote was nonbinding on its parliament, Sweden's Prime Minister Thorbjorn Falldin — a member of one of the nation's antinuclear political parties — promised to support the electorate's decision.

Sweden's nuclear program, which began in 1962, now provides 3.8 million killowatts or about 25 percent of the nation's electricity — the highest average anywhere. In addition to its six operating reactors, four are nearing completion and another two are in early stages of construction. Falldin, who fell from power once already — in September 1977 — over the issue of nuclear power, has said he would withhold operating authorization from two of the nearly completed plants if agreements are not concluded for the reprocessing of spent fuel.

Resource poor, Sweden imports more oil per capita than any other western nation. Although it does hold uranium — perhaps as much as 80 percent of Europe's known reserves — none is being mined. □

Well capped at last

Nearly 10 months after it began spewing oil (SN: 8/11/79, p. 99), the runaway Mexican well in the Gulf of Mexico has been capped. The more than 3.1 million barrels it spilled — twice what the *Amoco Cadiz*, previously the worst spill, had shed — fed massive fires and ribbons of crude that at times traveled more than 600 miles northward to foul Texas beaches. Plugs, fashioned from cement pumped down the 6,000-foot well shaft on March 23, hardened into seals hundreds of feet long. □

Additives at fault in hyperactivity

In the early 1970s a San Francisco allergist, Ben F. Feingold, proposed that food additives are a major cause of hyperactivity in children and that hyperactive youngsters can be successfully treated by eliminating food additives from their diets. Study results have been divided on whether Feingold's theory is valid (SN: 6/25/77, p. 406). But now three studies in the March 28 SCIENCE join the affirmative side.

James M. Swanson of the Hospital for

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