Meetings

Dimethyl Sulfoxide

The New York Academy of Sciences recently sponsored an international conference on dimethyl sulfoxide (DMSO), the remarkable and controversial solvent which has so many potential uses. The conference was arranged in cooperation with Stanley W. Jacob and Edward E. Rosenbaum (University of Oregon Medical School) who, with Robert J. Herschler (Camas, Washington) were among the first to suspect possible value in medicine of DMSO.

Extending for 3 days, various sessions of the conference were chaired by Norman David (University of Oregon Medical School), Murray Sanders (Fort Lauderdale, Florida), Kenneth Williams (Shrewsbury, Massachusetts), Marion Sulzberger (San Francisco and New York), Thomas Dougherty (Salt Lake City), Gordon McHardy (New Orleans), Arthur Scherbel (Cleveland, Ohio), and Albert Kligman (University of Pennsylvania).

A feature of the conference was an evening meeting on scientific and public responsibilities in evaluation of new drugs, chaired by Irving Wright (Cornell University Medical School). Jean Weston (AMA) discussed principles of drug evaluation, while Frank Fremont-Smith (New York Academy of Sciences) called for cooperation among scientists, clinicians, and public agencies in appraising new drugs. Arthur Ruskin (FDA) discussed public responsibilities in drug development, and Raymond McKeown (AMA) emphasized the responsibilities of members of the health professions in judging the value of drugs.

The conference opened with a discussion by Warren MacGregor (Camas, Washington) and David Rammler (Palo Alto) on the complex physical and chemical properties of DMSO. It was first synthesized by Alexander Saytzeff in 1866 and is now derived chiefly from lignin in the manufacture of paper. Crown Zellerbach Corporation holds a process patent on its preparation. Like ethanol, it mixes freely with water with the evolution of heat, and lowers the freezing points of aqueous solutions. Its molecule is pyramidal with sulfur, oxygen, and carbon at the corners. Due to the polarity of the sulfur-oxygen bond, the liquid has a high dielectric constant. The basicity of DMSO which results from enhanced electron density at the oxygen atom is slightly greater than that of water. DMSO forms crystalline salts with strong protic acids and coordinates with Lewis acids. It modifies hydrogen bonding.

M. J. Ashwood-Smith (Harwell, England) described the important cryoprotective properties of DMSO with regard to biological fluid and cellular systems. He also reported on its radioprotective effects. Both of these protective activities of DMSO may be associated with its relation to hydrogen bonding.

The absorption, distribution, fate, and excretion of DMSO with regard to living material was described in a series of reports from Erich Gerhards (Berlin), Charles W. Denko (Ohio State University), Karl-Heinz Kolb and colleagues (Schering Isotope Laboratories, Berlin), and others. The compound is rapidly absorbed and distributed in living material, loses its oxygen, and is excreted in part as dimethyl sulfide, which in mammals may give a garlic-like odor to the breath. Studies with radioactive sulfur in DMSO show that sulfur from the compound may remain in the sulfur pool of the body for several days.

Extensive toxicity studies on single and repeated dosage of DMSO were reported by Emil Smith and associates (Worcester, Massachusetts). Previous reports of low toxicity in mammals were confirmed. Clare Peterson and Ralph Robertson (University of Oregon Medical School) found no significant physiological changes with single intravenous doses as high as one gram per kilogram body weight in dogs. Fernand Caujolle and co-workers (Toulouse, France) reported predictable teratogenic effects from DMSO solutions injected into incubating chicken eggs. Caujolle, however, found no teratogenic effects after administering DMSO orally or intraperitoneally to pregnant rats or rabbits until lethal doses were attained.

The solvent and penetrant properties of DMSO have led to its wide testing in agriculture. R. Garren (Oregon State University) reported on the rapid uptake and distribution of labeled DMSO in plants when applied to leaves or stems. He noted its use as a carrier for nutritive element transport in pears and strawberries. Harry Keil (U.S. Department of Agriculture) reported better control of plant diseases with antibiotics in lower amounts when applied in solutions of DMSO, as in the case of bacterial leaf-spot disease of peaches. It was noted by L. Sciuchetti (Oregon State University) that growth and alkaloid content of drug-producing plants, such as *Datura*, are enhanced not only by growth regulators applied in DMSO but also by DMSO alone. C. Leonard (University of Florida) reported favorably on the use of DMSO as a carrier for iron salts in foliar applied sprays to citrus.

Dermal toxicological studies of DMSO in humans, documented by Albert Kligman (University of Pennsylvania) reveal that it releases histamine from mast cells in the skin. This is associated with skin reactions often noted on cutaneous application, as well as with occasional allergic manifestations. D. L. Berliner and A. Ruhmann (University of Utah) noted reversible inhibition of fibroblastic proliferation under the influence of DMSO, and C. Monder and M. Takayanagi (New York) described its use in isolating cell nuclei.

Ocular effects of DMSO were considered in detail. L. Rubin and K. Barnett (University of Pennsylvania and Cambridge University) reported that high doses given orally or topically for several weeks were followed by changes in the refractive power of the lens in swine, dogs, and rabbits. D. Wood and associates (Portland, Oregon) found no effects from direct application of varying aqueous solutions from 10 percent to full strength into the eyes of albino rabbits for a total dosage of between 0.1 and 0.2 g/kg body weight per day for 6

months. However, rabbits receiving daily doses as high as 10 g/kg orally or topically showed lines of discontinuity in their lenses. No cataract was seen after 10 weeks of such daily treatment, although discontinuous lens lines could be detected in about 2 weeks by slit-lamp examination. Chemical studies on these lenses revealed reduction in the usual concentrations of urea, glutathione, uric, and amino acids. Topical application at 10 g/kg daily was found to produce less chemical change and significantly less lens effect than oral administration. After high oral doses given daily for 3 weeks to dogs, Kurt-Eberhard Kleberger (Free University of Berlin) found increasing myopia in the center of the lens with increasing hyperopia toward the periphery.

D. Gordon (Cornell University Medical School) reported on 115 patients with ophthalmological disorders which were treated by daily intraocular applications of DMSO solutions for 1 to 15 months. Those suffering from corneal edema were benefited, and no untoward effects were noted, except in one 17-year-old boy under treatment for uveitis; he showed a lens opacity after 5 months. Since this condition did not increase during the subsequent 10 months with the same treatment, it was not believed to be related to DMSO. It was noted that hospital admissions indicate an incidence of 7 percent actual or incipient cataract in the general population. Gordon further noted no lens alteration in before-and-after ophthalmological examinations in 25 patients treated with up to 30 ml of DMSO topically applied daily for 19 months for various musculoskeletal disorders. G. Laudahn (West Berlin) described a slit-lamp study of the eyes of 40 patients receiving 22 ml of DMSO topically applied daily for 3 months. None had any change in lens.

Many reports were made on various aspects of the pharmacological actions of DMSO. Often its action was said to be similar to that of ethanol. Herbert and Nora Davis and Ann Clemons (University of Nebraska) demonstrated its procoagulant and nerve-blocking effects. H. J. Mallach (University of Tubingen) noted certain synergistic effects between DMSO and ethanol, and found that DMSO seems to aid in clearing alcohol from the circulation in mammals. G. F. Potts (Greenville, South Carolina) and his co-workers showed that DMSO is bacteriocidal in concentrations of more than 20 percent, but that it has no effect on antibiotics nor does it inhibit penicillinase. David Rammler (Palo Alto) reported that the mild action of DMSO on purified enzyme systems is *p*H dependent. Morgan Miller and John Ward (University of Utah) found that localized Shwartzmann phenomena are reduced by DMSO. M. C. Braude and R. R. Monroe (University of Maryland) told about the mild reserpine-like action of DMSO, and its lowering of thresholds to tonic convulsions induced by pentylenetetrazol in mice. W. M. Sams and his collaborators (San Francisco) reported that the slight cholinergic activity of DMSO is due to its inhibition of cholinesterase.

It was noted by G. L. Beckloff and H. J. Lerner (New Brunswick) that the instillation of undiluted DMSO for 1 hour daily into the bladders of dogs resulted in no structural or functional changes. This experimental study is important, since it was found by Lester Persky and Bruce Stewart (Cleveland) that the bladder instillation of 50 ml of 50 percent DMSO is very beneficial in the treatment of interstitial cystitis.

The effects of DMSO on skin were well described. T. J. Franz and J. T. Van Bruggen (University of Oregon Medical School) noted the high permeability coefficient of DMSO in a model frog-skin membrane system; they found osmotic effects and ability to facilitate movement of small molecular weight substances. Marion Sulzberger and his companions (Letterman General Hospital, San Francisco) showed penetration of dyes in DMSO solution through the stratum corneum of the skin but not below. DMSO increases penetration of low molecular weight allergens such as penicillin G, but not large molecular weight allergens, such as house dust. Rapid and deep penetration of DMSO into the horny layer aids in effectiveness of antibiotics and bacteriocidal agents in clearing pyodermas, dermatophystoses, and acnes. DMSO was being studied as a penetrant solvent for insect repellants for topical use on hands and heads. On single application of such repellants in DMSO solution there is penetration into the horny layers of skin with slow extrusion over several weeks, which could aid in reducing malaria and other insect-vectored diseases in such infested areas as Vietnam.

H. I. Maibach and R. J. Feldman (University of California, San Francisco) found a threefold increase in skin penetration of C-14 steroids when dissolved in DMSO over that obtained with conventional preparations. D. L. Gunberg and T. I. Djan (University of Oregon Medical School) showed effective functional response in rats to estradiol transported by DMSO through the skin. A. M. Kligman (University of Pennsylvania) found no significant untoward skin effects from long continued daily application of DMSO solutions. Leon Goldman and associates (University of Cincinnati) reported favorably on 1300 dermatological patients treated with topical applications of DMSO alone and in combination with steroids. He noted no significant skin reactions. M. Engel (Brunswick, Georgia) demonstrated histological improvement of keloids in patients treated with topical DMSO solutions. There was evidence of softening of collagen bundles.

W. Frommhold and companions (Berlin Auguste-Viktoria Hospital) found improvement, on the application of DMSO solutions, in subcutaneous fibrosis due to irradiation for malignancy. There was a gradual softening, with reduction in the size of the induration. This was accompanied by an increased rate of urinary excretion of hydroxyproline. Similar urinary increase of hydroxyproline was reported by A. Scherbel (Cleveland Clinic) following the successful use of topical DMSO solutions in scleroderma patients. G. Gries and colleagues (West Berlin) also correlated increased urinary excretion of hydroxyproline with reduction of symptoms in patients with swelling of tendons and connective tissue when treated with DMSO solutions.

Several reports were made on the use of DMSO in veterinary practice. M. B. Teigland and V. R. Saurino (Florida Atlantic University) observed anti-inflammatory response to DMSO solutions applied locally on open wounds and traumatic injuries in horses. Application of dilute DMSO was followed by improvement in bursitis and synovitis in 80 percent of a large number of equine subjects. This was further studied by hypersensitization to human gamma globulin which resulted, on antigen challenge, in massive erythema, necrosis, and slough, but which could be dramatically reduced by undiluted DMSO applied locally each hour after challenge. R. P. Knowles (University of Miami) found DMSO useful in relieving traumatic injuries to joints and muscles in racing

greyhounds, as a decongestant in mammary gland engorgement in dogs, and as a vehicle for various medicaments in skin disorders, including scabies. C. D. Dake (Ontario, Oregon) reported that intraperitoneal injections of 4 ml of 90 percent DMSO greatly reduces the usual high mortality of feline panleukopenia. F. Levesque (St. Hyacinth, Quebec) noted that topical application of 90 percent DMSO to open skin wounds in horses promotes granulation with healing within 10 days. R. Hill and D. Sasmore (Palo Alto) observed sedative effects in dogs from 10 ml/kg body weight of 90 percent DMSO given orally, and confirmed its efficacy on topical application in musculoskeletal disorders in dogs.

The possibility that DMSO might be carcinogenic was ruled out by several studies. W. S. Fletcher and D. L. Dennis (University of Oregon Medical School) found that DMSO causes nonfacilitation in the induction of breast cancer in rats. J. R. Armstrong and I. Cohn (Louisiana State University) could find no increase, after DMSO administration, in the incidence of tumors following implantation of cancer cells in rabbit peritoneal cavities. R. Schrek (Hines, Illinois) reported that 2 percent DMSO on incubation with suspended cells is much more cytotoxic for leukemia lymphocytes and myeloblasts from leukemic patients than for ordinary lymphocytes from healthy persons. J. E. Ayre and J. LeGuerrier (National Cancer Cytology Center, New York City) showed the clinical value of DMSO with growth-inhibiting chemicals in treating cancer of the cervix, and also found DMSO solutions useful in obtaining cervical smears for cytological examination. Florence Seibert and her colleagues (Cancer Research Laboratory, St. Petersburg, Florida) reported that 25 percent DMSO inhibits in vitro growth of pleomorphic organisms isolated from human tumors. J. T. Mallams and associates (Baylor Medical School, Houston) indicated that increased oxygenation of tumor tissue by intravenous infusions of dilute solutions of hydrogen peroxide with DMSO might be helpful in controlling malignant spread.

Baylor clinicians, J. A. Finney and associates, also successfully used hydrogen peroxide solutions in DMSO during experimental studies on ischemic hearts in pigs. It was found that DMSO in dilute solution alone could furnish enough oxygen to give protection. Other studies were reported on DMSO penetrability. G. Weissman (New York University) found that DMSO seems to enhance the action of endogenous steroids, and suggested that this might be due to better penetration at their sites of action on lysosomal membranes. H. John and G. Laudahn (Berlin), using plethysmographic methods, demonstrated objective improvement in peripheral arterial insufficiency in a large number of patients who were treated topically with DMSO. Referring to topical applications of DMSO as a "chemical hot-water" bottle, G. E. Bradham and J. Sample of the Medical College of South Carolina showed on dogs that the thermal effect of skin applications of DMSO solutions extends into the muscles beneath.

In burn injury studied experimentally, DMSO was not found to be helpful. F. L. Ashley and co-workers (University of California at Los Angeles) studied thermal edema in the legs of rabbits, and noted that leg volume was the same for treated and untreated groups at 3 and 24 hours, but that the leg volume was less at 6 hours in the animals treated with DMSO topically than in the controls. It was indicated in discussion that DMSO might aid in reducing pain and swelling in first- and second-degree burns, but that it would not be helpful in promoting healing in third-degree burns.

Clinical reports given at the conference were many and varied. J. F. Adamson (Norfolk, Virginia) noted that topical application of 70 percent DMSO four times daily prevents thrombosis and sloughing in pedicle flaps in skin surgery. In some 500 patients with problems connected with the ear, nose, and throat, M. Asen (West Berlin) found DMSO locally to be helpful as well as a useful solvent for antibiotics. L. Blumenthal (George Washington University) found that headaches induced by muscle tension would yield to DMSO applications on involved muscles. It was reported by Austin Kutscher and colleagues (Columbia University) that topical application of 70 percent DMSO helps to clear gingivitis without indication of untoward effect. In a double-blind study of pain relief after thoracotomy, D. S. Penrod and associates (Pennsylvania Hospital) found consistent benefit from postoperative local application of DMSO along the line of incision, with reduction in inflammation. On the other hand, I. C. Arno and colleagues (Albert Einstein Medical Center, Philadelphia) found no effect from DMSO applied topically in an attempt to reduce pain after postpartum episiotomy. However, J. L. Parsons and coworkers (Tucson) reported benefit from DMSO applied locally to "frozen shoulders," with marked reduction in pain on the first application in about half the patients and with anti-inflammatory effect in all. In recommending interval therapy, Marvin Paul (Toronto) noted high incidence of improvement in chronic musculoskeletal disorders with topical application of only 0.2 g/kg diluted DMSO twice weekly. All clinical reports emphasized relative lack of untoward effects, while admitting mild local erythema, itching, and garlic-like odor of the breath.

One of the most important clinical reports came from Arthur Scherbel and his colleagues (Cleveland Clinic), who found that the skin application of DMSO solutions was the first form of treatment to show real benefit in scleroderma. In their study, 26 of 42 patients with this peculiar disease were considerably improved with DMSO therapy.

The most intensive clinical study was reported by H. John and Gerhard Laudahn (Free Univesity of West Berlin). In 1025 patients with acute musculoskeletal traumatic injuries, there was 86-percent overall improvement with topical application of 2 to 5 ml of 90 percent DMSO thrice daily. In 3155 cases of chronic calcified bursitis and localized arthritis, objective improvement, including radiographic disappearance of calcifications, was noted with complete remission of symptoms in 49 percent, partial relief in 35 percent, and no relief in 16 percent. No serious untoward effects were seen. About half the patients got an unpleasant taste or garlic-like breath, but local dermatitis appeared in less than 1 percent. This report supplemented one given at the Berlin DMSO symposium held in July 1965. The proceedings were edited by Dr. Laudahn (*Dimethyl sulfoxide: DMSO*, Saladruck, Berlin, 1965, 126 pp.). Results on many similar patients, as reported by G. Boost (Palo Alto) and C. M. Demos (New Brunswick), were in essential agreement with the German experience. Demos used an average dose of 0.1 to 0.2 g/kg per day.

Takashi Sugiyama (Tokyo University School of Medicine) reported on 274 representative cases of rheumatoid arthritis selected from 20 Japanese medical centers by the Committee on Clini-

cal Drug Testing of the Japanese Rheumatism Association. Effectiveness was demonstrated in cases with grades I and II of rheumatoid arthritis. It was found that 90 percent DMSO applied topically was better than 50 percent, with both concentrations significantly superior to propylene glycol controls, using measurements of strength of grip, range of joint motion, and freedom from pain on pressure. Local skin irritation was greater with the higher concentration of DMSO. However, J. Zuckner and J. Uddin (St. Louis University Medical School) found only 30 percent improvement in 32 patients with rheumatoid arthritis followed for 1 month on topical DMSO, and with no suppression of immunological processes. M. Lockie (New York State University at Buffalo) described pain relief following topical DMSO in 23 of 27 patients with varying extent of rheumatoid arthritis. In various arthritic conditions, P. I. Day (University of Texas, San Antonio) confirmed patient benefit with topical DMSO in some 1000 patients, and noted fewer side-effects than with conventional therapy. A. Steinberg (Philadelphia) also confirmed patient benefit in various joint conditions, emphasizing the anti-inflammatory effect of DMSO and its value in steroid transport.

In a careful clinical study, using double blind methods, J. H. Brown (Seattle) found 10 percent DMSO applied locally in acute musculoskeletal injuries could serve as a placebo, whereas 60 percent to 90 percent DMSO gave significant improvement in 75 percent of the patients. R. Turner (University of California, Los Angeles) stressed the value of locally applied DMSO in speeding recovery from athletic bruises.

In reference to the penetrant properties of DMSO, V. Breckner and associates (University of California, Los Angeles) noted that 5 percent tetracaine base in undiluted DMSO achieves deep and lasting anesthesia of intact human skin. Intriguing was the indication by E. Ramirez and S. Luza (University of Peru Medical School, Lima) that DMSO may pass the blood-brain barrier, in showing that 5 ml of 80 percent DMSO intramuscularly thrice daily for 3 days may induce preconvulsive states as indicated by EEG, and will alert deeply depressed patients to helpful psychotherapy.

In concluding the 3-day session, in which 79 reports were opened for discussion, I ventured the remark that the well-known legal principle of *res ipsa loquitur* might well apply to the situation involving DMSO, and that rarely has a new drug come so quickly to the judgment of the members of the health professions with so much verifiable data from so many parts of the world, both experimentally and clinically, as to safety and efficacy.

CHAUNCEY D. LEAKE
San Francisco Medical Center,
University of California,
San Francisco

Forthcoming Events

July

5–8. **Lens Design** with Large Computers, intern. conf., Rochester, N.Y. (Inst. of Optics, Univ. of Rochester, Rochester 14627)

5–9. Technical and Industrial **Communications**, 9th annual inst., Colorado State Univ., Fort Collins. (B. K. McKee, Inst. in Technical and Industrial Communications, Rm. 322 Liberal Arts, Colorado State Univ., Fort Collins 80521)

5–9. American Soc. of **Pharmacognosy**, 7th annual mtg., Univ. of Minnesota, Minneapolis. (L. C. Schramm, College of Pharmacy, Univ. of Minnesota, Minneapolis 55455)

6–7. **Space Flight Mechanics**, specialist conf., Denver, Colo. (R. S. Novosad, Martin-Marietta Corp., Mail No. A127, Denver 80201)

6–8. Space and Ballistic **Missile Technology**, 11th symp., U.S. Air Force Academy, Colo. (C. T. Morrow, Aerospace Corp., P.O. Box 95083, Los Angeles, Calif. 90045)

6–9. National Soc. of **Professional Engineers**, annual mtg., Minneapolis, Minn. (The Society, 2029 K St., NW, Washington, D.C. 20006)

9–15. **Medical Women's** Intern. Assoc., 10th congr., Rochester, N.Y., and Niagara Falls, Ont. (The Association, 1790 Broadway, New York 10019)

10–15. **Power**, mtg., Inst. of Electrical and Electronics Engineers, New Orleans, La. (E. C. Day, IEEE, 345 E. 47 St., New York 10017)

10–16. American **Library** Assoc., annual conf., New York, N.Y. (D. H. Clift, 50 E. Huron St., Chicago, Ill. 60611)

11–14. **Aerospace Systems**, conf., Seattle, Wash. (Inst. of Electrical and Electronics Engineers, 345 E. 47 St., New York 10017)

11–15. International Council for **Bird Preservation**, world conf., Cambridge, England. (The Council, c/o British Museum of Natural History, Cromwell Rd., London S.W.7)

11–15. Use of **Isotopes in Milk Technology**, seminar, Munich, West Germany. (Intern. Agency Liaison Branch, Office of the Director General, Food and Agriculture Org., Via delle Termi di Caracalla, Rome, Italy)

11–15. **Weights and Measures**, 51st natl. conf., Denver, Colo. (Executive Secy. of the Conference, National Bureau of Standards, Washington, D.C. 20234)

11–16. **Graphic Design and Visual Communications Technology**, 2nd intern. congr., Bled Yugoslavia. (Intern. Council of Graphic Design Assoc., Herengracht 567, Amsterdam-C, Netherlands)

11–16. **Hydraulics** 2nd Latin American congr., Caracas, Venezuela. (M. Gonzalez, Colegio de Ingenieros de Venezuela, Apartado de Correos 2006, Caracas)

11–16. **Reaction Mechanisms of Inorganic Solids**, intern, symp., Aberdeen, Scotland. (General Secretary, Chemical Soc., Burlington House, London W.1, England)

11–16. **Statistical Mechanics and Thermodynamics**, intern. symp., Copenhagen, Denmark. (T. A. Bak, H. C. Ørsted Inst., Univ. of Copenhagen, Copenhagen)

12–14. **Failure Analysis**, William H. Eisenman conf., New York, N.Y. (J. V. Richard, American Soc. for Metals, Metals Park, Ohio 44073)

12–15. Use of **Radioisotopes and Radiation in Dairy Science** and Technology, seminar, Vienna, Austria. (P. Fent, Div. of Public Information, Intern. Atomic Energy Agency, A-1010, Kärntnerring 11, Vienna)

12–19. International Union of **Crystallography**, 7th general assembly and congr., Moscow, U.S.S.R. (J. Ibers, Chemistry Dept., Northwestern Univ., Evanston, Ill.)

14–16. **Listeriosis**, 3rd intern. symp., Bilthoven, Netherlands. (E. H. Kampelmacher, Natl. Inst. of Public Health, Sterrenbos 1, Utrecht)

14–16. Uses of **Plastics** in the Pacific Northwest, workshop, Richland, Wash. (R. A. V. Raff, College of Engineering, Washington State Univ., Pullman 99163)

15–19. **Tetanus**, intern. conf., Bern, Switzerland. (W. Mamie, Tiefenauspital der Stadt Bern, Bern)

17–21. Canadian **Veterinary Medical** Assoc., annual conv., Vancouver, B.C. (The Association, P.O. Box 416 C.P., Ottawa 2, Ont.)

17–22. **Control Procedures in Drug Production**, 2nd seminar, Hershey, Pa. (W. L. Blockstein, Extension Services in Pharmacy, Univ. of Wisconsin, Madison 53706)

17–22. American Soc. for **Pharmacology and Experimental Therapeutics**, mtg., Mexico City, Mexico. (E. B. Cook, The Society, 9650 Wisconsin Ave., NW, Washington, D.C. 20014)

17–23. **Animal Venoms**, intern. symp., São Paulo, Brazil. (Conference Secretary, Inst. Butantan, Caixa Postal 65, São Paulo)

18–20. American Inst. of **Aeronautics and Astronautics**, Interagency Chemical **Rocket Propulsion** Group, mtg., Washington, D.C. (Chemical Propulsion Information Agency, 8621 Georgia Ave., Silver Spring, Md.)

18–20. **Aerospace Reliability and Maintainability**, 5th mtg., New York, N.Y. (American Inst. of Aeronautics and Astronomics, 1290 Sixth Ave., New York)

18–22. World Federation for **Mental Health**, 19th mtg., Prague, Czechoslovakia. (J. E. Purkyne Czechoslovak Medical Soc., Sokolska 31, Prague)

18–22. Nuclear and Space **Radiation Effects**, annual conf., Stanford Univ., Palo Alto, Calif. (V. A. J. van Lint, General Atomics, Special Nuclear Effects Labora-