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.

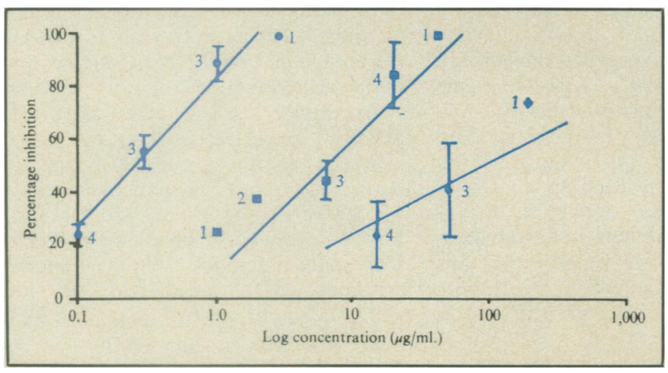
**The demonstration** that aspirin interferes with the local synthesis of prostaglandins may account for some of its therapeutic uses. The way in which aspirin reduces fever is linked with the observations in the past year or so that the prostaglandins are themselves among the most potent inducers of 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