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COVER A cluster of the sea star *Pisaster ochraceus* on a beach of the Pacific Rim National Park, Vancouver Island, British Columbia. The oocytes from this echinoderm have been used as a source of the mitogen-activated protein (MAP) kinase p44<sup>erk</sup>, which is now shown to be phosphorylated and activated by the lymphocyte protein tyrosine kinase p56<sup>erk</sup>. See page 853. [Photograph by Peter Thomas]
Two-fold serial dilutions of Rabbit IgG were spotted onto Du Pont’s PolyScreen PVDF transfer membrane (1 μL aliquots starting at 1 μg/mL). Spots were then detected using AntiRabbit-IgG-HRP and DAB, either unamplified (Panel A) or with Du Pont’s BLAST amplification systems (Panel B).

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Elephants, Monstrosities, and the Law

A
n elephant goes berserk at the circus, an elderly pillar of the community is discovered to be a child molester, a man admits to killing many young boys and storing parts of the bodies in the refrigerator, and a disgruntled employee shoots seven co-workers. Each of these news stories will be followed by a series of articles ofanguished soul-searching in which the educational system, the perplexity of life, the stress of modern society, or the brutality of zookeepers will play prominent roles. Yet each probably has a common origin: the simple fact that the brain is an organ, and like other organs—the heart, the lungs, the liver—has an internal biochemistry that can break down. Because of the special role of the brain, there are those who want to believe that it can only be affected by the environment; they refuse to face the fact that the brain, like other organs, while functioning correctly in most areas, may have one part go awry and cause major malfunction.

If we treat the brain as another organ, then the fact that an elephant or a human goes berserk is as easy to comprehend and as difficult to unravel as cystic fibrosis, tuberculosis, or AIDS. Sometimes the damage to the organ will be hereditary and sometimes environmental, but it is not mysterious that a large fraction of the organ can behave perfectly correctly while a small section has totally abnormal qualities.

An understanding of the chemistry of the brain should put us on the course of trying to identify biochemical causes of mental disease, a major advance over current views of such afflictions, which too often involve debates regarding the nature of evil and the definition of insanity. In the trial of the Milwaukee killer there is extensive discussion of whether he should be declared not guilty by reason of insanity, a kind of legal monstrosity first used in the last century. It is ludicrous to say that someone who has confessed to serial killings and cannibalism is sane in any normal sense, but in one sense any crime is insane to a normal citizen. There is no simple dividing line between sane crime and insane crime. Yet this sets up a curious standard: the more monstrous the crime, the more likely a criminal is to be declared “not guilty by reason of insanity” and perhaps even be released in a few years on psychiatric testimony that says he is cured.

“Not guilty by reason of insanity” was designed to protect those mentally ill individuals whom society recognized should not be placed in jails, but rather in mental hospitals. That was before the day when self-styled experts could blandly testify at trials that an individual was not guilty by reason of insanity, then later have that individual proclaimed to be cured and ready for safe release into the general population. When psychiatry is sufficiently advanced so that its practitioners can accurately predict future behavior, we may be able to prevent the damage caused by a berserk elephant or a berserk human being. But until such prediction is reliable, the concept that one guilty person should be released from a prison or hospital earlier than another individual on the basis of an expert’s testimony is nonsense. Such circumstances cause revulsion in society against all mentally ill individuals, most of whom are harmless to others. It also causes disdain for experts who appear to favor those who have the money to pay for expert witnesses.

There are a number of steps that we can take. The first is to increase the amount of research into mental illness so that in the future we can separate those who are likely to pose great danger to others from those who only pose dangers to themselves. The astonishing progress in cures or prevention of cancer would never have been achieved if we simply lumped all cancers together instead of recognizing that some are caused by viruses, some by heredity, and some by carcinogens and diet. Yet this lumping is routinely done in mental illness. Distinguishing among types of mental disorders on a scientific basis prevents the illogical procedure of release of an insane person who cannot profit from experience earlier than a sane one whose crime is less bizarre. The first step is to have trial procedures that simply determine whether the individual actually committed the crimes. At that point, the treatment he receives could be decided by a second process determining the type of illness and the appropriate treatment during the years of incarceration. Such a process would not only remove the temptation for phony appeals and dubious science, but would also help provide statistics on which treatment succeeded, leading in the long run to kinder treatment of individuals and prevention of future tragedies.—DANIEL E. KOSHLAND, JR.
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Heat of Fusion in the Hydrophobic Effect

In a technical comment (5 July, p. 88) on the hydrophobic effect, Judith Herzfeld suggests that, when one calculates the hydrophobic effect in protein denaturation, the enthalpy of fusion of the hydrophobic groups should be considered a factor distinct from the hydrophobic effect, per se, which is obtained from experiments in which a hydrophobe is transferred from liquid organic phase to water. This idea is correct, but had been proposed somewhat earlier (1) and had also been applied to the stabilization of protein-protein interfaces (2) and to the calculation of heat capacity at constant pressure of denaturation (3).

JAKE BELLO
Department of Chemistry, Roswell Park Division, State University of New York, Buffalo, NY 14263

REFERENCES


*Erratum: In the article "Subterranean waterworks of biblical Jerusalem: Adaptation of a karst system" by D. Gill (6 Dec., p. 1467), the scale bar in figure 1B represents meters and should have read 10 m.

*Erratum: Joyce Higgins should have been named as the source of the illustration on page 651 accompanying the Research News article "Playing tag with membrane proteins" by Michelle Hoffman (1 Nov., p. 650).
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for 30 hours at 30°C. Cultures were diluted and plated on SCM-Trp and SCM-Trp-Ura plates.


37. Y. Marahubes and B. Stillman, unpublished data.


48. For the mobility shift DNA binding assay and DNA bending assay, whole-cell extracts were prepared from S. cerevisiae strain BJ926 (24) as described (18). Restriction fragments and double-stranded oligonucleotides were 32P-end-labeled by standard procedures and extracted from a polyacrylamide gel (T. Maniatis et al., Molecular Cloning: A Laboratory Manual (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1982)). Binding reactions were as follows. Whole-cell extract (1 μl) was mixed with 6.5 μl of buffer A [25 mM tris-HCl, pH 7.5, 1 mM EDTA, 10 percent glycerol, 0.01 percent NP-40, 0.1 mM phenylmethysulfonyl fluoride (PMSF), and 1 mM dithiothreitol (DTT)], 0.5 μl of bovine serum albumin (BSA) (10 mg/ml), 1.0 μl of a solution (1 mg/ml) of poly(dI-dC), and probe (10,000 cpm) and incubated for 15 minutes at 30°C. The samples were then analyzed on a low ionic strength polyacrylamide gel (18), which was then dried and exposed to Kodak XAR film for 4.5 hours. For monitoring DNA bending, ARS1 fragments were excised from their plasmids with Eco RI and Hind III, subjected to electrophoresis in TBE buffer [0.089 M tris-borate, 0.089 M boric acid, 0.002 M EDTA, pH 8.0] in an 8 percent polyacrylamide gel at 4°C and 1.7 v/cm for 60 hours, then stained with ethidium bromide, and photographed.

49. We thank S. P. Bell, S. Brill, J. F. X. Diffley, and T. Tsukimoto for advice and interesting discussions; and M. Horvath for construction of the plasmids pARS/ WTA and pARS/WTB. Supported by NIH grant AI20460.

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Vignettes: A Discovery and a Solution

One day when the whole family had gone to a circus to see some extraordinary performing apes, I remained alone with my microscope, observing the life in the mobile cells of a transparent star-fish larva, when a new thought suddenly flashed across my brain. It struck me that similar cells might serve in the defence of the organism against intruders. . . . I felt so excited that I began striding up and down the room and even went to the seashore in order to collect my thoughts. I said to myself that, if my supposition was true, a splinter introduced into the body of a star-fish larva, devoid of blood vessels or of a nervous system, should soon be surrounded by mobile cells as is to be observed in a man who runs a splinter into his finger. This was no sooner said than done.

There was a small garden to our dwelling, in which we had a few days previously organized a “Christmas tree” for the children on a little tangerine tree; I fetched from it a few rose thorns and introduced them at once under the skin of some beautiful star-fish larvae as transparent as water.

I was too excited to sleep that night in the expectation of the result of my experiment, and very early the next morning I ascertained that it had fully succeeded.

That experiment formed the basis of the phagocyte theory, to the development of which I devoted the next twenty-five years of my life.

—Elie Metchnikoff, as quoted by Alfred I. Tauber and Leon Chernyak in Metchnikoff and the Origins of Immunology (Oxford University Press)

Hilde Proschohl . . . had been given by Speemann the assignment to transplant the Blastostat lip of a Triturus gastrula into the belly side of another gastrula. This she did in several hundreds of cases, but only some five of them survived . . . .

Speemann himself had no remedy for this high mortality rate. Well, I found a cure for it, and that was simple enough. Obviously, the denuded and defenseless embryos died of bacterial infection. Therefore, following the example of the medical profession, I proceeded to sterilize the instruments and glassware we used and to raise the embryos in a sterile medium. In addition, I devised an appropriate culture medium . . . . Having observed that embryos with open wounds disintegrated quickly in plain water, even if the water had been sterilized, I reasoned that water was strongly hypotonic, hence toxic, for the embryonic cells. This led me to experiment with salt solutions of different concentrations until I found an apparently isotonic, balanced salt solution which turned out to be an ideal culture medium (my “life elixir”) for our experimental embryos, even for isolated fragments of the embryo. Under the label “Holtfreter solution,” it became a widely used medium for explantation experiments. It amused me later to observe that it was this solution, perhaps more than anything else, by which I became known among the embryologists.


