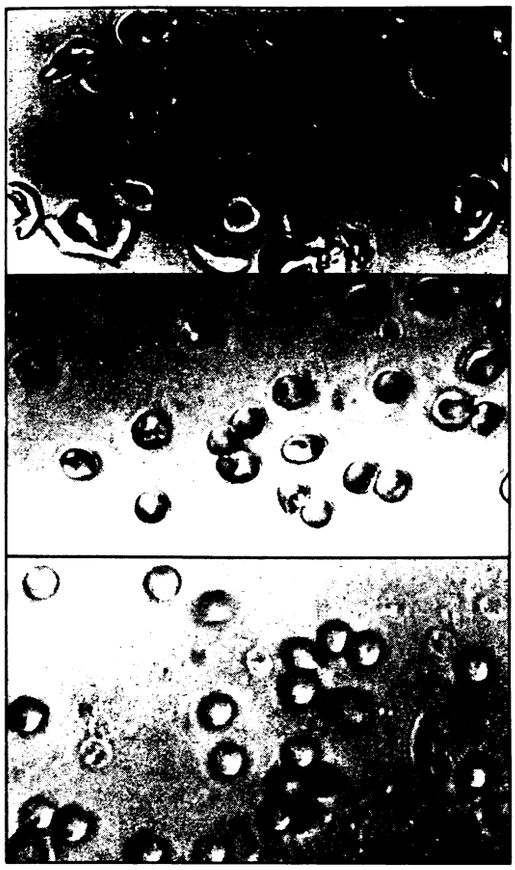

Rich et al./PNAS

Top to bottom: sickle cells; normal cells; cells treated with benzyl esters.

found that if they put certain small proteins (peptides) into red blood cells from sickle cell patients, the peptides would keep the red blood cells from sickling. But it took fairly heavy concentrations of peptides to penetrate red blood cells. Rich and his colleagues have since tested derivatives of the peptides and found them to be just as effective as the peptides but able to get into red blood cells easier. They report in the January PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES that peptide derivatives called amino acid benzyl esters do the trick nicely — apparently by binding to sickled hemoglobin molecules, by modifying the membranes of sickled red cells, or both.

After Rich and his co-workers determined that amino acid benzyl esters were able to prevent sickling of sickle cell patients' red cells, they compared the ability of various esters to produce the effect. They found that esters from amino acids with a high degree of hydrophobicity (aversion to water) were especially potent. They tested the esters on normal red blood cells' membranes to make sure that the esters did not damage them. Then they injected one of the most promising esters into mice and, as they hoped, it showed low toxicity. On the basis of all this data, they concluded: "Benzyl esters of hydrophobic amino acids and related compounds may prove to be useful in the treatment of sickle cell disease." □

R(3.17) or the color chemistry of quarks

Once upon a time the quark theory seemed like a fairly simple way of explaining the properties of nearly all the subatomic particles of physics. The particles were divided into two broad classes, the baryons, which are made of three quarks, and the mesons, which are made of two. Three varieties or "flavors" of quark, called up, down and strange, managed to serve to constitute all the particles known in various permutations.

Nothing in life stays simple. Theorists now see a need for six flavors of quark — charm, bottom and top have been added. This introduces new physical properties and increases the number of possible quark permutations. But until now the dual classification into baryons and mesons had held. Nobody had seen a single particle that had more than three quarks in it.

Evidence for just such a thing, a five-quark particle, may now have been found at the CERN laboratory in Geneva, according to a report at the recent meeting of the American Physical Society by Gerald A. Smith of Michigan State University. The finding was by a collaboration of physicists from Michigan State, the Universities of Birmingham, Cambridge, Glasgow and Paris, and CERN.

One of the recent complexities of quark theory is the attempt to study the behavior of quarks and their interrelationships inside particles. In such a quark dynamic study, one in which K mesons (a strange and an up quark) were struck against protons (two ups and a down), a particle appeared that gave indications of containing three strange quarks. Ordinary quark theory does not permit that combination.

A possible explanation of this unusual particle, which is being tentatively called R(3.17) is a "three-baryon resonance," a fleeting state in which three baryons are very temporarily stuck together. Its mass, 3.17 billion electron-volts, goes well with that supposition. The more exciting explanation is that the R(3.17) is a five-quark baryon, precursor of a whole new genus. Five-quark baryons (they have as yet no more distinctive technical name) are not part of the ordinary quark theory but are predicted by an extension called color chemistry. (Color is the name of the force that holds quarks together.) This is "chemistry" because the geometry of the configurations formed by the quarks is important. Smith suggests that R(3.17) consists of "two distinct clusters of two and three quarks respectively connected as on the ends of a dumbbell and rotating about its center with high velocity," a direct analogy to a molecule. If R(3.17) is a five-quark baryon, others should begin to appear. □

Pot: Off the streets, into the drugstores

In a move reminiscent of a pre-game pep rally, the government met with pharmaceutical companies Jan. 18 to whip up enthusiasm for Delta-9-Tetrahydrocannabinol (THC), the active ingredient in marijuana. The government's rallying cheer? Take THC to the marketplace!

Since then the National Institute on Drug Abuse and the Food and Drug Administration have met a second time with one of ten companies that attended the January session and plan similar meetings with four other drug companies that also have shown interest in marketing THC. Although government-sponsored sessions on potentially marketable drugs are not unusual, the history behind THC and the fact that several pharmaceutical companies now have shown interest in developing it weave an interesting tale.

Before it became an illegal substance in the 1930s, marijuana had been used in a number of medical preparations. But it was not until a young cancer patient noticed less nausea and vomiting, a side-effect of chemotherapy, after smoking street marijuana that interest was revived in marijuana as medicine. Researchers applied to FDA for grants to investigate the anti-nausea phenomenon and began experimenting with NIDA-supplied THC. Scientists have also found THC to be an effective treatment for glaucoma and the spasms associated with multiple sclerosis.

Still, from an economic viewpoint, the three potential applications of THC comprise only a "small market," causing drug companies to think twice about the high-risk investment of developing THC, explains Edward Tocus, a pharmacologist for the FDA's bureau of drugs. Furthermore, "THC has a reputation that some companies just don't want to mess with," Tocus says, referring to the social stigma attached to marijuana. Also, drug companies traditionally have shunned THC because of the red tape and security involved in researching a Schedule I drug — a substance classified as having high abuse potential and no redeeming medical value. Other deterrents include marijuana's notorious euphoria, the problem of encapsulating the resinous, sticky THC and the fact that THC is unevenly absorbed by the body when taken orally. Finally, although marketing processes can be patented, THC as a composition of matter cannot be patented.

Despite THC's complicating attributes, Robert Willette, chief of NIDA's research technology branch, believes THC already has passed through enough flaming laboratory hoops. Stephen E. Sallan and coworkers of Sidney Farber Cancer Institute

in Boston, Mass., for example, report in the Jan. 17 NEW ENGLAND JOURNAL OF MEDICINE the safe and effective antiemetic activity of THC in patients receiving chemotherapy. Patients who expressed preferences preferred THC over Compazine, one of the most commonly prescribed antiemetics, Sallan reports.

In another study, however, reported in the December 1979 ANNALS OF INTERNAL MEDICINE, Stephen Frytak and his colleagues, observing that past studies may have been limited in scope because they primarily involved young patients, "undertook to expand observations of THC as an antiemetic agent using a larger population of patients within the more typical cancer age groups." The research group, at the Mayo Clinic in Rochester, Minn., found that with their patient population of largely elderly adults, THC therapy showed antiemetic activity but resulted in an overall "more unpleasant treatment experience" than that noted with Compazine.

Meanwhile, the large pharmaceutical house Eli Lilly and Co. continues its work on Nabilone, a synthetic substance that is chemically similar to THC (SN: 8/5/78, p. 94). In the June 7 NEW ENGLAND JOURNAL OF MEDICINE, Terence S. Herman and colleagues of the University of Arizona in Tucson report the superiority of Nabilone over Compazine in reducing the nausea and vomiting in cancer patients undergoing chemotherapy. However, Lilly suspended clinical studies of Nabilone after observing the deaths of several dogs that received high doses of the synthetic drug. But because the company recognizes that Nabilone is metabolized differently in dogs and human beings, Lilly's loyalty to Nabilone has not waned; instead, the company is analyzing possible explanations for the adverse activity of Nabilone in dogs and soon will begin testing the THC analog in monkeys. Eventually, Lilly will decide whether or not to resume human testing of Nabilone, says Ronald Culp, spokesman for Lilly.

But one group involved in the "THC versus Nabilone" controversy — the National Organization for the Reform of Marijuana Laws (NORML) — argues that in the time it takes to perfect synthetics, cancer patients could benefit from the "natural form of THC." A November 1979 memorandum prepared by NORML reflects the organization's stance: "More conventional forms will undoubtedly be developed in coming years. But moral and social bias should not be allowed to prevent the use of marijuana cigarettes for medical purposes. ... If a cigarette seems an unconventional form of therapeutic administration we must weigh its conventionality against the relief it offers and make the determination on the basis of compassion, not past thinking and policy."

Now, the government is asking drug companies to re-evaluate this "past thinking and policy" for the more conventional, or oral, form of THC. If all goes well, Willette says, THC may be available in one to two years by prescription. □

Tea time lemon dilemma

Several scientists recently took the hot-tea plunge in an attempt to determine whether partaking of the beverage with lemon from a polystyrene cup is hazardous. The question arose when Michael Phillips of the University of Connecticut Health Center in Farmington was drinking tea with lemon and noticed the interior of the polystyrene cup "dissolving before my eyes and even perforating in places." In the Nov. 1 NEW ENGLAND JOURNAL OF MEDICINE he said, "This observation so thoroughly destroyed my appetite that I decided to pursue it in the laboratory."

Equipped with 16 polystyrene cups and teabags, Phillips decided to conduct an experiment with a twist — a lemon twist, that is (SN: 12/1/79, p. 376). His experiment showed that all the cups with tea and lemon experienced "erosions" and, surprisingly, a significant gain in weight. "The corrosion of the cups, combined with their gain in weight, suggests that substances in lemon tea solubilize polystyrene and possibly combine with it chemically," Phillips reported. He went on to cite a study implicating polystyrene as a carcinogen and explained that lemon tea drinkers who use polystyrene cups probably are also consuming parts of the container in solubilized form. "I suggest that the time is now ripe to return to the tradition of drinking lemon tea from cups of fine bone china," Phillips concluded.

Now, as a result of Phillips's initial report of the polystyrene cup caper, the pages of the Feb. 7 NEW ENGLAND JOURNAL OF MEDICINE runneth over with replies. From Edwin A. Chandross, of Murray Hill, N.J., for example, comes a possible explanation of the "Phillips phenomenon": "Foamed polystyrene would be penetrated readily by the oil at the temperature of hot tea, and the hot foamed beads would shrivel once plasticized by the low-molecular-weight material." Hence, the "corrosion" is really only a collapse of foamed polystyrene beads, writes Chandross.

Furthermore, argues John R. Lawrence, of The Society of the Plastics Industry in New York City, the carcinogen study cited by Phillips, which was first reported in 1948, is an example of "solid state" carcinogenesis. The researchers "observed that implantations in the form of film caused tumors, whereas textile fibers of the same materials did not. Scientists working in this field now do not believe that such results indicate that the materials tested were carcinogenic," Lawrence says. Still, Phillips says, no data are available on polystyrene effects on humans. □

Black holes: Do they remember?

"God does not throw dice": Albert Einstein. "Not only does God throw dice, He throws them where they cannot be seen": Stephen Hawking. Could Hawking's rebuke to Einstein be wrong? Don N. Page of The Pennsylvania State University believes that it might be and pursues the suggestion at some length in the Feb. 4 PHYSICAL REVIEW LETTERS.

In Hawking's study of the formation of black holes he found that black holes are subject to an evaporation process in which they emit particles and gradually shrink to nothing, exposing to view the "singularities" that lie at their centers. The exposure of this naked singularity brings the outside world into contact with a point where space and time disappear and the laws of physics, including principles of causality, are repealed. In addition, in the process of evaporation some of the particles produced come into the outside world, but some fall down the singularity. The particles carry information, and those that fall down the singularity take a certain amount of information beyond our reach. Without that information we cannot predict the future of such an evaporation process from its past. Hence Hawking's figure of the hidden dice.

Page proposes to apply some principles of particle physics to black hole formation and evaporation to see whether they will be able to restore to the situation at least the causal laws of quantum mechanics. These are not as strict as the ones Einstein preferred, but they are better than nothing. Such an outcome will be possible if the black hole process can be described mathematically in a particular way (by a superscattering operator that obeys the space-time and matter-antimatter symmetry principles of particle physics). Because there is as yet no satisfactory quantum theory of the gravitational forces that animate black holes, Page concedes that the hypothesis cannot be proved, but he maintains it is a tenable alternative. Other standing possibilities include Hawking's and a curious one (bonanza for historians) by which the past is entirely predictable from a knowledge of the future but not vice versa. □

Feb. 16 solar eclipse

A total solar eclipse will cross Africa and Southeast Asia Feb. 16 beginning at 2:12 a.m. EST and will allow researchers a unique chance to study the sun at maximum sunspot activity. National Science Foundation and NASA-sponsored studies will focus on the structure of the sun's atmosphere, changes in the earth's upper atmosphere and effects of ultraviolet sources on electron activity. □