

ANEXO I: CORPUS DE LOS ABSTRACTS.

ABSTRACTS DE DISTRIBUCIÓN SIMULTÁNEA (ADS).

3. PHARMACOKINETIC COMPARISON OF SUBLINGUAL LORAZEPAM WITH INTRAVENOUS, INTRAMUSCULAR, AND ORAL LORAZEPAM.

Abstract[] Ten healthy volunteers received single 2-mg doses of lorazepam on five occasions in random sequence. Modes of administration were: A, intravenous injection; B, deltoid intramuscular injection; C, oral tablets in the fasting state; D, sublingual dosage of oral tablets in the fasting state; and E, sublingual dosage of specially formulated tablets in the fasting state. Kinetic variables were determined from multiple plasma lorazepam concentrations measured during 48 hr. postdose. After intravenous lorazepam, mean (\pm SE) values were: elimination half-life ($T_{1/2\beta}$), 12.9 (\pm 0.8) hr.; volume of distribution, 1.3 (\pm 0.07) liters/kg; total clearance, 1.21 (\pm 0.1) ml/min/kg. Absorption of intramuscular lorazepam was rapid. Peak plasma levels were reached at 1.15 hr. after dosage, with absorption half-life averaging 14.2 (\pm 4.7) min. Absorption of oral and sublingual lorazepam tended to be less rapid than intramuscular injection although differences were not significant. Times of peak concentration were 2.37, 2.35, and 2.25 hr. postdose for trials C, D, and E, respectively; values of absorption half-life were 32.5, 28.5, and 28.7 min. Absolute systemic availability for trials B, C, D, and E averaged 95.9, 99.8, 94.1, and 98.2% respectively; none of these differed significantly from 100%. Values of $T_{1/2\beta}$ were highly replicable within individuals regardless of the administration route. Thus, sublingual lorazepam is completely absorbed and is a suitable administration route in clinical practice.

* keyphrases: Lorazepam-sublingual, pharmacokinetic compared with intravenous, intramuscular and oral doses forms / Pharmacokinetics-sublingual, pharmacokinetic compared with intravenous, intramuscular and oral doses forms / Dosage forms-sublingual, pharmacokinetic compared with intravenous, intramuscular and oral doses forms.

>> *Journal of Pharmaceutical Science*, vol. 71/2, p.248, Feb. 1982.

4. NITROGEN-PHOSPHOROUS DETECTION OF PHENCYCLIDINE IN BLOOD SERUM.

Abstract[] A method for quantitating phencyclidine in blood serum of rhesus monkeys with a solvent extraction procedure followed by gas chromatography with nitrogen-phosphorous detection is reported. Phencyclidine was extracted with ether from 0.5 ml of serum (pH 13.5) made basic with 2M NaOH, followed by back-extraction into 0.5M sulfuric acid. After the addition of 2M sodium hydroxide, phencyclidine was extracted into a small volume of ether for concentration and injection into the gas chromatograph. The limit of quantitation of phencyclidine in serum was 5 ng/ml. Recovery averaged $51.9 \pm 4.3\%$. Standard curves were linear between 5-50 ng/ml and 100-2000

ng/ml. Comparison between serum and aqueous standards indicated no interference by serum components in the extraction procedure. Pentobarbital, caffeine, and the monohydroxy metabolites of phencyclidine did not interfere with the analysis. This procedure is a rapid and sensitive method for determination of serum phencyclidine levels in animal studies requiring analysis of large numbers of samples.

* keyphrases: Phencyclidine-analysis using gas chromatography with nitrogen-phosphorous detection, rhesus monkey blood serum. Gas chromatography-nitrogen-phosphorous detection of phencyclidine in rhesus monkey blood serum. Drugs of abuse-phencyclidine, analysis using gas chromatography with nitrogen-phosphorous detection, rhesus monkey blood serum.

>> *Journal of Pharmaceutical Science*, vol. 71/2, p.194, Feb. 1982.

5. EFFECT OF CARBOXYLIC ACIDS ON PERMEATION OF CHLORPROMAZINE THROUGH DIMETHYL POLYSILOXANE MEMBRANE.

Abstract[] The effect of carboxylic acids on the permeation of chlorpromazine was investigated through a demethyl polysiloxane nonpolar membrane. The permeability of the diffusate, at pH 5.8, increases considerably in the presence of carboxylic acids or phosphate, probably due to an ion-pair formation between the relative anions and chlorpromazine.

* Keyphrases: Chlorpromazine-permeation through a demethyl polysiloxane membrane, effect of carboxylic acids. Diffusion-chlorpromazine, through a dimethyl polysiloxane membrane, effect of carboxylic acids. Carboxylic acids-effect on chlorpromazine diffusion through a dimethyl polysiloxane membrane.

>> *Journal of Pharmaceutical Science*, vol. 71/2, p.239, Feb. 1982.

6. ASCORBIC ACID ABSORPTION IN HUMANS: A COMPARISON AMONG SEVERAL DOSAGE FORMS.

Abstract[] There have been few studies conducted to determine the efficiency of ascorbic acid absorption in humans. Differences in the extent of its absorption among individuals may contribute to the outcome of clinical trials. Ascorbic acid absorption in four subjects was investigated from several oral dosage forms containing 1 g of the vitamin (solution, tablet, chewable tablet, and timed-release capsule). Approximately 85% of an intravenous dose was recovered in the urine as ascorbic acid and its major metabolites. In contrast, only ~30% of the dose was recovered from the solution and tablet forms. A considerably smaller fraction of the dose (~14%) was recovered from the timed-release capsule. There was considerable intersubject variation in ascorbic acid absorption and there appeared to be good and poor absorbers of the vitamin. Consideration should be given to the influence of the extent of ascorbic acid absorption on the results of clinical trials.

* Keyphrases: Ascorbic acid-comparison of absorption of several dosage forms, humans. Absorption-ascorbic acid, comparison of several dosage forms, humans. Vitamin C-comparison of absorption of several dosage forms, humans.

>> *Journal of Pharmaceutical Science*, vol. 71/3, p.282, Mar. 1982.

7. KINETICS AND STABILITY OF A MULTICOMPONENT ORGANOPHOSPHATE ANTIDOTE FORMULATION IN GLASS AND PLASTIC.

Abstract[] An aqueous solution of trimedoxime bromide, atropine, and benactyzine hydrochloride was formulated to have maximum stability as an antidote in organophosphorus poisoning. The stability of the mixture in glass and plastic cartridges was determined. Glass cartridges were more desirable than plastic; there was less vapor loss, color formation, and anomalous reaction. Trimedoxime was stable losing 1.4% of its potency after 1 year at 25° and atropine was more stable than trimedoxime. Considerable degradation of benactyzine occurred; 20% of its potency was lost after 1 year at 25°. Equations for predicting the shelf life of each ingredient at selected temperatures are presented.

* Keyphrases: Benactyzine-in formulation, kinetics and stability in glass and plastic /Atropine-in formulation, kinetics and stability in glass and plastic /Trimedoxime-in formulation, kinetics and stability in glass and plastic.

>> *Journal of Pharmaceutical Science*, vol. 71/3, p.321, Mar. 1982.

8. TRANSITION-STATE ALKYLATION GEOMETRIES OF 7,8-DIHYDROXY-9,10-EPOXY-7,8,9,10-TETRAHYDROBENZO (α) PYRENE ENANTIOMERIC ISOMERS WITH NUCLEIC ACID DIMERS.

Abstract[] The steric contact spaces associated with the reaction of the enantiomeric isomers of 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[α]pyrene (I) with the exocyclic amino group of guanine of dinucleoside dimer structures were examined for a fixed transition-state geometry. This reaction is sterically prohibited for the B form DNA conformation. If, however, the nucleic acid structure is deformed, such that the distance between two adjacent base pairs (one containing guanine and cytosine) is maximized, sterically allowed transition-state geometries can be identified. It was not possible to uniquely identify the preferred transitionstate complex with respect to nucleic acid structure or isomer of I. However, two types of general transition-state geometries were observed. In one, I was located "outside" the nucleic acid structure; in the other geometry, I was intercalated between adjacent base pairs in the transition state. The intercalation process might serve as a physicalcatalyst for the alkylation of NH₂-guanine by I.

* Keyphrases: 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[α]pyrene-enantiomeric isomer, alkylation of dinucleoside dimers, transition state geometry. Dinucleoside dimers-alkylation by enantiomeric isomers of 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[α]pyrene, transition-

state geometry. Transition state geometry of the alkylation of dinucleoside dimers by enantiomeric isomers of 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[α]pyrene, intercalation.

>> *Journal of Pharmaceutical Science*, vol. 72/7, p.800, Jul. 1983.

9. INVESTIGATION OF DIGOXIN, QUINIDINE, AND DISOPYRAMIDE INTERACTIONS IN RATS UTILIZING PAROTID SALIVA, BLOOD, AND OTHER TISSUES.

Abstract[] Blood, parotid saliva, heart, liver, and kidney concentrations of digoxin and quinidine were determined in rats chronically treated with digoxin and in nontreated (control) rats after the administration of quinidine (20 mg/kg ip) and disopyramide (10 mg/kg ip). The results indicated that digoxin concentrations increased significantly and proportionally in parotid saliva and plasma after quinidine, but did not increase after disopyramide. With the exception of the liver, which showed an increase in digoxin concentrations, tissue concentrations of digoxin did not differ from control animals. In rats pretreated chronically with digoxin, quinidine concentrations in plasma, parotid saliva, or heart tissue did not differ significantly from control animals, but were significantly lower than controls in liver and kidney tissues. The results presented here lend additional support to the hypothesis that the increase in digoxin plasma concentration following quinidine administration is primarily due to interference with renal excretion and displacement of digoxin by quinidine binding sites. Furthermore, it was demonstrated that disopyramide has little or no effects on plasma digoxin levels in rats.

* Keyphrases: Digoxin-interaction with quinidine and disopyramide in parotid saliva, blood, and other tissues. Quinidine-interaction with digoxin and disopyramide in parotid saliva, blood, and other tissues. Disopyramide-interaction with digoxin and quinidine in parotid saliva, blood, and other tissues.

>> *Journal of Pharmaceutical Science*, vol. 71/2, p.211, Feb. 1982.

12. STABILITY OF ASPIRIN IN DIFFERENT MEDIA.

Abstract[] Aspirin rapidly hydrolyzes in various aqueous, organic, and biological media. The purpose of this investigation was to study the decomposition of aspirin in the media that comes in contact with it during analysis in biological fluids for pharmacokinetic studies. These media included water, water-polyethylene glycol 4000, water-methanol-acetic acid, phosphate buffer, freshly drawn blood and plasma from control rats and rat deprived of water for 36 hr. and blood precipitated with acetonitrile. Studies were also conducted to determine the decomposition as a function of temperature and pH. Of the various solvent systems studied, aspirin was found most stable in water-polyethylene glycol (4:1,v/v), which provides an excellent medium for preparation of intravenous dosage forms. Phosphate buffer showed significant catalysis of aspirin hydrolysis. A More than fivefold increase in the hydrolysis of aspirin was noted when the temperature was raised

to 37° from 22.5°. The hydrolysis of aspirin in rat blood was 13 times faster than that in plasma, with an average half-life in blood approx.13 min. This creates significant problems in aspirin disposition kinetic studies. Mixing the blood sample immediately after collection with twice the volume of acetonitrile and then centrifuging gives a plasma-acetonitrile mixture in which no lysis of blood cells is observed.

* Keyphrases: Aspirin-stability in media, human blood and plasma, hydrolysis kinetics. Kinetic-aspirin hydrolysis in media human blood and plasma, stability. Stability-of aspirin in media, human blood and plasma, hydrolysis kinetics.

>> *Journal of Pharmaceutical Science*, vol. 72/9, p.1024, Sep. 1983.

15. INFLUENCE OF FOOD AND FLUID VOLUME ON CHLOROTHIAZIDE BIOAVAILABILITY: COMPARISON OF PLASMA AND URINARY EXCRETION METHODS.

Abstract[] The bioavailability of chlorothiazide from oral tablet was examined under fasting and nonfasting conditions in healthy male volunteers. Bioavailability was determined from urinary excretion data and plasma chlorothiazide concentrations. Two fasting treatments and one nonfasting treatment yielded similar plasma chlorothiazide profiles, characterized by sharply ascending and descending segments until 12-13 hr. postdosing, followed by a prolonged period with variable and erratic chlorothiazide levels. A triexponential function that adequately described mean data from each treatment could not be applied to individual plasma curves because of their variable nature. Chlorothiazide absorption was not influenced by different accompanying water volumes in fasted individuals but was doubled when tablets were administered immediately after a standard meal. Urinary excretion for chlorothiazide correlated well with plasma drug concentrations; 48-hr. urinary recovery accounted for 24.7% of a 500-mg dose in nonfasted subjects compared to 12.3 and 14.9% in fasted subjects receiving the drug with 20 and 250 ml of water, respectively. Observed relationships between chlorothiazide dosage and absorption efficiency are consistent with previous suggestions that chlorothiazide absorption from the GI tract is saturable and site specific.

* keyphrases: Chlorotiazide-effect of food and fluid volume on bioavailability plasma and urinary excretion methods compared. Bioavailability-chlorotiazide, effect of food and fluid volume, plasma and urinary excretion methods compared. Diuretic-chlorotiazide, influence of food and fluid volume on bioavailability, plasma and urinary excretion methods compared.

>> *Journal of Pharmaceutical Science*, vol. 71/1, p.32, Jan. 1982.

16. IMMUNIZATION STUDIES WITH ATTENUATED STRAINS OF BACILLUS ANTHRACIS.

Abstract[] Live, attenuated strains of *Bacillus anthracis* lacking either the capsule plasmid pX02, the toxin plasmid pX01, or both were tested for their efficacy as vaccines against intravenous challenge

with anthrax toxin in Fischer 344 rats and against aerosol or intramuscular challenge with virulent anthrax spores in Hartley guinea pigs. Animals immunized with toxigenic, nonencapsulated (pX01⁺, pX02⁻) strains survived toxin and spore challenge and demonstrated postimmunization antibody titers to the three components of anthrax toxin (protective antigen, lethal factor, and edema factor). Immunization with two nontoxigenic, encapsulated (pX01⁻, pX01⁺), Pasteur vaccine strains neither provided protection nor elicited titers to any of the toxin components. Therefore, to immunize successfully against anthrax toxin or spore challenge, attenuated, live strains of *B. anthracis* must produce the toxin components specified by the pX01 plasmid.

>> *Infection and Immunity*, vol. 52/2, p.454, May 1986.

17. IN VIVO DEGRADATION OF BACTERIAL CELL WALL BY THE MURALYTIC ENZYME MUTANOLYSIN.

Abstract[] The muralytic enzyme mutanolysin can act in vivo to eliminate chronic erosive arthritis induced in rats by polymers of peptidoglycan-polysaccharide isolated from group A streptococci (PG-APS). The amounts of PG-APS in the livers and spleens of rats treated with mutanolysin were significantly reduced compared with the amounts in control rats treated with phosphate-buffered saline. However, the amounts of PG-APS in the limbs of mutanolysin- and phosphate-buffered saline-treated rats were comparable. PG-APS polymers extracted from the livers, spleens, and limbs of mutanolysin-treated rats were extensively degraded, whereas PG-APS extracted from phosphate-buffered saline-treated rats had a high molecular weight. We propose that mutanolysin abrogates arthritis in rats by degrading PG-APS polymers to a size which is no longer able to induce chronic erosive arthritis, even though the polymers are still present in the limbs.

>> *Infection and Immunity*, vol. 52/2, p.459, May 1986.

18. UREAPLASMA INFECTION OF CELL CULTURES.

Abstract[] Studies were performed to characterize the effects of ureaplasmas in HeLa, 3T6, and CV-1 cell cultures. The ureaplasmas studied were human *Ureaplasma urealyticum* T960 (serotype VIII), bovine *U. diversum* T95, simian strain T167-2, ovine strain 1202, canine strain D1M-C, and feline strains 382 and FT2-B. FT2-B was the only ureaplasma to grow in the cell free culture medium, Dulbecco modified Eagle-Earle medium containing 10% fetal bovine serum. The growth pattern of the ureaplasmas varied in the different cell cultures, but each strain grew in at least two of the cell cultures, suggesting a requirement for a product of the cell culture and for low concentrations of urea. When growth occurred, organisms grew to concentrations that approached, but did not equal, those observed in 10B broth. Most, but not all, ureaplasmas grew quickly, reaching peak titers 2 days after infection. Canine strain D1M-C did not grow in 3T6, but showed rapid growth in He La and CV-1 cells, killing both cultures. In some systems, e.g., *U.*

urealyticum T960 and simian strain T167-2, the infection persisted, and ureaplasmas could be recovered from cell cultures four passages after infection, when studies were terminated. The cell culture ureaplasmas grew on T agar, but not on mycoplasma agar medium.

>> *Infection and Immunity*, vol. 52/2, p.437, May 1986.

19. OPSONIZATION OF *LISTERIA MONOCYTOGENES* TYPE 4b BY HUMAN ADULT AND NEWBORN SERA.

Abstract[] We studied the requirements for opsonization of *Listeria monocytogenes* type 4b with chemiluminescence and bactericidal assays and electron microscopy. Preopsonization with 3% adult serum had good opsonic activity (27,300±11,000 standard deviation counts, chemiluminescence assay), while 3% newborn cord serum was not opsonically active (820±530 counts, P<0.001 versus adult serum). In addition, organisms opsonized with cord serum were not killed (0% bacterial killing) and were less frequently visualized intracellularly on electron micrographs (0 to 4 bacteria per cell) than organisms opsonized with adult serum (70% killing and 10 to 20 bacteria per cell). Opsonic requirements for *L. monocytogenes* type 4b at low concentrations of serum were studied in detail with Sepharose-protein A-treated adult serum to obtain immunoglobulin G (IgG) and IgM fractions and zymosan-absorbed and C4 inactivator-treated serum to obtain alternative and classical complement pathway-deficient sera, respectively. In the presence of complement, IgM was opsonically active (59% of control) while IgG was not (6% of control). In addition, classical complement activity was required for efficient opsonization (>100% of control) while the alternative complement pathway was unnecessary (3% of control). Since IgM is absent and classical complement activity is low in neonatal serum and at the common sites of neonatal *Listeria* infection, the requirement for IgM and classical complement activity for efficient opsonization of *L. monocytogenes* type 4b at low serum concentrations may be a factor in the pathogenesis of neonatal disease.

>> *Infection and Immunity*, vol. 52/2, p.493, May 1986.

20. PATHOPHYSIOLOGY OF EXPERIMENTAL LEISHMANIASIS: PATTERN OF DEVELOPMENT OF METASTATIC DISEASE IN THE SUSCEPTIBLE HOST.

Abstract[] A clear understanding of the etiology of the various forms of leishmaniasis will require knowledge of how physiological properties of the parasite and host immunity influence the pattern of development of the disease. Of particular importance are how these factors affect the growth rate of *Leishmania* spp. at the site of inoculation in the skin, their capacity to disseminate to visceral and distant cutaneous sites, and their capacity to multiply once there. This paper details the pattern of development of disseminated *Leishmania major* infection in susceptible BALB/c *nu/+* and BALB/c *nu/nu* mice. It was found that the parasite disseminates from the hind footpad to distant

cutaneous sites soon after metastatic foci are established in the liver and spleen. Both mononuclear phagocytes and neutrophils may be the vehicles for the transport of the parasite in the blood. Once visceral and cutaneous metastases are established the parasites in those foci increase in number progressively. *L. major* has the capacity to multiply at visceral and cutaneous sites at the same rate. Despite the presence of viable parasites in a number of skin sites, cutaneous metastatic lesions developed almost exclusively on the feet and the tail. Furthermore, these lesions appeared to develop preferentially at sites near joints, suggesting that factors other than temperature may influence the development of cutaneous metastatic lesions.

>> *Infection and Immunity*, vol. 52/2, p.364, May 1986.

21. RECOMBINATION NEAR THE ANTIBIOTIC RESISTANCE LOCUS *penB* RESULTS IN ANTIGENIC VARIATION OF GONOCOCCAL OUTER MEMBRANE PROTEIN I.

Abstract[] In gonococci, the nonspecific antimicrobial resistance locus *penB* is known to be closely linked to loci designated *nmp* that alter the M_r and antigenicity of the outer membrane porin protein I (P.I.). We report that after selection for the linked donor *penB* locus, occasional recombinants expressed P.I. with some epitopes from each parent. These hybrid P.I. antigens were stable on subculture and were transformed at a locus closely linked to *penB*. The hybrid P.I. antigens were detected with monoclonal antibodies in both coagglutination and Western blot assays. The alterations of P.I. antigenicity may have resulted from recombination between structural genes for P.I. that are closely linked to *penB*.

>> *Infection and Immunity*, vol. 52/2, p.529, May 1986.

22. DELAYED-TYPE HYPERSENSITIVITY AND IMMUNITY TO *SALMONELLA TYPHIMURIUM*.

Abstract[] Studies were carried out to correlate immunity and expression of delayed-type hypersensitivity (DTH) in mice of the C3H lineage immunized with an avirulent strain of *Salmonella typhimurium* (strain SL3235). This strain belongs to a class of *aroA*⁻ organisms which are being considered as vaccine strains for humans and veterinary use. In a systematic study, the relationship between the mouse strain and the immunizing dose of strain SL3235 on the development of protective immunity and DTH was examined. It was found that in hypersusceptible C3H/HeJ and C3HeB/FeJ mice, several doses of strain SL3235 afforded protection against intravenous challenge doses as high as 1,300 50% lethal doses. Despite these significant levels of immunity to challenge, mice of these two strains never mounted significant DTH responses following immunization with the doses of strain SL3235 tested, which spanned 3 orders of magnitude. Nonresponsiveness was not due to antigen oversoad, as all of the mouse strains were comparably colonized with strain SL3235 at the time of DTH elicitation. Further, it was found that the ability of responsive C3H/He NCrIBR mice to display DTH was dependent on the immunizing

dose of strain SL3235 and that a dosage could be found that resulted in increased resistance to challenge in these mice without a concomitant display of DTH. Thus, while both induction of protective immunity and DTH were vaccine dosage dependent in the responsive mouse strain (C3H/HeNCrIBR), DTH was a less sensitive measure of protective immunity than survival. Vaccine dosages ranging over three orders of magnitude failed to yield positive footpads to the *Salmonella* elicitor in the nonresponsive mice. The data suggest that caution should be observed in interpreting *Salmonella* DTH tests that are used as screens of immune status to typhoid fever in humans, as the extent of discordance between immunity and DTH in humans is unknown.

>> *Infection and Immunity*, vol. 52/2, p.504, May 1986.

23. PATHOGEN-RELATED ORAL SPIROCHETES FROM DENTAL PLAQUE ARE INVASIVE.

Abstract[] Spirochetes that share pathogen-restricted antigens with *Treponema pallidum* subsp. *pallidum* have been identified in dental plaque and diseased gingival tissues, but it is not known whether these spirochetes possess virulence characteristics. In this study, plaque spirochetes were able to transmigrate a tissue barrier in vitro and were identified on the other side by using monoclonal antibodies specific for pathogen-restricted determinants from *T. pallidum* subsp. *pallidum*. This invasive capability is shared with *T. pallidum* subsp. *pallidum*, but cultured oral and intestinal treponemes did not perforate the tissue barrier. Cocultures indicated that invasive treponemes do not create opportunities for cultivable oral treponemes to cross the barrier. These findings indicate that gingival tissues may be a port of entry for previously unrecognized invasive spirochetes in humans.

>> *Infection and Immunity*, vol. 59/10, p.3377, Oct 1991.

24. ANTIMALARIAL ANTIBODIES OF THE IMMUNOGLOBULIN G2A ISOTYPE MODULATE PARASITEMIAS IN MICE INFECTED WITH *PLASMODIUM YOELII*.

Abstract[] Previous studies have demonstrated the importance of antibodies in mediating immunity to malaria, but the relative contribution of the different immunoglobulin isotypes has not been assessed. In this study, hyperimmune plasma was generated against *Plasmodium yoelii* and separated by protein-Sepharose chromatography into fractions containing immunoglobulin G1 (IgG1), IgG2a, IgG2b, or IgG3 antibodies and the remaining nonbinding plasma proteins, including IgM. Following concentration, the antimalarial titer of each isotypic fraction was approximately equivalent to the corresponding isotype in hyperimmune plasma. The isotypic fractions were passively transferred to BABL/c and outbred ICR mice prior to challenge with virulent *P. yoelii* 17XL and CBA/CaJ mice challenged with avirulent *P. yoelii* 17XNL. Only mice receiving IgG2a antibodies experienced an altered course of infection. Immunoprecipitation studies showed that all four IgG

isotypes appear to recognize a similar set of antigens. These results suggest that antimalarial antibodies of the IgG2a isotype play a dominant role in modulating *P. yoelii* parasitemias.

>> *Infection and Immunity*, vol. 59/10, p.3547, Oct 1991.

25. CONSTRUCTION AND EXPRESSION OF PLASMIDS CONTAINING MUTATED DIPHTERIA TOXIN A-CHAIN-CODING SEQUENCES.

Abstract[] We previously demonstrated that cells can be killed through transfection of an expression plasmid that encodes the diphtheria toxic A-chain fragment (DT-A). This report describes the construction of expression plasmids containing three mutant DT-A-coding sequences substituting glutamic acid 148 with aspartic acid, serine, or glutamine which are known to have 100- to 300-fold-reduced ADP-ribosylation activity measured in vitro. The toxicity of these constructs was determined in cotransfection experiments using HeLa and 293 cells with a luciferase expression plasmid as the reporter. Dose responses were compared for the three new DT-A mutant plasmids and for the corresponding plasmids containing wild-type DT-A and the previously characterized *tox* 176 mutant. The dose required to produce 50% inhibition of control luciferase expression in 293 embryonic kidney cells for the five plasmids ranged from 0.01 µg for wild-type DT-A to 1.2 µg for the least toxic plasmid, which replaces glutamic acid 148 with glutamine. In conclusion, a wide range of DT-A toxicity can be achieved by using plasmid expression vectors that encode different DT-A mutations.

>> *Infection and Immunity*, vol. 59/10, p.3562, Oct 1991.

26. COMPARISON BETWEEN *XANTHOMONAS CAMPESTRIS* PV. *MANIHOTIS* (ISPP LIST 1980) AND *X. CAMPESTRIS* PV. *CASSAVAE* (ISPP LIST 1980) BY MEANS OF PHENOTYPIC, PROTEIN ELECTROPHORETIC, DNA HYBRIDIZATION AND PHYTOPATHOLOGICAL TECHNIQUES.

Abstract[] *Xanthomonas campestris* pv. *manihotis* (ISPP List 1980) and *X. campestris* pv. *cassavae* (ISPP List 1980) strains, isolated from cassava (*Manihot esculenta*) plants of different geographical origin, were studied by numerical analysis of 267 phenotypic features, computer-assisted comparison of gel electrophoregrams of soluble proteins, mol% G+C determinations, DNA: DNA hybridizations and virulence tests. *X. campestris* pv. *manihotis* and pv. *cassavae* constituted separate biological entities which could be differentiated from each other by four biochemical features, their symptoms on cassava, their soluble protein electrophoregrams and their DNA characteristics. Within each pathovar no correlation was found between phytopathogenicity, geographic origin and year of isolation of the strains, on the one hand, and the biochemical, physiological and protein electrophoretic properties on the other. Two yellowish *Xanthomonas* strains, CIAT 1164 and CIAT 11165, isolated from cassava in Colombia were

genetically and electrophoretically similar to *X. campestris* pv. *poinsettiicola*, but were unable to infect *Euphorbia pulcherrima*. *X. campestris* pv. *poinsettiicola* was genetically more related to the *X. campestris* pv. *manihotis* cluster than to the *X. campestris* pv. *cassavae* cluster.

>> *Journal of General Microbiology*, vol. 133, p.57, 1987.

27. REGULATION OF GENE EXPRESSION DURING AEROBIC GERMINATION OF *MUCOR RACEMOSUS* SPORANGIOSPORES.

Abstract[] The pool of mRNA stored in dormant sporangiospores of *Mucor racemosus* and expressed during early germination in air has been investigated. Total RNA was extracted from dormant and germinating spores and translated in a cell-free rabbit reticulocyte system containing L-[³⁵S] methionine. Isotopically labelled *in vitro* translation products were analysed by PAGE and autoradiography and were compared with labelled proteins synthesized *in vivo* at the same stages of development. This comparison revealed several significant findings about the fates of individual mRNA populations as templates in translation: (i) a pool of mRNA, presumably represented entirely or in part by a recoverable polyadenylated RNA fraction, can be extracted from dormant spores in a translatable form; (ii) most of the differential gene expression displayed at the level of protein synthesis during germination results from concomitant changes in functional mRNA levels; (iii) some of the stored mRNA species may be activated and others inactivated by post-transcriptional processing mechanisms; and (iv) a small population of gene products may be regulated at the level of selective translation of pre-existing messages.

>> *Journal of General Microbiology*, vol. 133, p.141, 1987.

28. REQUIREMENT FOR VITAMIN B₁ FOR GROWTH OF *EUGLENA GRACILIS*.

Abstract[] *Euglena gracilis* Z showed an absolute requirement for vitamin B₁ for growth. Increase of cell number in vitamin B₁-deficient cultures occurred on the addition of vitamin B₁ and depended on the amount added. The phosphate esters of vitamin B₁ also supported growth. *E. gracilis* cells exhaustively took up vitamin B₁ within about 2h of addition. Of the total amount of vitamin B₁ taken up, as much as 96% existed in the free form irrespective of the forms added. The addition of 4-amino-5-hydroxymethyl-2-methylpyrimidine, but not 5-(2-hydroxyethyl)-4-methylthiazole, to the vitamin B₁-deficient cells enhanced cell number at the same rate as the addition of vitamin B₁, indicating that *E. gracilis* Z is unable to synthesize the pyrimidinemoiety of vitamin B₁.

>> *Journal of General Microbiology*, vol. 133, p.25, 1987.

29. LEPTOMYXID AMEBA, A NEW AGENT OF AMEBIC MENINGOENCEPHALITIS IN HUMANS AND ANIMALS.

Abstract[] Amebae belonging to the order Leptomyxida are regarded as innocuous soil organisms incapable of infecting mammals. We report here the isolation of a leptomyxid ameba from the brain of a pregnant baboon (*Papio sphinx*) that died of meningoencephalitis at the San Diego Zoo Wild Animal Park. By using rabbit anti-leptomyxid serum in the immunofluorescence assay, we have identified the leptomyxid ameba in the brain sections of a number of human encephalitic cases from around the world as well as a few cases of meningoencephalitis in animals in the United States, which suggests that the leptomyxid amebae are potential etiologic agents of fatal meningoencephalitis in humans and animals.

>> *Journal of Clinical Microbiology*, vol. 28/12, p.2750, Dec. 1990.

30. DIAGNOSIS OF EPSTEIN-BARR VIRUS INFECTION IN HAIRY LEUKOPLAKIA BY USING NUCLEIC ACID HYBRIDIZATION AND NONINVASIVE TECHNIQUES.

Abstract[] The presence of Epstein-Barr virus (EBV) DNA in the epithelial cells of oral hairy leukoplakia is the confirming criterion in the diagnosis of this lesion, which occurs mainly in persons infected by the human immunodeficiency virus. Because hairy leukoplakia often presages the development of the acquired immune deficiency syndrome, it is important that suspicious lesions be accurately diagnosed. Commonly, biopsy tissue is removed for detection of EBV DNA by in situ hybridization, but biopsy is contraindicated in some patients. This study evaluated filter and cytopsin in situ hybridization, two noninvasive techniques that examine epithelial cells swabbed from the surfaces of the lesions, for their sensitivity in detecting EBV DNA. As compared with tissue in situ hybridization, the filter and cytopsin techniques had sensitivities of 100 and 92%, respectively. We conclude that these two noninvasive techniques can provide the clinician with an accurate alternative to biopsy whenever this human immunodeficiency virus-associated lesion is suspected.

>> *Journal of Clinical Microbiology*, vol. 28/12, p.2775, Dec. 1990.

32. LABORATORY INVESTIGATION OF ACANTHAMOEBA KERATITIS.

Abstract[] Following the diagnosis of *Acanthamoeba* keratitis in a contact lens wearer, the antimicrobial susceptibility of the clinical isolate and the environmental source of the infection were investigated. Contrary to previous reports, in vitro antimicrobial testing showed that the infecting strain was inherently resistant to propamidine isethionate. Restriction endonuclease digestion analysis of *Acanthamoeba* whole-cell DNA of strains isolated from the patient's cornea, contact lens storage container, saline rinsing solution, and kitchen cold-water tap showed that the isolates were identical. This implicates, for the first time, domestic tap water as the source of *Acanthamoeba* sp. in this infection. It is therefore recommended that the use of homemade saline solutions and the rinsing of contact lenses in tap water be strongly discouraged.

>> *Journal of Clinical Microbiology*, vol. 28/12, p.2722, Dec. 1990.

33. PROPERTIES OF GROUP B STREPTOCOCCI WITH PROTEIN SURFACE ANTIGENS X AND R.

Abstract[] A total of 128 bovine and 134 human group B streptococci were serotyped by conventional methods. Among the bovine cultures, 60 (47%) had type antigen X, and among the human cultures, 53 (39%) had type antigen R. The occurrence of type antigens X and R was significantly related to the growth pattern of the bacteria in fluid media. Type X- and R-positive cultures and most of the nontypeable cultures predominantly formed long chains and grew as granular sediment with clear supernatant. In addition, group B streptococci with surface antigen X or R showed compact colony formation in soft agar and reacted positively in the salt aggregation test. These properties, possibly caused by the surface charges of the X- and R-positive cultures, might be related to bacterial pathogenicity.

>> *Journal of Clinical Microbiology*, vol. 28/12, p.2834, Dec. 1990.

34. EFFECT OF TRICARBOXYLIC ACID CYCLE INTERMEDIATES ON ACETIC ACID PRODUCTION BY *ACETOBACTER ACETI*.

Abstract[] The stimulative effect of tricarboxylic acid (TCA) cycle intermediates on the acetic acid production of *Acetobacter acetii* M23 was investigated in batch and continuous cultures. Cell growth was hardly affected by the supplement of the TCA cycle intermediates; however, the acetic acid production rate in a continuous culture at the dilution rate of 0.097 h^{-1} increased 3.2 times in the medium supplemented with 2 mM citric acid. The optimum concentration of citric acid as an additive in the medium was 10 mM. Acetic acid production was enhanced by adding citric acid only when there was an insufficient supply of oxygen.

>> *Journal of General Applied Microbiology*, vol. 36, p.105, 1990.

35. SOLUBILIZATION OF ROCK PHOSPHATE BY *RHIZOBIUM* AND *BRADYRHIZOBIUM*.

Abstract[] The potential of strains of *Rhizobium* and *Bradyrhizobium* to solubilize rock phosphate was evaluated in vitro. Almost all organisms tested effectively solubilized rock phosphate and lowered the medium pH. The presence or absence of $(\text{NH}_4)_2\text{SO}_4$ made little difference in the solubilization of rock phosphate. Among the strains, *Rhizobium leguminosarum* biovar *viceae* BICC635 was the most effective solubilizer. Maximum solubilization of phosphate and acid production was achieved after 3 days of incubation. The strain produced 2-ketogluconic acid in the culture medium, the primary cause of rock phosphate solubilization. Increasing the phosphate status of the medium had little effect on the extent of dissolution of Purulia rock phosphate. Adding calcium as CaCl_2 , CaCO_3 and $\text{Ca}(\text{OH})_2$ reduced the phosphate solubilization from phosphate

rocks. The results indicated that pH, per se, is of less importance in phosphate solubilization. EDTA increased the extent of rock phosphate solubilization, possibly by chelation of the calcium ions that the solubilization produced.

>> *Journal of General Applied Microbiology*, vol. 36, p.81, 1990.

36. THE DETERMINATION OF MEAN RESIDENCE TIME USING STATISTICAL MOMENTS: IS IT CORRECT?

Abstract[] The estimation of mean residence time using statistical moment theory is shown to lead to the true mean residence time only in the case of a concentration-time curve which is a single exponential. In other cases, including the commonly encountered double exponential, there is a systematic error present which can lead to the result being incorrect by as much as a factor of 2. For the case of instantaneous input, an alternative estimation procedure is suggested which gives an estimate much closer to the true mean residence time.

* Keyphrases: mean residence time; statistical moment theory; decumulation; plasma drug concentrations; Co.

>> *Journal of Pharmacokinetics and Biopharmaceutics*, vol. 13/1, p.93, 1985.

37. A THEORETICAL CONSIDERATION OF PERCUTANEOUS DRUG ABSORPTION.

Abstract[] The percutaneous drug absorption process and its clinical significance are not fully known. In this article we propose a theoretical method to obtain two parameters (K_d and k_c) of percutaneous drug absorption from in vivo data. These parameters are related to diffusion of a drug through the skin and removal process at the skin-capillary boundary, respectively, characterizing several pharmacokinetic aspects of the drug applied to the skin. Moreover, by employing these two kinetic constants, a simulation of percutaneous drug absorption can be theoretically generated. On the basis of our theoretical considerations on the percutaneous drug absorption process described herein, we conclude that the percutaneous drug absorption process is better understood by employing two kinetic constants in a mathematical model and that its clinical application would be highly possible.

* Keyphrases: percutaneous drug absorption; pharmacokinetic model; diffusion model; lag-time *in vivo*; mean residence time (MRT) and variance of residence of a drug (VRT) through the skin; statistical moment theory.

>> *Journal of Pharmacokinetics and Biopharmaceutics*, vol. 13/1, p.55, 1985.

39. LOCALIZATION OF PHOSPHATIDYLETHANOLAMINE IN MICROSOMAL MEMBRANES AND REGULATION OF ITS DISTRIBUTION BY THE FATTY ACID COMPOSITION.

Abstract[] Rat liver microsomes were incubated with the monofunctional aminoreagent fluorescamine. Although the probe easily penetrated the membranes, two pools of phosphatidylethanolamine (PE) could be detected. The first pool rapidly reacted with the probe and comprised 80% of the total PE. The second pool exhibited a very slow interaction. The two pools showed differences in fatty acid composition as well as in their sites of attachment. In vivo labeling with ethanolamine, glycerol, and palmitic and stearic acid resulted in a higher specific activity in the first pool after 1 hr.; equilibration with the second pool took about 3 hr. No equilibration between the pools could be detected under in vitro conditions. In vivo incorporation of labeled fatty acids showed that palmitic and stearic acids were mainly incorporated into phosphatidylethanolamine by the novo synthesis, while linoleic and arachidonic acids were introduced through deacylation-reacylation processes. Injection of liposomes consisting of labeled synthetic phosphatidylethanolamines into the portal vein was followed by uptake by the hepatocytes and incorporation of the lipids into the microsomal membranes. Depending on the fatty acid composition of the injected lipid, one of either of the two pools became labeled.[] It is suggested that the fatty acid composition of a given phospholipid molecule exerts a signal function directing the lipid to its final intramembranous location.

>> VALLTERSSON, C., L. FILIPSSON, AND G. DALLNER. Localization of the phosphatidylethanolamine in microsomal membranes and regulation of its distribution by the fatty acid composition. *J. Lipid Res.* 1986. 27:731-741.

* Supplementary key words: fluorescamine phosphatidylethanolamine pools lipid translocation
× signal function deacylation-reacylation.

>> *Journal of Lipid Research*, vol. 27, p.731, 1986.

40. FREE FATTY ACID RELEASE FROM ENDOTHELIAL CELLS.

Abstract[] Cultured bovine aortic endothelial cells that have been previously enriched with fatty acid are able to release free fatty acid (FFA) into the intracellular fluid. No stimulus other than the presence of albumin in the medium is needed to elicit the FFA release. Intracellular triglycerides appear to be the source of most of the FFA that is released. The released FFA is composed of a mixture of fatty acids, with the fatty acid used to enrich the cells contributing about half of the total. Under certain conditions sufficient fatty acid can be released to increase the FFA concentration of the extracellular fluid. Cells enriched initially with arachidonic acid released 1.7- to 2.9-times more FFA as compared to cells enriched with corresponding amounts of oleic acid. Neither prosta glandins nor lipoxygenase products contributed appreciably to the amount of FFA released from cells enriched with arachidonic acid. Porcine pulmonary artery endothelial cells also can release net amounts of FFA [] These findings indicate that endothelial cells have the capacity to release fatty

acid in the form of FFA. This process could possibly play a role in the transfer of fatty acids, particularly arachidonic acid, across the endothelium.

Supplementary key words: arachidonic acid; oleic acid; albumin; triglyceride.

>> *Journal of Lipid Research*, vol. 27, p.771, 1986.

41. EFFECTS OF ESTRADIOL AND ENVIRONMENTAL TEMPERATURE CHANGES ON RAT LIVER $\Delta 6$ MICROSOMAL DESATURASE ACTIVITY.

Abstract[] The regulation of $\Delta 6$ desaturase activity by environmental temperature changes was studied in the microsomal membranes from female and ovariectomized female rat liver. Female rats adapted at 30^o-32^oC for 20-25 days and then shifted to 13^o-15^oC for 5 days showed an increased $\Delta 6$ desaturase system. Ovariectomized rats adapted under the same conditions did not show significant changes in this enzyme. The fatty acid compositions of microsomal phosphatidylcholine showed a decrease in arachidonic acid in female rats at 30^oC compared to females at 15^oC and ovariectomized rats at both temperatures. These results suggest that a modification of ovarian sex hormone levels might be responsible for the different $\Delta 6$ desaturase activity in female rats acclimated at both temperatures. In this regard, serum estradiol radioimmunoassay yielded slight differences between the two groups of female rats, suggesting that estradiol could play a role in the regulation of the $\Delta 6$ desaturase. The administration of a pharmacological dose of 17- β estradiol to female and ovariectomized rats kept at 30^o and 15^oC decreased the $\Delta 4$ microsomal desaturase activity. These data suggest that estradiol levels are involved in the regulation of the $\Delta 6$ desaturase during cold adaptation.

>> *Lipids*, vol. 21/7, p.440, 1986.

42. A LIQUID CRYSTALLINE PHASE IN HUMAN INTESTINAL CONTENTS DURING FAT DIGESTION.

Abstract[] A viscous, gel-like phase was found in ultracentrifuged human upper intestinal contents collected during rapid fat lipolysis. This "gel" phase was layered in the ultracentrifuge tube between the micellar and oil phases. The gel contained lipids typical of the micellar and not the oil phase. The concentration of the lipids was lower in the gel than in the micellar phase. The gel, unlike the micellar phase, was birefringent between crossed polarizers. These data demonstrate that lipids in this gel phase can form liquid crystals in the gut during fat digestion.

>> *Lipids*, vol. 21/7, p.444, 1986.

43. EFFECTS OF NICOTINE ON FINGER TAPPING RATE IN NON-SMOKERS.

Abstract[] Five experiments were conducted investigating the effects of nicotine on finger tapping rate in non-smokers. In each experiment subjects tapped as fast as possible a fixed number of times with one finger on a conventional computer keyboard. In the first experiment tapping rate was increased by two 2 mg doses of a nasal nicotine solution (NNS) but not by an inactive solution. The second study was carried out double-blind and showed that a single 2mg dose of NNS improved tapping performance by about 5% whereas a very low dose (0.15mg) NNS and a placebo had no effect. The effect of the NNS was to bring about a sustained increase in tapping rate from the start of each trial. The third study found that the effect of nicotine on tapping was reduced by a single 2.5 mg dose of the central cholinergic blocking agent, mecamylamine, but not a placebo. Experiment four followed tapping rate for one hour after a dose of two 2 mg NNS and showed that within a subject this behavioral measure can provide a very consistent and sensitive bio-assay of the time course of nicotine effects. The final experiments found that repeated dosing with one 2 mg NNS on an hourly schedule for six hours produced a reliable increase in tapping speed after each dose with no evidence of acute tolerance. The results indicate that nicotine can substantially improve performance by non-smokers on a simple motor task, probably via its action on cholinergic pathways, NNS provides for the first time an effective means of examining the effects of nicotine on nonsmokers.

* Keyphrases: Nicotine. Finger tapping. Non smokers.

>> *Pharmacology Biochemistry and Behavior*, vol. 25, p.727, 1986.

44. EFFECTS OF HALOPERIDOL ON THE BIOPHYSICAL CHARACTERISTICS OF OPERANT RESPONDING: IMPLICATIONS FOR MOTOR AND REINFORCEMENT PROCESSES.

Abstract[] Food-deprived rats were reinforced with sweetened condensed milk for pressing a force-sensing operandum on a continuous reinforcement basis. Force was continuously recorded (every 0.00195 sec) during each response, and measures derived from the resulting force-time waveforms serves as the basis for evaluating neuroleptic challenge in the form of haloperidol (0.04, 0.08, 0.16 mg/kg). Significant dose-related drug effects included a decrease in response rate, an increase in mean emitted peak force, and an increase in overall response duration. Additional quantitative analyses revealed that the drug-induced increase in response duration resulted primarily from a slowing in the animal's paw removal from the force-sensing operandum. The findings are analogous to deficits in Parkinson's disease and suggest a behavioral mechanism that might account for much of the rate attenuating effects of neuroleptics. Implications for motor and reward interpretations of the actions of dopamine antagonists are also discussed.

* Keyphrases: Haloperidol. Neuroleptics. Force of response. Duration of response. Motor effects. Anhedonia.

>> *Pharmacology Biochemistry and Behavior*, vol. 25, p.791, 1986.

45. CROSS-TOLERANCE BETWEEN MORPHINE- AND BOMBESIN-INDUCED INHIBITION OF INTESTINAL TRANSIT IN RATS.

Abstract[] Intracerebroventricular (i.c.v.) injection of either morphine or bombesin to rats inhibits intestinal transit of a intraduodenally administered radiochromium marker. In this work, we show that tolerance develops to this effect of bombesin after i.c.v. infusion of the peptide (0.5 µg/h for 4 days via an s.c. implanted Alzet 2001 osmotic minipump). Tolerance also develops to the inhibition of intestinal transit associated with i.c.v. morphine after s.c. injections of morphine. Bombesin-induced delay of transit is not attenuated by naltrexone (10 mg/kg. s.c.), a standard narcotic antagonist. Nevertheless, two-way cross-tolerance develops between bombesin and morphine in this system. This is a surprising result since both bombesin and morphine are believed to act on different receptors and cause opposite effects on intestinal motility in rats.

* Keyphrases: Bombesin. Morphine. Intestinal transit. Tolerance.

>> *European Journal of Pharmacology*, vol. 114, p.175, 1985.

46. SPATIAL AND TEMPORAL CHANGES OF NITRIFYING BACTERIAL POPULATIONS IN FISH PONDS OF DIFFERING MANAGEMENT PRACTICES.

Abstract[] Practices of three types of fish farming (polyculture, monoculture and traditional) resulted in density differences of ammonia oxidizers which occurred in maximal numbers in polyculture and minimal in traditional systems. This distribution pattern was attributed to their nutrients status. The sine and cosine waves of periodic functions were a good fit with the seasonal data showing a sharp peak in winter. The correlation studies revealed that seasonal changes of ammonia oxidizers of these fish ponds were largely dependent upon pH, concentrations of different forms of nitrogen, phosphate, dissolved oxygen, organic carbon and organic matter as well as the ratio of C to N.

>> *Journal of Applied Bacteriology*, vol. 59, p.195, 1985.

48. DNA REPLICATION IN *ESCHERICHIA COLI* MUTANTS THAT LACK PROTEIN HU.

Abstract[] DNA replication in *Escherichia coli* cells lacking protein HU was studied. HU has been suggested to be involved in the initiation of replication from in vitro studies. The isolated HU mutants, however, are viable under normal growth conditions (M. Wada, Y. Kano, T Ogawa, T. Okazaki, and F. Imamoto. J. Mol. Biol. 204:581-591, 1988) Chromosomal replication in the mutants appeared to be normal with respect to bidirectional replication from *oriC* and to its dependence on *dnaA* and some other *dna* gene products. No significant defect was observed in DNA synthesis in vitro with a crude enzyme fraction prepared from mutant cells. These results, along with the earlier in vitro studies, suggest that other histonelike protein(s) may substitute for HU in the initiation of replication in the mutant cells. Minichromosomes were more unstable in the mutants. In the

absence of either the *mioC* promoter, from which transcription enters *oriC*, or the DnaA box (DnaA protein-binding site) just upstream of the *mioC* promoter, the minichromosomes were especially unstable in the HU mutant and were integrated into the chromosomal *oriC* region under conditions selective for the plasmid-harboring cells.

>> *Journal of Bacteriology*, vol. 171/10, p.5672, Oct. 1989.

49. THIOL-SENSITIVE GENES OF *ESCHERICHIA COLI*.

Abstract[] The effect of 1-thioglycerol on the expression of genes of *Escherichia coli* was investigated. Pulse-labeled proteins from aerobically growing, 1-thioglycerol-treated *E. coli* were separated by two-dimensional gel electrophoresis, and their radioactivities were compared with those of identical proteins from nontreated cells. The first 10 min of exposure to thiol stimulated the synthesis of 10% of the observed proteins and inhibited the production of 16% of the proteins. After 30 min of growth with thiol, the synthesis of 44% of the observed proteins was inhibited and synthesis of 18% of the proteins was stimulated. In general, the expression of genes of carbohydrate metabolism, amino acid metabolism, and protein biosynthesis were inhibited, while nucleic acid synthetic and repair gene expressions showed mixed responses. Synthesis of transport proteins was not affected. Transient stimulation of oxidative-stress proteins and sustained stimulation of the expressions of *trxB*, *ompA*, and *ompB* genes and those of several unidentified gene products were also observed. Whether these complex responses merely reflect adjustments by cellular subsystems to a suddenly reducing environment or whether they are manifestations of a reductive-stress regulon will have to await genetic analysis of this phenomenon.

>> *Journal of Bacteriology*, vol. 171/10, p.5607, Oct. 1989.

ABSTRACTS DE REVISTAS DE ABSTRACTS (ARA).

1. THE PATHOGENICITY AND DEVELOPMENT OF *BACILLUS THURINGIENSIS* IN TERMITES.

Studies on pathogenicity and development of *Bacillus thuringiensis* in termites, *Microcerotermes championi* and *Bifiditermes beesoni*, were carried out. Both the termites were found susceptible to the infection caused by *B. thuringiensis* developed earlier in *M. championi* as compared to *B. beesoni*. In the case of *B. beesoni*, the bacterial rods reached near the peritrophic membrane after 24 hours, attacked epithelial and regenerative cells after 48 hours and reached the basement membrane of the midgut 72 hours after infection.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.100, 1986.

2. ROLE OF THE MOSS CELL WALL IN GAMETOPHORE FORMATION INDUCED BY *AGROBACTERIUM TUMEFACIENS*.

The induction of buds and gametophores on the moss *Pylaisiella selwynii* by *Agrobacterium tumefaciens* was inhibited by cell walls (CW) isolated from dicots (potato, tomato bean) but not by those from monocots (asparagus, onion). Pectin and polygalacturonate were also inhibitory; the latter was more effective. CW from *Pylaisiella* protonema also inhibited gametophore induction by *A. tumefaciens*; CW from *Pylaisiella* gametophores were less inhibitory; and *Polytrichum commune* protonema or gametophores showed little inhibitory activity. The absence of suitable *Agrobacterium* adherence sites on *Polytrichum* CW and the generation of such sites by pectinesterase action account for these results.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.100, 1986.

3. EVOLUTION AND SPREAD OF IncFIV PLASMIDS CONFERRING RESISTANCE TO TRIMETHOPRIM.

Twenty-one IncFIV-group plasmids conferring trimethoprim resistance in *Escherichia coli* isolates from humans and pigs were examined. Three evolutionary lines of plasmids were identified on the basis of restriction enzyme analysis. All R plasmids readily transferred to laboratory strains, and evidence was found for transfer to other biotypes of *E. coli* in the environment. The *Tp^r* genes from representatives of the plasmid lines were cloned and compared by restriction analysis and by hybridization with two characterized *Tp^r* dihydrofolate reductase genes. The sequences flanking the *Tp^r* genes were different for each line, but all showed homology with the type 2 dihydrofolate

reductase gene, irrespective of whether they were of human or animal origin. There was no hybridization to the type 1 gene. The remarkable degree of similarity among plasmids of the third line provided clear evidence of the exchange of plasmid-bearing *E. coli* between humans and pigs.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.42, 1986.

4. SELECTION OF SOME POTENTIAL CYTOSTATIC AGENTS FROM NEW ANTIBIOTIC PREPARATIONS OF BIOSYNTHESIS.

The "in vitro" action of some new antibiotic preparations of biosynthesis on HeLa cell culture development was investigated. The significant modification of the protein dynamics considered as an expression of the cytostatic action of the drugs tested by the authors allowed the selection of some potential cytostatic agents. These should be included in the "in vivo" screening circuit on tumor bearing animals in order to characterize them as cancerostatics.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.42, 1986.

5. INTERRELATION BETWEEN ACTIVITY OF *ACTINOMYCES RECIFENSIS* VAR. *LYTICUS* 2435 PRODUCING LYTIC ENZYMES AND ITS POPULATION VARIABILITY.

Spontaneous variability of *Actinomyces recifensis* var. *lyticus* 2435 producing a complex of lytic enzymes was studied. A correlation between the strain activity and the content of the variants of the main morphological type in the population was shown. The carbon sources influenced the proportion of different type variants in the population. Strain 2435 was rather stable with respect to the level of the synthesis of yeast-like enzymes and showed a significant variation with respect to the level of the biosynthesis of the bacteriolytic complex. The population variation of strain 2435 with respect to the staphylolytic (synthesis of specific endopeptidases and muramidase activity) was most pronounced.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.43, 1986.

8. STIMULATED SALIVARY FLOW RATE, PH AND *LACTOBACILLUS* AND YEAST CONCENTRATIONS IN PERSONS WITH DIFFERENT TYPES OF DENTITION.

The flow rate of stimulated whole saliva did not differ significantly in relation to dentition in men and premenopausal women in an unmedicated population. In the postmenopausal women the flow rate was lower in full denture wearers and in those having a highly reduced number of occluding pairs of teeth. Full denture wearers had salivary yeasts and lactobacilli more often and with higher counts than fully dentate persons, a group which in any case showed a difference in the yeast distribution between the sexes.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.74, 1986.

9. REDUCTION OF ORAL FLORA WITH RIFAMPIN IN HEALTHY VOLUNTEERS.

The effect of a short course of rifampin on the oral microflora was evaluated in 17 healthy volunteers. Salivary specimens were collected before and after two 600-mg doses of rifampin administered 6 h apart. Salivary bacteria were identified to species, and total quantitative colony counts were determined for each isolate. Clinical studies are needed to clarify the significance of the in vitro data and to delineate a possible role for rifampin in preoperative prophylaxis of patients undergoing head and neck cancer surgery.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.74, 1986.

10. RAPID DIAGNOSIS OF DYSBACTERIOSIS BY THE DETECTION OF β -ASPARTYL-GLYCINE IN FECES UNDER EXPERIMENTAL CONDITIONS.

In experiments on Fischer rats, both with common microflora and germ-free, the influence of the systemic destination of different antibiotics (tetracycline + ampicillin, gentamicin + kefzol, gentamicin, fradizine) on the intestinal microflora, the content of β -aspartyl-glycine in feces and the colonization resistance of the intestinal tract to *Staphylococcus aureus* B-243 and *Pseudomonas aeruginosa* No. 93 has been studied. The early appearance of β -aspartyl-glycine in the supernatant of fecal samples has been shown to be the first sign of dysbacteriosis and to indicate the decrease of the colonization resistance of the intestine to opportunistic bacteria.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.74, 1986.

11. PSEUDOTUMOR RESULTING FROM ATYPICAL MYCOBACTERIAL INFECTION: A "HISTOID" VARIETY OF *MYCOBACTERIUM AVIUM-INTRACELLULARE* COMPLEX INFECTION.

A 54-year-old immunosuppressed cardiac transplant recipient with a six-month history of progressive swelling of the hand, with nodules and linear lymph node chain enlargement, diagnosed as a sporotrichoid *Mycobacterium avium-intracellulare* pseudotumor is described. The microscopic features closely resembled the previously described histoid variety of lepromatous leprosy. Routine hematoxylin and eosin staining suggested a spindle cell neoplasm rather than an infectious or inflammatory process. An infectious etiology was pursued on the basis of the clinical setting.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.74, 1986.

12. EFFICACY OF LOW-CONCENTRATION IODOPHORS FOR GERMICIDAL HAND WASHING.

The efficacy of iodophor germicides containing different concentrations of available iodine against transient (inoculated) bacteria and the natural hand microflora was compared with chlorhexidine gluconate (2 and 4%) liquid detergent (Hibitane), non-germicidal soap and a tap water rinse. The tap water rinse was ineffective compared with all other treatments. Only 4% chlorhexidine gluconate liquid detergent and iodophor containing 0.75% available iodine were significantly better than the non-germicidal soap for reduction of transient bacteria, *Escherichia coli* and *Pseudomonas fluorescens*, that had been inoculated onto hands. These agents also caused a significant reduction in the number of "natural" microorganisms released from hands after a standard 15 s hand wash.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.74, 1986.

15. INHIBITION OF BACTERIAL GROWTH BY TETRACYCLINE-IMPREGNATED ENAMEL AND DENTIN.

Tetracyclines can react with enamel and dentin to form relatively insoluble fluorescent compounds. The purpose of this study was to evaluate the possible antimicrobial effect of these reaction products on various microorganisms associated with human dental plaque and periodontal disease. Slabs of native dentin and enamel as well as demineralized dentin were immersed in aqueous solutions of tetracycline HCl, oxytetracycline HCl and doxycycline HCl for periods of 1 h or 24 h. With the exception of enamel impregnated for 1 h in 0.01mg/ml tetracycline solution, all test specimens caused growth inhibitions zones, varying in size according to concentration of the drug, immersion period and bacterial species. The results indicate that tetracyclines react with enamel and dentin to form slightly soluble compounds with a pronounced antibacterial effect. In comparison, the antimicrobial effect of dentin treated with penicillin was small.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.75, 1986.

16. SUCRASE AND MALTASE ACTIVITIES IN SUPRAGINGIVAL PLAQUE IN HUMANS OF STREPTOCOCCAL, ACTINOMYCETES AND LACTOBACILLI SPECIES.

20 Reference strains and 72 isolated strains from dental plaque of streptococci-, *Actinomyces*, and lactobacilli species were examined for sucrase and maltase activities. The type of sucrase in the different strains was determined by use of the-glucosidase inhibitor, acarbose. The enzyme activities were determined as formation of monosaccharide, and quantitated spectrophotometrically. Although variations occurred in enzyme activities between reference and isolated strains, the same general pattern was noticed. Strains of *Streptococcus mutans* and *S. salivarius* showed regularly the highest sucrase activities, followed by strains of *Actinomyces viscusus* and *A.*

naeslundii. Most lactobacilli belonged to the bacteria with low sucrase activity like *S. sanguis* and *S. mitior*. In some lactobacilli strains, however, a high sucrase activity was observed.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.75, 1986.

17. ENDOCRINE PROFILE AND SEMINAL PLASMA COMPOSITION IN HANSEN'S DISEASE.

Endocrine profile and seminal plasma composition in 45 patients with tuberculoid-type Hansen's disease are reported. There was marked reduction in sperm count and motility, with an increase in abnormal forms of spermatozoa. The levels of serum prolactin and oestradiol-17 B were increased significantly with a marked reduction in serum FSH, LH and testosterone. The possible significance of these findings may help further to understand male reproductive function in Hansen's disease.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.75, 1986.

18. A CONTROLLED CLINICAL TRIAL OF PROPHYLACTIC TINIDAZOLE FOR CHEMOPROPHYLAXIS IN THIRD MOLAR SURGERY.

A randomised double-blind placebo-controlled clinical trial was carried out to assess the efficacy of a single dose anaerobicidal prophylactic regimen using a 2 g oral dose of tinidazole administered prior to the surgical removal of bone impacted lower third molar teeth. Fifty patients completed the trial in whom 89 lower third molars were removed. Four sockets out of a possible 45 became infected in the tinidazole group whereas 20 out of 45 became infected in the placebo group. These differences were statistically significant. The results suggest that this anaerobicidal regimen which is free from the requirements of patient compliance significantly improves postoperative recovery after third molar surgery.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.75, 1986.

19. FIBRONECTIN BINDING AND CELL-SURFACE HYDROPHOBICITY OF ATTACHING EFFACING ENTEROPATHOGENIC *ESCHERICHIA COLI* STRAINS ISOLATED FROM NEWBORN AND WEANLING RABBITS WITH DIARRHOEA.

32 different strains of *Escherichia coli* isolated from rabbits with diarrhoea were studied for cell-surface properties which may be involved in intestinal colonisation. Based on the findings, the authors propose that binding to intestinal cell surface (mucus)-associated fibronectin may be an early important step in intestinal colonisation of the small bowel in enteropathogenic *E. coli* (EPEC) diarrhoea in rabbits and other animal species.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.95, 1986.

20. STUDIES ON *MYCOPLASMA MYCOIDES* SUBSP. *MYCOIDES* (LC) IN LAMBS AND CALVES.

Six cesarean-derived lambs were inoculated either with 4.5×10^4 , 4.5×10^6 or 4.5×10^8 *Mycoplasma mycoides* subsp. *mycoides* intratracheally. One animal receiving the intermediate dose died four days postinoculation, the two receiving the high dose died six days postinoculation, while one receiving the low dose died eight days postinoculation. The two surviving lambs were challenged on day 20 postinoculation with 1×10^8 organisms subcutaneously and 2×10^9 organisms intravenously. One animal died eight days following this challenge while the other survived and was killed. Six conventionally reared lambs challenged with 90 to 8500 organisms by intranasal and intraocular instillation failed to become infected. Three conventionally reared calves were each inoculated with 1×10^8 organisms by each of intratracheal, subcutaneous and intravenous routes. They were killed 20 days postinoculation without having shown any clinical signs.

>> *Microbiology Abstracts*. Bacteriology, vol. 21/6, p.95, 1986.

21. EFFECT OF CONTAINER MATERIAL, STORAGE TIME AND TEMPERATURE ON DETERMINATIONS OF CADMIUM LEVELS IN HUMAN URINE.

The effects of container material, viz, polyethylene, polypropylene, polystyrene, borosilicate glass and flint glass, storage time (up to 86 days), and temp. (4° and 22°) were studied. No loss of added Cd occurred during 10 and 28 days when samples were stored in polyethylene at 22° , or for 3 to 4 days storage at 22° ; the other four materials were all suitable. The loss of Cd, especially from actual samples, was, for all types of containers, greater at 4° than at 22° . All determinations of Cd were by graphite-furnace a.a.s.

>> *Analytical Abstracts*. Biochemistry, vol. 47/12, p.1144, Dec. 1985.

23. SIMPLE, RAPID AND SENSITIVE ALTERNATING-CURRENT TASTPOLAROGRAPHIC METHOD FOR LEAD DETERMINATION IN BONES.

The dried sample (0.13 g) of rat bone is kept overnight at ambient temp. in 4 ml of conc. $\text{HNO}_3\text{-HClO}_4$ (1:1), the resulting soln. is evaporated to dryness, the residue is four times heated to dryness with H_2O , and the product is dissolved in 5 ml of aq. 20% citric acid. Polarography of this soln. is carried out with a dropping-mercury electrode, a platinum auxiliary electrode and a KCL-saturated silver-AgCL micro reference electrode. A sinusoidal alternating component (15 mV) is superimposed on the linearly rising potential applied to the electrodes, and the integrated first harmonic of the a.c. is recorded between -0.2 and -0.6 V for the last 0.2 s of the drop life. Peak height at -0.356 V is evaluated by using a calibration graph or the standard-additions method. Citric

acid completely binds the Ca present and avoids matrix interference. The sensitivity corresponds to 2 ppm of Pb in the bone, and this method is suitable for rapid screening in the range 2 to 1000 ppm; the more time-consuming a.a.s. method is required only for Pb contents in the ppb range.

>> *Analytical Abstracts*. Biochemistry, vol. 47/12, p.1144, Dec. 1985.

24. DETERMINATION OF VITAMIN A[RETINOL] AND E[α -TOCOPHEROL] IN PHARMACEUTICAL PREPARATIONS BY H.P.L.C. METHOD.

The cited vitamins were extracted from tablets, capsules, creams or veterinary preparations with a 1:1 mixture of CHCl₃ with aq. 95% ethanol-CHCl₃ (7:3). The extracts were filtered through Na₂SO₄ and dried on a rotary evaporator. The residue was dissolved in the mobile phase [CHCl₃-hexane (1:4)] for h.p.l.c. on a column (25 cm x 4mm) of μ Porasil with a mobile-phase flow rate of 1ml min⁻¹ and 287-nm detection. Recoveries were 94.4, 99.2 and 98.9 % for tocopheryl acetate, retinyl palmitate and retinyl acetate, respectively; standard deviations were <5.0%.

>> *Analytical Abstracts*. Pharmaceutical Chemistry, vol. 47/12, p.1182, Dec. 1985.

27. HIGH-PERFORMANCE LIQUID-CHROMATOGRAPHIC DETECTION OF THE ADDITION OF GRAPEFRUIT JUICE TO ORANGE JUICE.

The addition of >10% of grapefruit juice to orange juice can be detected by the determination of naringin, which is the dominating flavanone glycoside of grapefruit. Unfiltered juice is applied to a column (80 mm x 25 mm) of polyamide equilibrated with H₂O. The column is washed with H₂O and percolated with methanol, and the methanol eluate is evaporated to dryness. A soln. of the residue is analysed by h.p.l.c. on a steel column (12.5 mm x 5 mm) packed with Hypersil 5 ODS, with methanol-1% acetic acid (33:67) as mobile phase (0.8 ml min⁻¹) and detection at 280 nm. Naringin was detected in the presence of narirutin and hesperidin in an adulterated orange juice. The remainder of the polyamide eluate is evaporated to dryness, benzoylated and analysed by normal-phase h.p.l.c. Pure orange juice contains no naringin but shows the presence of narirutin and hesperidin.

>> *Analytical Abstracts*. Food, vol. 47/12, p.1192, Dec. 1985.

28. COMPARATIVE INVESTIGATIONS INTO THE DETERMINATION OF PROTEIN BY THE KJELDAHL METHOD AND N.I.R. (NEAR-INFRA-RED) TECHNIQUE.

Prepared mixtures of wheat flour with a free amino-acid, gluten or cellulose powder (30 samples in all) were analysed by the conventional Kjeldahl method, with use of a factor of 5.7 to convert percentage of N into that of protein, and by near-i.r. reflectance spectrophotometry on a Cary model 14 prism-grating instrument under computer control. The i.r. spectrum was scanned

from 1000 to 2638.4 nm at 0.2-nm intervals, the resulting 8192 readings being compressed into 1024-point curves. The curves were transformed to log. (1/R) form to afford rectilinear correlation with concn., and the second-derivative curve was obtained. Values measured at 2177.6 and 2062.4 nm showed high correlation with "Kjeldahl protein" and with calculated protein, respectively. Measurements of phenylalanine at 1140.8 nm and of cellulose at 2336.0 nm showed excellent correlation with concn. present.

>> *Analytical Abstracts*. Food, vol. 47/12, p.1189, Dec. 1985.

29. EVALUATION OF AN EXPOSED-ELECTRODE GALVANIC CELL DISSOLVED-OXYGEN ANALYSER USED IN BREWERIES.

Accuracy, range, inter-instrumental variation, drift and pH dependence are examined in exposed-electrode galvanic cell instruments used for determining dissolved O in beer. Such analysers produce results that are too variable and unreliable to make them suitable for determination of <600 $\mu\text{g l}^{-1}$ of dissolved O in beer.

>> *Analytical Abstracts*. Food, vol. 47/12, p.1192, Dec. 1985.

30. PHARMACOKINETIC DRUG INTERACTIONS WITH CIMETIDINE (TAGAMET).

The mechanism of drug interactions of cimetidine (I) and their clinical and therapeutic relevance were presented.

The drug-metabolizing enzymes in the liver are inhibited by I, which leads to higher blood levels and adverse effects of other drugs, especially with preparations having a narrow therapeutic range, such as anticoagulants, theophylline, or phenytoin. The influence of I on the absorption, distribution and elimination of other pharmaceutical preparations is low.

>> *International Pharmaceutical Abstracts*. Drug Interactions, vol. 21/6, p.524, Mar. 1984.

31. CLINICAL PHARMACIST IMPACT ON PARENTERAL CEPHALOSPORIN PRESCRIBING.

A study was undertaken to evaluate clinical pharmacists' influence on parenteral cephalosporin prescribing patterns in a 940 bed hospital.

Two intervention methods were evaluated: 1) publication of a pharmacy newsletter for physicians containing specific recommendations and emphasizing the primary use of cefazolin, and 2) personal interaction between the clinical pharmacy staff and physicians promoting the recommendations outlined in the newsletter. The methods were compared with each other as well as with an initial time span during which no influencing efforts were made.

The effect of the pharmacy newsletter as a sole means of influencing physician prescribing of parenteral cephalosporins was minimal. The effect of pharmacist-physician interaction, either as

a sole means or in conjunction with a pharmacy newsletter, resulted in an increased use of cefazolin. An annual cost savings of up to \$11,265.88 was projected.

It was concluded that physicians can be influenced by clinical pharmacists in their prescribing of parenteral cephalosporins, leading to significant cost savings.

>> *International Pharmaceutical Abstracts*. Institutional Pharmacy Practice, vol. 21/6, p.499, Mar. 1984.

33. HEMODYNAMIC EFFECTS OF DOPAMINE ADMINISTRATION IN PATIENTS WITH SEVERE CHRONIC CONGESTIVE HEART FAILURE: COMPARISON OF TWO DOPAMINE PRODUCTS.

The hemodynamic effects of dopamine hydrochloride (I), as a generic preparation or as Intropin, were compared in 10 patients with chronic severe congestive heart failure who received 5mcg/kg/min of either drug for 30 min.

During the infusions, there was no significant difference in hemodynamic responses between the 2 preparations. In addition, the acute infusion of I to patients with chronic congestive heart failure and elevated pulmonary capillary wedge pressures was associated with a significant improvement in cardiac output without significant changes in left ventricular filling pressure and/or symptoms.

It was determined that the generic and standard preparations of I are bioequivalent.

>> *International Pharmaceutical Abstracts*. Biopharmaceutics, vol. 21/6, p.524, Mar. 1984.

34. CLINICAL TRIAL OF AN ORAL CONTRACEPTIVE CONTAINING DESOGESTREL AND ETHINYL ESTRADIOL.

In a clinical trial, the efficacy of an oral contraceptive combination (Marvelon) containing 150 µg of desogestrel and 30 µg of ethinyl estradiol was determined in 1159 women who used the preparation for a total of 15,222 observed cycles.

The drug was administered in cycles of one tablet daily for 21 days, followed by 7 tablet free days.

There were no pregnancies attributed to tablet failure. Cycle control during the trial was good. No serious side effects occurred, and the incidence of minor complaints was lower than during a nontreated cycle.

It was determined that the combination is an effective oral contraceptive and that desogestrel suppresses the undesired effects of estrogen on the endometrium but does not interfere with its beneficial effects on certain metabolic functions.

>> *International Pharmaceutical Abstracts*. Investigational Drugs, vol. 20/2, p.22, Jan. 1983.

35. SIMULTANEOUS ADMINISTRATION OF INFLUENZA AND PNEUMOCOCCAL VACCINES.

The antibody responses and adverse reactions of 126 participants (aged 18-26 yr.) given influenza and pneumococcal vaccines at the same time, or on separate occasions, were compared.

Results showed that simultaneous administration of the 2 vaccines did not result in any increase in local or systemic reactions, except for transient myalgia. Study participants who received the vaccines simultaneously had pneumococcal antibody responses comparable with those of participants who received pneumococcal vaccine alone, although the response rate for both groups was low. There was also no difference between the simultaneous administration group and the group that received influenza vaccine alone in antibody response to the influenza A/Texas antigen. Antibody responses to the influenza A/Brazil and B/Hong Kong antigens were adequate for both groups, although the group that received influenza vaccine alone achieved higher postvaccination antibody titers.

It was concluded that simultaneous administration of influenza and pneumococcal vaccines is as safe and effective as giving either vaccine alone.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.25, Jan. 1983.

37. LABETALOL AND PLATELET FUNCTION IN PRE-ECLAMPSIA.

Pre-eclampsia patients whose diastolic blood pressure was still above 95 mm Hg after 4 days of hospital rest were randomly allocated to traditional bed rest only or to receive increasing doses of oral labetalol (I) until their blood pressure was below 90 mm/Hg.

All patients with diastolic blood pressure above 110 mm Hg were treated with I. After 7 days, platelet counts in the I-treated patients had risen into the normal range while counts in the controls had continued to fall; the difference was significant.

It was suggested that part of the beneficial effect of I therapy was mediated through PGI₂ stimulation.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.414, Jan. 1983.

38. EFFECTS OF AGE AND SMOKING ON THE PHARMACOKINETICS OF PINDOLOL AND PROPRANOLOL.

In a randomized crossover study, the effects of age and cigarette smoking on the pharmacokinetics of pindolol (I) (15 mg daily) and propranolol (II) (240 mg daily) were studied in 32 healthy men.

Neither age nor smoking was shown to have any influence on the time to reach a peak plasma level after I or II. Age, on the other hand, significantly increased the peak plasma levels and

the areas under the plasma concentration time curves, and decreased the elimination rate constants, the differences between the age groups being more pronounced for II than for I. No effect of smoking on these parameters was observed. Differences were found between I and II in respect of time to reach a peak plasma level, peak plasma levels and area under the plasma concentration time curves in the groups of old (over 60 yr.) non-smokers and young (aged 20-30 yr.) smokers when related to the young non-smokers control group. Changes observed tended to be less for I and were considered to be of little clinical significance.

>> *International Pharmaceutical Abstracts*. Drug Interactions, vol. 20/2, p.709, Jan. 1983.

39. TREATMENT OF BASAL CELL EPITHELIOMA WITH TOPICALLY APPLIED SOLCODERM.

The efficacy of topical Solcoderm (a solution containing acetic acid, copper ions, lactic acid, nitrates, and oxalic acid) as a sole method of treatment of basal cell epithelioma of the skin was evaluated in 96 patients.

Fifty-seven (59.3%) of the patients were in complete clinical remission after up to 30 months of follow-up. In 22 of these patients (39%), posttreatment histological examination confirmed the absence of tumor. The cosmetic results were good. Nineteen patients (19.7%) showed recurrence during the observation period. Essentially all of these recurrences occurred in lesions which were originally over one cm in diameter or were lesions recurring after treatment by other methods. Twenty patients (20.8%) with very thick or ulcerated lesions failed to respond. No local or systemic side effects were noticed during this trial period.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.708, Jan. 1983.

40. FIVE YEAR CLINICAL TRIAL OF LEVONORGESTREL SILASTIC IMPLANTS (NORPLANT).

Silastic (dimethicone) intradermal implants containing levonorgestrel were tested as a long term contraceptive system in 101 women over a 5 yr. period.

No pregnancies occurred in the population. The continuation rate was 54%. Menstrual irregularities were the most frequent reason for termination of use but only during the first yr. Some of the subjects elected to continue use of the implants beyond 5 yr., allowing release rate data to be obtained for a 6 yr. period.

From the second to the sixth yr. of use, the implants delivered a constant 30 mcg/day of drug; 57% of the original drug content remained in the device even after 6 yr.

Return of fertility following removal was essentially immediate and not related to time of use. Medical reasons for removal were infrequent and no pattern was discernible.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.708, Jan. 1983.

41. COMPARISON OF FLURBITROFEN, ASPIRIN AND PLACEBO IN POSTPARTUM UTERINE PAIN.

In a double blind randomized trial, the efficacy of single oral doses of flurbiprofen (I), 50 mg, was compared to that of aspirin (II), 650 mg, and placebo, in 96 women with moderate or severe postpartum uterine pain.

Using subjective reports as indices of response, patients rated pain intensity, pain relief, and side effects at periodic intervals for 6 hr.

All measures of peak and summed analgesia exhibited significant differences among the 3 treatment groups with I and II virtually equal; each was significantly superior to placebo. Side effects were not significant.

It was suggested that analgesia with I compares favorably with II in postpartum uterine pain.

>> *International Pharmaceutical Abstracts*. Investigational Drugs, vol. 20/2, p.22, Jan. 1983.

42. DETAILS OF CONTAMINATED DRESSINGS REPORT.

The procedure used in the microbiological contamination testing of 65 batches of nonadhesive sterile first aid dressings available in the British market, and the degree and type of microbial contamination in the dressings examined, are discussed in the report of the Public Health Laboratory Service.

Results showed that 22 of 38 batches of dressings imported from India exhibited a substantial degree of microbial contamination. None of the 27 batches of British dressings examined showed a comparable degree of contamination. Of the organisms associated with contaminated dressings, aerobic spore forming bacilli and fungi predominated.

>> *International Pharmaceutical Abstracts*. Pharmaceutical Technology, vol. 20/2, p.106, Jan. 1983.

43. INSTRUMENTATION OF A DOSING DISK AUTOMATIC CAPSULE FILLING MACHINE.

The instrumentation of a Hofliger-karg GKF 330 automatic capsule filling machine is described, and preliminary analyses of the relationship of the machine's operating variables to capsule fill weight are presented.

The principles of the dosing disk method of capsule filling illustrated by this machine were compared with piston-tamp principles. Relationships between compression force, piston setting and final fill weight of capsules were evaluated. Final fill weight of the capsules, using the automatic equipment, was found to be dependent on a complex interaction of all compression stations.

>> *International Pharmaceutical Abstracts*. Pharmaceutical Technology, vol. 21/6, p.498, Mar. 1984.

44. MEDROXYPROGESTERONE ACETATE AND HOMOZYGOUS SICKLE CELL DISEASE.

The hematological and clinical effects of IM medroxyprogesterone acetate (Depo-Provera; I), 150 mg/3 months, in homozygous sickle cell (SS) disease were assessed in a 2-yr. placebo controlled crossover trial completed by 23 patients.

Hematological indices remained steady during the placebo phase, but during the I phase, fetal hemoglobin, total hemoglobin, red cell count, red cell mass and red cell survival rose significantly, and reticulocytes, irreversibly-sickled cell counts and total bilirubin fell significantly. Painful crises were significantly less frequent during the I than the placebo phase.

The results are compatible with an inhibition of in vivo sickling in patients with SS disease during I treatment.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.414, Jan. 1983.

45. FAILURE OF RIFAMPICIN AND CO-TRIMOXAZOLE IN Q FEVER ENDOCARDITIS.

A case of a 38-yr-old man with *Coxiella burnetti* infection, resistant to rifampin (rifampicin; I) and Co-trimoxazole (sulfamethoxazole, combination, trimethoprim), is reported.

The immediate clinical response with Co-trimoxazole seemed satisfactory, but after 10 months of continuous treatment there was relapse with fever. Rifampin was added to the regimen. A surgical exploration of the valve was undertaken after 3 wk. of I. Both valve and diaphragm were excised and a disc-valve prosthesis inserted. *C. burnetti* colonies were seen microscopically. Rifampin and Cotrimoxazole were continued during and after the operative period.

After 16 months of continuous treatment with Cotrimoxazole, and 5 months with I and Co-trimoxazole in combination, the patient died.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.414, Jan. 1983.

46. PREVENTION OF RHINOVIRUS COLDS BY HUMAN INTERFERON ALPHA-2 FROM *ESCHERICHIA COLI*.

Forty-one susceptible volunteers were treated with repeated doses of high titer interferon alpha-2 (I) derived from *E. coli* or an identical placebo in a randomized double blind trial.

The subjects were challenged with rhinovirus type 9 on the second day of treatment. Volunteers who received I were protected against rhinovirus infection. This schedule of I was well tolerated by 10 volunteers who were not challenged with virus.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.414, Jan. 1983.

47. DICLOFENAC IN THE TREATMENT OF PRIMARY DYSMENORRHEA.

In a double blind study, the effects of diclofenac sodium (I; Voltaren; Voltarol), 50-150 mg, were compared to those of placebo, in 30 women with primary dysmenorrhea.

A better analgesic effect was demonstrated in the group of patients treated with I compared with the control group. The consumption of additional rescue analgesics was statistically significantly lower in the active treatment group compared with that in the placebo group. The patients treated with I stated a decrease of the amount of bleeding. No change in bleeding was reported in the control group. The difference between the groups was statistically significant. The number of patients willing to continue treatment with the drug received was significantly greater in the group treated with I. No patient discontinued treatment owing to side effects and there was no difference in the frequency of side effects between the groups.

>> *International Pharmaceutical Abstracts*. Investigational Drugs, vol. 20/2, p.22, Jan. 1983.

48. FLOW RATE ACCURACY OF A NEW VOLUMETRIC CONTROLLER.

A description of the Rateminder volumetric controller and an evaluation of its accuracy in delivering solutions of varying viscosity from different containers are presented.

In-vitro-testing showed that the accuracy of the device for all solutions was 98.7-101.5% of the set flow rate of either 60, 125 or 175 ml/hr.

>> *International Pharmaceutical Abstracts*. Pharmaceutical Technology, vol. 21/6, p.498, Mar. 1984.

49. SELECTIVE INTRA-ARTERIAL STREPTOKINASE THERAPY IN THE IMMEDIATE POSTOPERATIVE PERIOD.

A case of 25-yr-old patient successfully treated with selective intra-arterial streptokinase for acute distal thrombosis, 7 hr. after repair of a common femoral artery laceration and retroperitoneal dissection, is reported.

No systemic effects or complications developed.

It was concluded that local intra-arterial thrombolytic therapy is more effective and safer than IV systemic therapy and should be considered in the immediate post-operative period, providing the drug is delivered downstream from the operative site.

>> *International Pharmaceutical Abstracts*. Drug Evaluations, vol. 20/2, p.25, Jan. 1983.