Send information for publication on this page to:
Sam Lee Pool, M.D.
18711 Prince William
Houston, TX 77058

SPACE MEDICINE BRANCH REPORT

SALIVA: A WAY TO OBTAIN SPECIMENS IN AN OPERATIONAL SETTING

Dr. Phil Johnson

The observation that a wide range of physiological and biochemical changes occur during exposure to microgravity suggested that microgravity-induced changes might alter the pharmacodynamics of drugs administered during weightless flight. These changes might affect drug absorption as had been suggested by Dr. Leach who was instrumental in starting the NASA pharmacodynamics group. It might also cause metabolism changes as a result of altered blood flow to the kidneys and liver. For NASA flight surgeons, this possibility is of considerable clinical significance since many crewmembers experience space sickness during the first 48–72 h of orbital flight and because returning crewmembers regularly show decreased tolerance to upright posture in gravity. Both sets of symptoms should be preventable or should at least be ameliorated with targeted pharmacological interventions. Most crews have no medically trained member on board so parenterally administered medications are both inconvenient and are not preferred by a symptomatic individual about to be injected by an inexperienced fellow crewman. There are other problems with administering drug therapies in orbit since the most common and important crew afflictions are regularly associated with nausea and, in extreme cases, regurgitation at irregular and unpredictable intervals. Loss of stomach contents likely would include any recently ingested medication. Some NASA personnel believe that this space sickness is associated with cessation of small bowel motor activity so that ingested medications might remain in the stomach for considerable periods delaying the time to reach therapeutic levels and possibly making the medication ineffective.

Classic pharmacology regularly uses invasive methods, such as multiple venopunctures, to follow the absorption and disposition of experimental drugs. In operational missions it is not practical to obtain multiple blood specimens from crewmembers busy with other duties. There are other problems also. The crewmembers generally have only the rudimentary medical training given them by the flight surgeons as a minor part of preflight preparations. These lectures contain just enought information to help the crew in emergencies to respond correctly to suggestions from the flight surgeon in Mission Control. Because there is no way to process blood samples in the Shuttle Orbiter, it would be necessary to bring along a relatively heavy and power-hungry centrifuge to process blood samples. There is no freezer available to store samples until the end of a mission. Even a simple icebox is not ordinarily carried in the Shuttle. NASA scientists and flight surgeons have realized these problems but, until recently, no one has come forth with a practical way to solve them without using a dedicated Shuttle mission with subjects willing to stop what they are doing to allow an inexperienced phlebotomist to obtain multiple blood specimens.

JSC scientists Dr. Nitza Cintron and Dr. James Vanderploeg combined their talents with Northrup Services scientist Dr. Lakshmi Putcha and suggested that drug absorption might be measured by the use of salivary samples, which require no special handling or storage. In practice, a cotton ball or small section of dental dam is placed in the mouth and allowed to saturate with saliva. It is then formed into a cylinder by the tongue and pushed into a test tube, which is sealed. Postflight, as much as 1 ml of saliva can be expressed from each collection. In addition, from a crewmember's point of view, expectorating into a tube is a lot more fun than allowing someone to draw your blood.

For the first studies, a drug was needed that was familiar to the crews, would not produce noticeable side effects, and was known to be safe for nearly everyone. As might be predicted, an over-the-counter medication was preferred. After considerable discussion, acetaminophen was chosen as a first demonstration drug since it is already being used as a treatment for headaches and minor pains by orbiting crewmembers. Preliminary JSC laboratory studies showed that acetaminophen is found in detectable levels in the saliva and that salivary/plasma ratios remain close to unity over a wide range of plasma concentrations.

In the first study, an orbiting crewman afflicted with space sickness showed erratic salivary concentrations compared to the matched preflight control study. This suggests, as has been suspected but never proven, that gastrointestinal function changes during symptomatic space sickness. After the crewman had recovered and during a time when he felt well, the peak concentration was decreased and the time to peak was delayed, indicating a decreased rate of absorption. While this is an N of 1, it did confirm anecdotal comments by other crewmembers from previous missions that, while they were in orbit, drugs seemed to take longer before a salutary effect was noted. In this study, the elimination half-time did not show a difference from control, suggesting that liver-kidney function in relationship to this drug's metabolism was unchanged in microgravity.

There are plans to try to use and study other drugs which also are excreted in the saliva and which show nearly constant salivary/plasma ratios through wide ranges of concentrations. Generally, any drug which distributes into total body water should appear in the saliva. The space sickness medication most commonly taken by susceptible individuals is a combination of scopolamine and dextroamphetamine. This combination medication was studied one time in one crewman while in orbit but, unfortunately, the samples obtained were unsatisfactorily small. Perhaps this resulted because these drugs decrease the rate of salivary production. There are plans to repeat this study in future missions. Further drug testing is planned to obtain statistically valid numbers.

Obtaining salivary samples seems to be popular with crewmembers who have participated so far since they, like almost anyone, would prefer not to experience the pain and inconvenience of multiple blood specimens. NASA management likes this program since it is a low budget, low power, and low weight way of obtaining operationally significant data. Salivary specimens to obtain endocrine measurements were suggested and studied by Dr. Craig Fischer, who directed the Clinical Laboratories at the Johnson Space Center during the Gemini-Apollo era. In those early days, a cup was attached over the parotid duct to quantitatively collect the needed, relatively uncontaminated, saliva samples. While studies were undertaken, the salivary collection cups were never used in flight. Until the present series of inflight drug studies, no NASA scientist had taken advantage of salivary samples to eliminate inflight phlebotomies.

These bright investigators have demonstrated a way to obtain valid drug absorption data under the operational constraints of a routine Shuttle mission. Perhaps other members of this Space Medicine Branch might find ways to use salivary specimens for this or other purposes. Salivary collections may be a convenient way to advance the field of aerospace physiology when the investigator must use subjects involved in operational activities. We look forward to the continuation of this innovative approach to space medicine research.

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