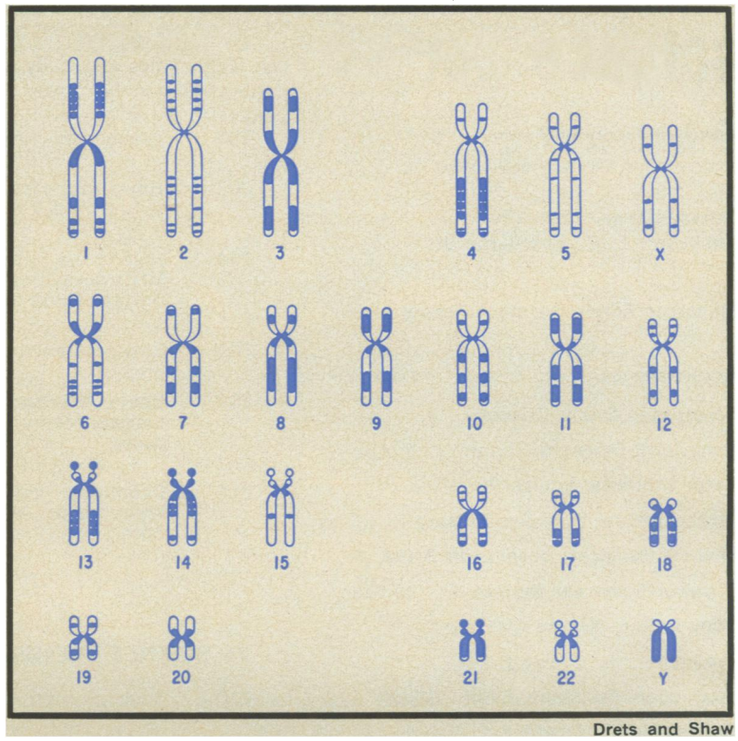
Sorting out chromosomes

New staining technique helps geneticists distinguish each of the 23 pairs of chromosomes



Giemsa stain reveals reliable patterns for each chromosome.

Karyotyping, systematically arranging and analyzing the chromosomes of a single cell, has been accomplished in the past by photographing a dividing cell and then examining silhouettes of the chromosomes. This, however, allowed scientists to positively distinguish and identify only 4 of the 23 pairs of human chromosomes.

Early last year, karyotyping was advanced by the development of chromosome analysis under a fluorescent microscope by the Swedish scientist T. Caspersson. His process revealed various details on the chromosomes but its general use was limited by the price of the microscope—$12,000. Then in the summer of 1970 Francis E. Arrighi and T. C. Hsu of the M. D. Anderson Hospital and Tumor Institute at the University of Texas in Houston discovered a staining procedure that differentiated specific regions of certain chromosomes without the use of a fluorescent microscope. Their paper, published in the current CYTOGENETICS, concluded that "without question the technique described here will be simplified and improved in the future."

This prediction has now come true. Rather than wait for publication, Hsu sent advance copies of the work to various investigators. The results were what he expected. Other researchers experimented with and modified the original procedure and produced a more detailed description of chromosomes.

In the Aug. 27 SCIENCE Shivanand R. Patil, Suzanne Merrick and Herbert A. Lubs of the University of Colorado Medical Center in Denver reported observation of regional staining of chromosomes with the Giemsa staining procedure (that used by Arrighi and Hsu). They undertook a systematic study of certain of the variables involved in the Giemsa procedure to improve the technique. The result, they reported, was "the identification of each human chromosome."

Two weeks ago at the International Congress of Human Genetics in Paris the same findings were reported by a number of other scientists. One even reported a reverse stain. Hsu says that "all of these stem from our original work, and this is just the beginning." Although he has not had time to try all of the modifications, he says he did not have good luck with the Denver group's method. "The reproduction was not so good." The best method he has found so far is reported by Maximo E. Drets and Margery W. Shaw (also at the M. D. Anderson Hospital) in the September PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

They report on a modification of the Arrighi-Hsu technique that results in a permanent preparation and allows precise identification of every human chromosome by a specific banding. In addition to the sex chromosomes, 20 of the 22 autosomal pairs have been identified by this technique, and the remaining two are tentatively classified. The genetic terrain, previously only partially mapped, is now completely known. This should allow researchers to localize genes in specific chromosome segments more accurately.

The method, however, has its drawbacks, says Merrick of the Denver group. The procedure takes three days, she explains, and the chromosomes appear to have come partially uncoiled by the denaturing and heat processes used. Their method, on the other hand, is less complicated and takes only a few minutes. As Hsu complains, though, the reproduction is not as distinct. But Merrick says her group is working on further refinements and hopes to develop a cheaper, routine method that will be readily accessible to all researchers.

The Houston researchers also plan to work on further refinements. In the meantime, Felix L. Haas, head of the biology department at the M. D. Anderson Hospital, says the findings "should significantly advance knowledge concerning human birth defects, drug damage, mental retardation and illness, effects of viruses and pollutants on cells, problems of the aging and cancer."

This may be somewhat optimistic but Robert L. Ledley, a geneticist and president of the National Biomedical Research Foundation in Washington, believes the new process is of "extremely great significance." Now "we can identify each individual chromosome, pick out further abnormalities and, in the case of translocation of chromosome arms, even tell which arm is translocated," he says. And because of the distinct banding patterns on each arm, it allows researchers to know exactly what they are looking at. Concludes Ledley: "This gives another dimension in the identification of genetic diseases, opens up the chemical analysis field and is a brand new shot in the arm." □