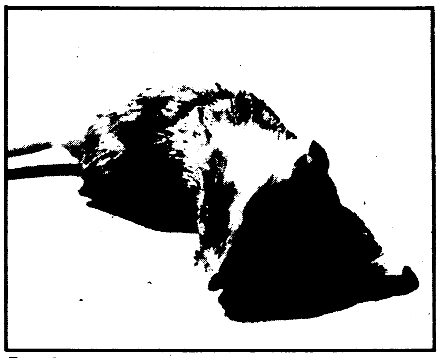
A mouse of two species

The fine art of producing living patchworks has expanded into a new range of possibilities with animals composed of cells from two distinct species. Manipulation of embryos in recent years has created chimeric mice with six parents (SN: 10/14/78, p. 261) and others partly descended from tumor cells (SN: 1/27/79, p. 60). In 1973, scientists attempted to construct a rat-mouse combination by introducing rat cells into mouse embryos. Although the rat cells functioned early in gestation, the pups born appeared to be pure mouse.

To avoid such massive selection against one set of cells, Janet Rossant recently put together embryonic cells of two mouse species. She reasoned that these cells would be more likely to interact normally than would cells of widely disparate species. She chose to work with the standard laboratory mouse species, *Mus musculus,* and a smaller, pointy-nosed, wild species from Asia called *Mus caroli.* "When I say 'wild,' I mean wild," Rossant told the meeting in Washington of the Gerontological Society. Behavioral differences between the two species are pronounced, and the species don't interbreed.

When Rossant introduced cells from a wild-mouse embryo into a laboratory-mouse embryo, and implanted it into a laboratory-mouse foster mother, more than 80 percent of the pups born contained cells from both species. Because the lab mouse is white and the wild mouse is agouti (a grizzled gray), many chimeras are obvious by their coat color. Individual mice vary in the distribution of species characteristics, including behavior. Rossant says that the more the chimeric mouse looks like *M. caroli,* the less docile is its behavior.



Rossant

Patchy coat indicates inter-species mouse.

The scientists also have examined the distribution of an enzyme that is distinguishable between the two species. They find that internal tissues can contain cells of both species types, and in skeletal muscle cells of the two species can fuse normally to make extended cells with a mixed enzyme type.

The chimeric mice, unlike natural cross-species progeny such as the mule, can mate with the original species and produce offspring. Even the germ cells can be of mixed origin; one chimeric female, mated with *M. musculus,* produced both *M. musculus* and hybrid pups.

The intention behind this research really is not to blur species lines, but rather to provide tools for tracing how early embryonic cells contribute to a developing animal. Rossant and collaborators at Brock University in Ontario, Canada, are working to find antibodies that will bind only to cells of one mouse species or the other. With such markers they hope to map the descendants of embryonic cells of each species and thus determine which give rise to each adult tissue. □

DNA rules: Revisions, not exemptions

In a revision of the rules for recombinant DNA research, National Institutes of Health director Donald S. Fredrickson last week basically agreed with the recommendations of the Recombinant DNA Advisory Committee (SN: 9/29/79, p. 214), but he quibbled with their wording. In September the committee proposed that experiments involving the enfeebled bacteria *Escherichia coli* K-12, used in the vast majority of recombinant DNA experiments, be "exempted" from the guidelines except for a few special instances. Those experiments, however, still would be required to meet the minimal (P1) safety requirements described by the guidelines. Those requirements include decontamination of biological wastes and a prohibition against pipetting material by mouth.

In his proposal, published in the Nov. 30 FEDERAL REGISTER, Fredrickson states that he would not exempt those experiments from the guidelines, but simply lower their safety requirements to P1 and require them to be registered with a local institutional biosafety committee, rather than with the national Office of Recombinant DNA Activities. For experiments in which recombinant DNA is deliberately programed to produce plant or animal proteins in the bacteria, Fredrickson proposes that the local committee must give prior approval. "I remain committed to shifting responsibility to local institutions for adherence to uniform, sensible guidelines," he says.

Frederickson says that the word "exempt" should be reserved for experiments in which no special safety requirements and no registration are required. He points out that keeping the experiments under the guidelines means that industrial scale-up of experiments to more than 10 liters still needs prior NIH approval. The guideline revisions are available for public comment until December 30. □

Channeling radiation from electrons

Looking at a venetian blind from one angle a person will find the view totally blocked and nothing of the outside visible. Shifting the head radically changes this impression. Channels open between the slats, and at the proper angle the outside becomes almost totally visible. The same trick can be played with a crystal: At the proper orientation clear channels open up between the planes of atoms that make the crystal lattice — provided the observer is an electron or a positron or similar particle.

A charged particle moving through one of those channels should have a bumpy ride because of the forces exerted on it by the atoms of the lattice, and as a result it should radiate light or X-rays. In fact a group of experimenters from Stanford University, the Lawrence Livermore Laboratory and Oak Ridge National Laboratory reported last spring that they had succeeded in demonstrating such channeling radiation using positrons as the radiators (SN: 5/12/79, p. 311). The effect is the source of intense, highly directed, tunable beams of X-rays.

Now the same group, Richard L. Swent, Richard H. Pantell and Mark J. Alguard of Stanford, Barry L. Berman and Stewart D. Bloom of Livermore and Sheldon Datz of Oak Ridge, report in the Dec. 3 PHYSICAL REVIEW LETTERS that they have succeeded with electrons.

They started with positrons, Berman said in an interview with SCIENCE NEWS, because positrons are "easier to use." There was a theoretical prediction of how the channeling radiation spectrum from positrons would look. There was none for electrons. Positrons have positive charge as do the ions in the crystal lattice. The mutual repulsion between them as the positrons move down the channel produces back and forth kicks that can be analyzed according to classical physics, "a classical harmonic oscillator potential," as Bloom called it in the same interview. In the radiation spectrum, this meant a single peak wavelength for a given channel and a given positron energy.

When the experimenters did the experiment with electrons, they found a family of lines in the spectrum instead of a single peak wavelength. As soon as they saw that family of lines, says Bloom, they knew they had to use quantum mechanics to explain it. The forces between the negative electrons and positive lattice are better analyzed by a model that takes electron and lattice as a total system and speaks of discrete quantum mechanical energy states (bound states) of the system. The family of spectral lines represents transitions between different bound states. In their Dec. 3 publication the group stresses the finding that quantum mechanics must be invoked to explain channeling radiation.

For the immediate future Berman and Bloom stress that they would like to learn more about aspects of the physics that they do not understand well. They want to see how many bound states there are in the spectrum. They want to know how the effect changes with the energy of the incident particle. They have so far done electrons at two energies and positrons at two energies. They have worked at generally high energies, and they would like to see what happens at very low energies. The electron accelerators in hospitals, where channeling radiation might find important applications, work mostly at very low energies.

They want to know the angular distribution of the photons — that is, how far away from the direction of the incident particle beam they appear. They want to know what happens if they use a thinner crystal. They want to know the number of photons produced per incident particle, an important consideration for designing practical devices.

They want to see what happens with a different kind of crystal. So far they have used only silicon. "We have a South African-English-Dutch connection," says Berman, and through it they expect to get a diamond cut just the right way. Diamond has the same crystal structure as silicon, but a slightly different atomic number and so different lattice spacing. This means being able to study the effect of a small known change.

Eventually there may be practical devices. Bloom and Berman think more must be learned about the physics, but in not too long the Standford members of the group intend to begin work on one. If successful it could have uses in many lines of scientific research and in medical diagnostics and therapeutics. □

Do cool incubators make male sea turtles?

Scattered programs throughout the world have attempted to restock declining wild sea turtle populations with animals raised from eggs incubated in captivity. But good intentions aside, scientists may be doing about as much harm as good by inadvertently skewing the sex ratios of the animals they raise, according to research reported last week at the World Conference on Sea Turtle Conservation (SN: 12/1/79, p. 372).

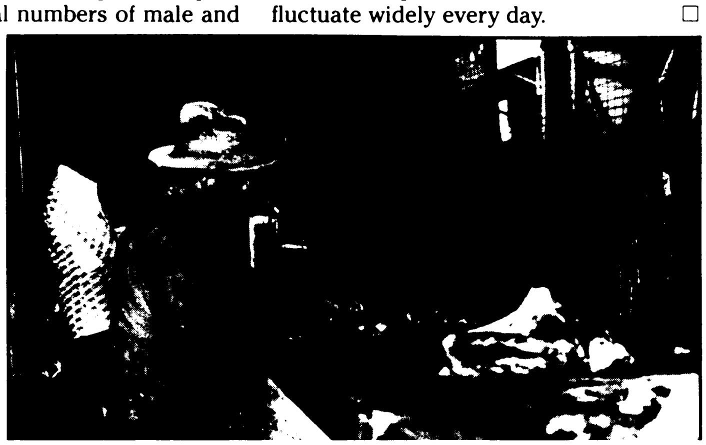
The reasoning behind captive incubation is simple: It increases the chance that a turtle will survive its weeks of unprotected incubation on what are often public beaches, such as those in Ft. Lauderdale, Fla. Predation by hungry animals or by humans harvesting eggs for sale in local markets has been known to wipe out 100 percent of the eggs within only a day or two of when they were laid.

But a previously unknown problem facing eggs incubated in captivity was outlined by University of Toronto zoologist Nicholas Mrosovsky. Research he is conducting with C.L. Yntema of the Upstate Medical Center in Syracuse, N.Y., shows that the sex of sea turtles is — like that of some of their landed cousins — determined by the temperature at which they incubate. The pivotal temperature is 30°C. Eggs incubated at that temperature produce roughly equal numbers of male and female hatchlings. But raise the temperature just 2° and the hatchlings are all female, lower it 2° and male turtles are hatched.

This finding was made possible by the development of a technique that permits simple identification of the sex of hatchlings via microscopic examination of the tissue structure of an animal's gonads. Until now, scientists had not been able to identify the sex of a sea turtle until just before it reached sexual maturity — something long assumed to take seven years. As a result of a number of reinforcing studies and observations reported last week, however, it now appears sea turtles in the wild probably take somewhere between 12 and 60 years — perhaps even longer — to reach sexual maturity.

Since harvesting of adult turtles primarily involves nesting — therefore reproductive — females, it would be of questionable benefit to restock overharvested populations with only male animals.

Mrosovsky worries that without auxiliary heating, styrofoam hatching boxes, which most hatcheries use, may cool and thereby masculinize eggs. He cautions against ignoring another variable, however. His work has so far only involved eggs incubated at constant temperatures, but the temperature of beach sand can fluctuate widely every day. □



Smithsonian Tropical Research Inst., Panama

Hanging pot (right) contains eggs — often eaten raw — from oviducts of butchered turtles. In Panama, turtle meat sells for $.40 a pound while the cheapest beef is $1.25 per pound.

The genetic price of heroin abuse

The ability of radiation and certain toxic chemicals to wreak genetic havoc and in some cases contribute to cancer is well documented. But in other cases, such as drug abuse, genetic damage has been inferred but not observed. "Not all chemically induced mutations result in observable changes," says Arthur Falek, director of the Human and Behavioral Genetics Research Laboratory of the Georgia Mental Health Center in Atlanta. "Mutations can hide in the genetic pool for generations without producing any apparent disorder."

However, Falek and his colleagues report perhaps the first direct observation of genetic damage caused by heroin abuse. Moreover, they have found that straight withdrawal from heroin, or the substitution of methadone, appears to at least partially reverse such drug-induced changes in chromosomes. And as part of the same study, the researchers report that cigarette smoking may hamper a person's ability to self-repair genetic damage.

The investigators studied the chromosomes in white blood cells of heroin addicts and controls as the cells underwent the normal process of division. The ability of the chromosomes to self-repair — after damage induced by heroin or experimentally by ultraviolet radiation — was examined in 38 street heroin addicts, 18 methadone maintenance patients and 90 non drug users.

"We have found that opiate addicts have more DNA damage than controls based on our findings of significantly increased chromosome damage in their white blood cells and of their much lower ability to repair DNA damage," Falek said last week at an informal news conference sponsored by the Alcohol, Drug Abuse and Mental Health Administration. The study appears in the November PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

The researchers found a "significant increase" among heroin addicts in the number of "poor" repairers of genetic material; the poor repairers displayed only one-fourth the capacity of control group members to repair damaged DNA. "After long-term methadone treatment, however, there was no significant difference between the DRS [DNA Repair Synthesis] mean ... for these patients and those for controls," they report. "Finally, withdrawal from street heroin without any methadone treatment also results in a decrease in chromosome aberration."

The only factor among sex, age, alcohol, tobacco and coffee use that seems to affect repair capacity is tobacco use. Among the non-addicts who smoked, none were classified as "high repairers," although smoking did not produce repair scores as low as those for addicts.