AFFECTS PROSTAGLANDINS

How aspirin works

The mechanism of probably the most widely used medication in the world—aspirin—has eluded discovery for many years. Now two teams of London researchers, for a long time unaware of each other's research although they worked down the corridor from each other, have come up with an identical, well-documented and reasonably cogent explanation. It is that aspirin inhibits synthesis of prostaglandins, local hormone-like regulators that affect various organs and tissues. Prostaglandins are fast becoming one of the hottest research subjects in the biological sciences (SN: 10/10/70, p. 306).

Using guinea-pig tissue, Dr. John Vane of the Pharmacology Department of the Royal College of Surgeons in London found that three aspirin-like drugs impede synthesis of a particular prostaglandin. The drugs used were sodium aspirin, indomethacin and sodium salicylate, which is used to treat rheumatoid arthritis. Then with two colleagues, Drs. Sergio Ferreira and Salvador Moncada, Dr. Vane showed that aspirin and indomethacin block the release of prostaglandin from the spleen.

Working independently in the RCS Pharmacology Department, Drs. J. Bryan Smith and Anthony Willis found that platelets in the blood of volunteers who took aspirin were no longer able to produce prostaglandin.

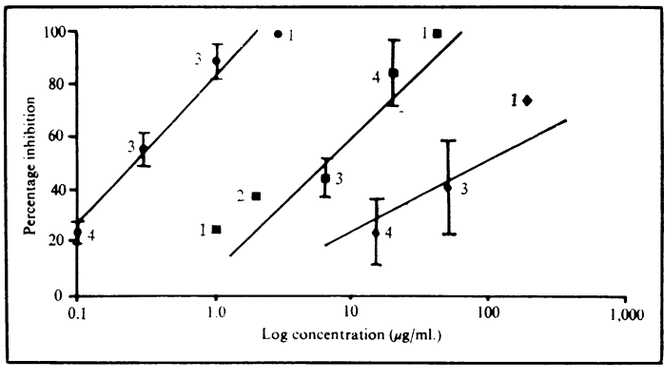
The demonstration that aspirin interferes with the local synthesis of prostaglandins may account for some of its therapeutic uses. The way in which aspirin reduces fever is linked with the observations in the past year or so that the prostaglandins are themselves among the most potent inducers of fever. In the same way, there is good reason to believe that the prostaglandins are implicated in the production of inflammation, so that a drug that inhibits the production of prostaglandins should be effective in reducing inflammation.

The RCS discoveries may also explain why intrauterine devices are not always successful in preventing pregnancy. Some, but by no means all, scientists speculate that IUD's work by stimulating the release of prostaglandins. If this is so, then taking aspirin while using an IUD might spark operational failure.

But Dr. Vane says there is at present no reason to believe that the sensation of pain is mediated by the prostaglandins, so there is no ready explanation for aspirin's analgesic activity. If anything, evidence suggests that the analgesic effects of aspirin may be more psychological than physiological, since it is difficult to demonstrate in controlled trials that the drug really does have an analgesic action separate from placebo effects. Moreover, how aspirin inhibits prostaglandins at the biochemical level is still unknown. Most drugs are believed to work by interfering with one or more of the cell's macromolecules, such as genes or enzymes.

Dr. Vane foresees two crucial spin-offs from his and his colleagues' work. First, the ability to block prostaglandin synthesis with aspirin-like drugs will open up a whole new field of experimentation aimed at elucidating roles of the ubiquitous prostaglandins. Second, a precise understanding of aspirin's action will allow better aspirin-like drugs to be developed. For instance, it may be possible to design drugs that will inhibit the synthesis of prostaglandins by the skin, while leaving untouched those in the stomach. This might well elimate the gastrointestinal side effects of drugs used to treat rheumatoid diseases. Aspirin-type drugs are now given in massive doses to keep body temperatures down in cases of rheumatic fever. The development of more effective treatment has been hampered by uncertainty about how aspirin does its job. Now much-improved drugs for rheumatic fever may became possible.

Among the many who attempted to explain the action of aspirin before the RCS teams came up with definitive evidence, perhaps the most prescient was Dr. Harry Collier of Miles Laboratories in Buckinghamshire, England. Dr. Collier suggested in the early 1960's that aspirin performs an "antidefensive" role, checking an over-exuberance on the body's part in mounting defense actions to various diseases. Within the last few years the prostaglandins have been increasingly implicated in these defensive reactions. □



Three aspirin-like substances inhibit prostaglandin activity.

Vane/Nature

BLAMED IN DEATHS

Soyuz seal failure

The report was terse. Moscow, July 12, Tass: "From the government commission for investigating the causes of the death of the Soviet pilot-cosmonauts G. T. Dobrovolsky, V. N. Volkov and V. I. Patsayev.

"After studying the recordings of the flight parameters for the Soyuz 11 spaceship, it has been established that up to the descent trajectory the ship's flight proceeded normally. The cosmonauts . . . performed according to the flight program.

"On the ship's descent trajectory, 30 minutes before landing, there occurred a rapid drop of pressure within the descent vehicle, which led to the sudden death of the cosmonauts. This is confirmed by the medical and pathological-anatomical examinations.

"The drop in pressure resulted from a loss of the ship's sealing. An inspection of the descent vehicle, which made a soft landing, showed that there are no failures in its structure.

"A technical analysis allowed to establish a number of probable causes of the seal failure, the study of which continues."

Worldwide speculation amidst the shock over the June 30 deaths had been rampant (SN: 7/10/71, p. 22) over not only the cause but also the effects they would have on both Soviet and American space programs. News from a sorrowing Moscow, however, portrayed not a faltering space program but one determined to forge ahead with continued manning of Salyut.

It was not the Soviet Government but Victor Louis, a reporter for the London Evening News and a Soviet citizen, who first wrote that the cabin pressure loss resulted from a faulty sealing of the hatch following the undocking with Salyut. Force exerted on the hatch during reentry jerked the seal open, he said. While the official report does not eliminate this possibility, it indicates that several things could have caused the loss of sealing.

On the day of the tragedy, the National Aeronautics and Space Administration said there would be no significant changes in the American space schedule. The Apollo spacecraft differs from Soyuz. While the Soyuz cabin has about one atmosphere of pressure of a

mixed gas (80 percent nitrogen and 20 percent oxygen), the Apollo has only one-third of an atmosphere of pure oxygen. Any loss of oxygen or pressure would occur more slowly. For example, if a half-inch hole was created the astronauts would have five minutes to suit up. Apollo also has many redundant systems Soyuz doesn't have.

Despite these differences, NASA was expected to announce soon that the Apollo 15 astronauts due to be launched toward the moon July 26 (SN: 7/10/71, p. 28) will suit up—just to be safe. This change will occur at least once on the mission during the time most comparable to the Soyuz-Salyut separation—the jettisoning of the ascent stage of the lunar module. David Scott, James Irwin and Alfred Worden will put on "soft suits"—the same suits that are worn on the lunar surface, but not pressurized. They can be pressurized within seconds should an emergency arise. No crew has suited up for LM jettisoning since the Apollo 9 crew did in March 1969. □

DEBATE ON AEROSOLS

Question for the (ice) ages

The question of the extent to which man may be inadvertently modifying the earth's climate by tampering with the composition of the atmosphere has aroused concern and controversy throughout the scientific community. The concentration of atmospheric carbon dioxide, the agent that slows down surface cooling, has increased by seven percent in the last few decades. At the same time, some meteorologists have blamed an observed cooling of world climate on increases in the amount of fine particles, called aerosols, in the atmosphere (SN: 11/15/69, p. 458).

Drs. S. I. Rasool and S. H. Schneider of the National Aeronautics and Space Administration's Goddard Institute for Space Studies have made separate estimates of the climatic effects of increases in the concentration of carbon dioxide and dust in the atmosphere.

To perform their calculations, they adopted a model atmosphere that reflects present-day global conditions and then calculated the effects of carbon dioxide increases. A doubling of carbon dioxide produced a temperature increase of 0.8 degrees C. in the troposphere, they report in the July 9 SCIENCE. But as more carbon dioxide is added, the rate of temperature increase declines and eventually levels off. Even an increase by a factor of eight—an increase the researchers believe is highly unlikely in the next several thousand years—produced an increase in surface temperature of less than two degrees.

Calculating the effects of aerosols was much more complicated, since particles, depending on their composition, number, size and shape, will scatter and absorb both radiation from the sun and heat radiated from the earth. Drs. Rasool and Schneider estimated the magnitude of scattering and absorption of visible and infrared radiation by typical atmospheric aerosols. They found that aerosols produced surface cooling, the rate of cooling increasing with greater opacity of the aerosols.

Several recent studies have indicated that the dust content of the atmosphere may have doubled in the last 60 years. The NASA scientists also point to estimates that man's potential to pollute will increase six- to eightfold in the next 50 years. If this increased rate of injection of particulate matter into the atmosphere were to raise the present opacity by a factor of four—an increase that cannot be ruled out as a possibility in the next hundred years—Drs. Rasool and Schneider calculate that the mean surface temperature of the earth could be lowered by as much as 3.5 degrees C.

A temperature decrease of this magnitude, if sustained over a period of several years, might be sufficient to trigger an ice age, the scientists said in their report. In the week since its publication, that statement has received considerable attention, but Dr. Rasool said this week that it was not meant as a prediction of an impending ice age but was intended merely to emphasize the importance of a global change of even a few degrees.

Even with a radical decrease in temperature, points out Dr. J. Murray Mitchell Jr. of the National Oceanic and Atmospheric Administration's Environmental Data Service, an ice age must await cooling of the oceans, a process that would take several centuries. Also, though he agrees with the NASA scientists' calculations on a global scale, Dr. Mitchell says the problem of climatic change as a result of pollutants is much more complex locally, and that the moistness of the underlying surface must be taken into account, (SN: 4/24/71, p. 274). □

The poetry of plate tectonics

The theory of plate tectonics has revolutionized thinking in all the geological sciences in the last few years, so maybe it's not too surprising that it has also inspired some poetry. It isn't Shakespeare, but then scientific reports in the journal NATURE, where this venture into geo-verse appeared last week, don't usually read like the scripts of Elizabethan plays either. Some excerpts from the "paper" by earth scientists B. C. King of Bedford College in London and G. C. P. King of Cambridge University:

They put a girdle round the Earth
And named it the Worldwide Rift;
It helps explain the ocean floor
And Continental Drift.

Vine and Matthews sailed away
Exploring the ocean bed;
It took much longer getting them back;
They said it was seafloor spread.

It appears that the oceans were mostly formed
By Cenozoic streams
Of mantle flooding up the cracks
And gumming up the seams.

* * * *

And so the plate has been revived
In present day tectonics,
Though sial and sima still remain
As crustal term mnemonics.

Both kinds of crust now constitute
The grander types of plates
And as they move upon the Earth
They suffer subtle fates.

The edges which are growing still
Are hid beneath the oceans,
While those around the island arcs
Show self-consuming motions.

Yet others seem to hit or slide
Performing curious functions,
And where they can't make up their minds
You there have triple junctions.

On continents the crustal plates
Are edged by earthquake foci,
And little plates proliferate
By joining up the loci.

As alchemists once sought the stone
For magic transmutations,
The motions of the plates are shown
By seismic computations.

Geologists naively thought
That rifts were due to faulting,
By subsidence of crustal strips
Along a pre-rift vaulting.

Their evidence was solely based
On visual observations
Of structure and stratigraphy
And such out-moded notions.

But others now hold better views
And think that each "mañana"
Brings Africa a step more close
To the fate of old Gondwana.

McKenzie sees his moving plates
Wedging the rift asunder,
And one day ships will sail the rift
To maritime Uganda.