medical sciences

Gathered at the meeting of the Academy of Pharmaceutical Sciences last week in Washington

ARTHRITIS

Cyclophosphamide and immunity

Cyclophosphamide, a widely used immunosuppressive drug against rheumatoid arthritis, definitely improves the majority of subjects treated, but not necessarily by suppressing the immune responses, according to Dr. Nathan J. Zvaifler of Georgetown University Medical Center in Washington, D.C.

The drug, he says, is known to reduce pain and swelling of the joints usually within 8 to 10 weeks. Because rheumatoid arthritis is supposedly an immunologic phenomenon, it would be reasonable to use an immunosuppressive agent to treat it. But, he adds, "this is not the whole story."

To test the effectiveness of cyclophosphamide, Dr. Zvaifler administered the drug to patients with rheumatoid arthritis and found that the majority did improve. But interestingly, the drug blocked the immune responses of antibodies and the rheumatoid factor to the same extent in those patients who responded as in those who did not. Therefore Dr. Zvaifler concludes that the response cannot be due entirely to immunosuppression. Although an immune factor is important, he says, some unknown factor is also part of the picture of rheumatoid arthritis.

INFLAMMATION

Roots in immunology

Although there are numerous ways to control chronic inflammation, none of them are particularly effective. According to Dr. J. C. Houck of Children's Hospital, Washington, D.C., acute inflammation heals and chronic does not; therefore the answer might lie with the difference between the two.

Chronic inflammation, he says, can be induced by a constant irritant that prevents healing, as contrasted to the temporary, acute inflammation caused by such effects as burns or bruises. Human inflammation-linked disease might therefore be caused by some immunologic defect that acts as an irritant to prevent healing.

In determining the difference between acute and chronic inflammation, Dr. Houck found that with the acute form white cells, or monocytes, move out of circulation into the wound and then die. In the chronic form these white cells divide in the wound. Whether or not this has any effect on healing, it suggests that some unknown agent in the inflammation encourages the cell division.

Finding out what causes the cell division might solve the riddle of chronic inflammation, Dr. Houck says.

ANTIBIOTICS

The shape of tetracycline

Although theories and generalizations abound, lack of understanding on the molecular level of how antibiotics exert their action hinders development of new drugs. The conformation of steroids and certain other fixed systems, such as penicillin, are understood, but this is not generally the case with most antibiotics.

Dr. L. A. Mitscher of Ohio State University in Columbus investigated the shape of tetracycline. Both the molecular shape and orientation (the direction some constituents point) but not necessarily the chemical configuration are important for maximum biological activity, he reports.

Tetracycline is L-shaped, like a book lying flat on a table with one end sticking up. If changes are made at the hinge point, Dr. Mitscher says, the shape is drastically changed and the drug becomes inactive. If the nitrogen atom that projects outward is altered to project inward, activity also changes. On the other hand, if such groups as chlorine, hydroxyl, or carbonyl are interchanged, neither the shape nor activity is changed, Dr. Mitscher says.

HALLUCINOGENS

LSD, others alike

Various psychedelic drugs produce similar psychotropic effects but are chemically different. If any similarity could be established, drugs that heighten self-awareness could be synthesized.

Dr. S. H. Snyder of the Johns Hopkins University School of Medicine in Baltimore studied a molecular model of LSD (d-lysergic acid diethylamide) to explain this paradox and found that the shape of the molecules is what produces the psychedelic action.

He found that three other potent hallucinogenic compounds, tryptamine, phenylethylamine and amphetamine, have approximately the same shape as the three-ringed LSD molecule.

HEMOSTASIS

Drugs for bleeding

A complex mechanism in the body helps control the bleeding of blood vessels by reducing blood flow and allowing platelets to aggregate and clot. With severe trauma, this mechanism is aided by suturing, or application of certain hemostatic agents such as gel foams.

Most recently, alpha-cyanoacrylates have evoked medical interest because they adhere firmly to moist tissue and, when sprayed against bleeding surfaces, rapidly produce clotting.

Dr. Fred Leonard of the Walter Reed Medical Center in Washington, D.C., studied a series of these chemicals and found that they do indeed fulfill all the requirements for a clotting agent. They are nontoxic, nonallergenic, thicken rapidly, form a tight film to coat the tissue and are degraded biochemically.

These compounds are particularly valuable for use on organs that are bleeding extensively and cannot be sutured. Already, Dr. Leonard says, n-butyl-cyanoacrylate has been used in combat casualties in Vietnam to control bleeding of liver and kidney wounds.