SELECTED ABSTRACTS ON ANIMAL MODELS FOR BIOMEDICAL RESEARCH - II

Charles B. Frank, et al

National Academy of Sciences-National Research Council

Prepared for:
Office of Naval Research
National Cancer Institute
National Science Foundation
Atomic Energy Commission
Agricultural Research Service

1972

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SELECTED ABSTRACTS
ON
ANIMAL MODELS FOR
BIOMEDICAL RESEARCH - II
This publication was supported in part by Contract PH43-64-44 with the Cancer Chemotherapy National Service Center, National Cancer Institute, and the Animal Resources Branch, National Institutes of Health, U.S. Public Health Service; Contract AT (11-1)-3369 with the Atomic Energy Commission; Contract N00014-67-A-0244-0016 with the Office of Naval Research, U.S. Army Medical Research and Development Command, and U.S. Air Force; Contract 12-14-140-2341-91 with the Agricultural Research Service, U.S. Department of Agriculture; Contract NSF-C310, Task Order 173, with the National Science Foundation, Grant RC-1M from the American Cancer Society, Inc.; and contributions from pharmaceutical companies and other industry.

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INSTITUTE OF LABORATORY ANIMAL RESOURCES
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INSTITUTE OF LABORATORY ANIMAL RESOURCES

The Institute of Laboratory Animal Resources (ILAR) was founded in 1952 within the Division of Biology and Agriculture. It serves as a coordinating agency to disseminate information, survey existing and required resources, establish standards, promote education, hold conferences, and generally to upgrade laboratory animal resources.

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This publication is the second in a series containing abstracts selected from the biomedical literature pertaining to animal models. These abstracts were accumulated during 1972 and represent only a select portion of papers appearing in journals during the period 1970 - 1972. An earlier edition, published in 1971, contained abstracts of papers appearing in the literature from 1969 - 1970.

There are many papers in the scientific literature pertaining to potential animal models in various fields, and this publication does not purport to be all inclusive. A more comprehensive listing of recent citations appears in the quarterly newsletter, ILAR News, available from the Institute of Laboratory Animal Resources.

In addition to the abstracts presented in this compendium, a special section has been appended that includes a brief review of several recent books or symposium reports specifically related to animal models for research. The appendix (pages 45-56) includes a summary and lists the pertinent papers in these publications.

Since July 1969, the Institute has maintained the Animal Models and Genetic Stocks Program, an information exchange program developed to assist scientists in the selection and location of animal models and genetic stocks for biomedical research. The program accumulates references and major characteristics describing animal models or genetic stocks, the names and addresses of scientific consultants, and a genetic stock registry listing sources of supply and the location of unique animal colonies and mutant stocks throughout the United States. The data are made available without charge to interested individuals in response to specific inquiries and through periodic publication in the ILAR News.

Information is continuously accumulated on colonies of animals that can serve as models for biomedical research. ILAR is asking investigators to assist in the development of its data bank by providing information on animal models or genetic stocks maintained within their institutions. A sample colony data form appears on page 57. Your cooperation in completing this form and providing the information to ILAR will aid in the further development of the Animal Models and Genetic Stocks Information Exchange Program.

The support of investigators is essential if a comprehensive listing of the animal models and genetic stocks being used throughout the country is to be maintained. Interested persons are urged to make suggestions for improving the program and to furnish whatever information they may have concerning potential models or genetic stocks. Readers are requested to complete and return the questionnaire on page 59 to assist ILAR in evaluation of this publication. Correspondence should be addressed to:

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Six dogs were administered excessive quantities of ethanol daily through an esophageal feeding, for periods ranging from 10 to 18 months. Ethanol levels of venous blood after alcohol was administered ranged from 315 to 477 mg%. Animals were fed a balanced diet. Serial biopsy specimens of the liver revealed fatty metamorphosis in 4 of 6 dogs, as well as degenerative changes of the hepatocytes, including eosinophilic hyaline bodies, cell death, infiltration with polymorphonuclear leukocytes and centrolobular fibrosis. These histologic alterations of the liver are comparable to those observed in patients with alcoholic hepatitis or alcoholic liver disease other than cirrhosis. In 3 control dogs, there were no changes in hepatic function or in the histologic appearance of the liver. Liver function abnormalities which developed included elevations of serum alkaline phosphatase, serum glutamic pyruvic transaminase and glutamic oxalacetic transaminase, and decreased serum albumin levels. The present investigation indicates that daily administration of excessive amounts of ethanol over a prolonged period can produce hepatic lesions similar to those observed in human alcoholic liver disease. -Authors' abstract.


Evidence is presented that viral hepatitis in marmosets is caused by an actual transmission of human agents and is not an activation of latent marmoset viruses. The investigators summarize the attempts of various laboratories to induce hepatitis in marmosets and to pass the disease serially from animal to animal. In this study, inoculation of marmosets with coded human specimens was carried out using sera or plasmas from normal individuals; from volunteers before inoculation with Willow Brook MS-1 virus and acute phase specimens from the same volunteers. None of the normal human sera or plasmas induced disease in any of the experimental animals, whereas the acute phase specimens induced hepatitis in 21 of 27 white lipped and in 6 of 9 cotton topped marmosets. The authors conclude that there is little doubt left that human infectious hepatitis can be transmitted to marmoset monkeys and can be passed serially from animal to animal. The physical, chemical and antigenic characteristics of the transmissible agent(s) have been partially identified and final identification should be possible with this consistently reliable animal assay system. - M.J.A.

Investigation of the function of human sling fibers is not feasible with the use of technics currently available for animal experiments. Thus, this study examined the anatomy of the gastric sling fibers in 22 dogs and 16 cats to determine if either or both resemble that of the human. In both species, the gastric sling fibers hooked around the notch between the gastric fundus and distal esophagus, and traversed the stomach, anterior and posteriorly, parallel to the lesser curve, finally disappearing near the incisura angularis. A constrictor cardiac muscle was found at the upper limit of the sling fibers in both species. The muscularis propria of the distal esophagus of the dog was found to be striated. In contrast, smooth muscle was present in the distal esophagus of the cat. Furthermore, a vestibule, analogous to that described in man, was found in the cat but not in the dog. It has been postulated that the sling fibers play a role in the sphincteric mechanism of the distal esophagus. The finding that the anatomy of the sling fibers and the distal esophagus in the cat resembles that of man suggests that it would be a more suitable model than that of the dog. - Authors' abstract.


Caesphagi were infused with a standard acid-pepsin solution for 1/2, 1, 2, 4, or 7 hours. The esophagitis scores for each infusion time were closely clustered and the depth of esophageal injury was directly related to infusion time. A model of experimental injury was directly related to infusion time. A model of experimental esophagitis was developed which permits: prediction of esophagitis scores for a given infusion time; esophagitis production of desired depth by selection of the appropriate infusion time. - Authors' abstract.


This paper presents some of the problems of using rodents as experimental models for research in periodontal disease. The scope of the paper has been confined to experimental systems of rats and hamsters. A selective citation has been made of relevant studies within the field, rather than attempting complete coverage of the extensive literature available on the use of rodents in periodontal disease research. An attempt was made to focus on certain aspects of the problem deemed pertinent to continued development of the model for future needs. It was felt that this approach could be aided by a more careful consideration of animal models in general. Inherent weaknesses and limitations of the model have been pointed out. These should be balanced against certain special advantages of the model to make it a useful research tool for future studies. - Author's conclusions modified.
6. Kirkpatrick, J. J. (Department of Surgery, Wayne State University 
   School of Medicine, 540 East Canfield Avenue, Detroit, Michigan 
   Res. 11:608-611.

   The methods and criteria for creating a standard liver injury in the 
   experimental animal were presented. A variety of animals were studied to 
   find a species with liver anatomy closely paralleling the human. Sheep 
   were found to be ideal subjects for this type of study. Their liver has 
   two main lobes and their biliary, arterial, venous, and portal circulations 
   differ only slightly from those of man. In this study, it was found that 
   a bursting injury produces the most consistent and lethal results. Immediate 
   and profound hypotension out of proportion to blood loss is often seen after 
   this type of injury. It is hoped that this experimental model will be of 
   benefit in comparing present methods of therapy in the treatment of severe 
   liver injuries. - Author's summary modified.

7. Lisboa, P. E. (Clinica Universitaria de Patologia Medica, University 
   Hospital of Santa Maria, Lisbon, Portugal). 1971. Experimental 
   hepatic cirrhosis in dogs caused by chronic massive iron overload. 
   Gut 12:363-368.

   In this study 19 dogs were subjected to massive parenteral iron loading 
   using intravenous iron-dextran and intramuscular iron-sorbitol. Although 
   13 animals died, in many cases the deaths were attributable to fighting. 
   The large doses of iron employed (up to 5.8 g/kg) were well tolerated by the 
   surviving animals, and after 35 to 47 months five of the six survivors had 
   developed hepatic cirrhosis with massive siderosis; the dog which had not 
   yet developed cirrhosis received the smallest iron load. The liver pathology 
   in many ways resembled that of human haemochromatosis, and may provide an 
   experimental model for the study of chronic iron-induced liver injury. - 
   Author's summary modified.

8. McSherry, C. K. (Department of Surgery and of Medicine, Cornell 
   University Medical College, New York Hospital, New York, New York 
   10021), F. Glenn, and N. B. Javitt. 1971. Composition of basal 
   and stimulated hepatic bile in baboons, and the formation of cho-

   The baboon, Papio, has been found to be a model for the study of the 
   pathogenesis of cholesterol cholelithiasis in man. Studies of the physiologic 
   variations in hepatic bile composition indicate a cyclic pattern to the 
   proportions of cholesterol, lecithin, and bile salt in hepatic bile. During 
   reabsorption of the bile salt pool from the intestines (stimulated flow), 
   hepatic bile is characteristically undersaturated with cholesterol. After 
   reabsorption of the bile salt pool (basal flow), hepatic bile is character-
   istically supersaturated with cholesterol. This typical pattern of basal 
   and stimulated hepatic bile occurs irrespective of the presence of cholesterol 
   stones in the baboon. Recognition of these two types of hepatic bile and 
   their interrelationship during admixture in the gallbladder provides new 
   insight into the pathogenesis of gallstone formation. - Authors' abstract.

Marmosets have been shown to develop hepatitis after inoculation of serum from patients with viral hepatitis. The activity alterations of lactate dehydrogenase, isocitrate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, glutamate dehydrogenase, glucose-6-phosphate dehydrogenase, and phosphogluconate dehydrogenase in serum and liver tissue of marmosets with hepatitis suggest that these animals suffer from a mild but relatively protracted hepatocellular injury. Although the enzyme patterns are not identical to those seen in human viral hepatitis, they appear to resemble more closely the picture seen in that disease than in any other. - Authors' abstract.


Hepatitis was induced in male albino rats treated with D-GalN-HCl (1.5g/kg) in vitro. Incorporation of alanine-U-14C, pyruvate-2-14C, and glutamine-3,4-14C acid into glucose by liver slices from GalN-treated animals was found decreased to 20-25% of the control values. The CO2 production from these substrates was impaired by 50%. Activity of gluconeogenic enzymes was measured. PEP carboxykinase and pyruvate carboxylase exhibited the most important changes and FDPase and G-6-Pase were also significantly decreased but failed to respond to fasting. It is suggested that this GalN-induced hepatitis might be a good model to use to reproduce a study of hypoglycemia found sometimes in human viral hepatitis and other liver damage. - Authors' summary.


As a model for the study of hepatic function during a severe viral induced injury to the liver, modified acute infectious canine hepatitis offers several desirable characteristics. In this paper a method for production of a severe and prolonged form of canine hepatitis is presented. The clinical course, which is characterized by fever, lethargy, anorexia, marked elevations of serum enzymes, and impaired BSP removal, is most severe 7 to 10 days after infection. The predictable recovery, ensuing by the end of 3 weeks, permits sequential studies from the normal healthy state through a severe hepatitis to recovery. Study of this disease and definition of the recovery sequence may yield additional information and understanding of the physiologic abnormalities in hepatitis. - MJA.

Two simple methods for the production of clearly defined, deep gastric and duodenal ulcers in rats and cats were reviewed. 1.) Acetic Acid Injection Model. By injection of acetic acid (1-30%, 0.05 ml per rat or 20%, 0.5 ml per cat) into the submucosal layer of the stomach, penetrating experimental ulcers which are confirmed by the contiguous organs (mainly liver) can be induced. Such ulcers in the rat rapidly diminish in size and depth in the early phase of recovery, but even at 200 days are present, presumably by repeated healing and re-aggravation. Histologically the healing processes closely resemble those of human peptic ulcer disease. In the cat, the gastric ulcers heal within 6 weeks and symptoms of re-ulceration were not observed at 0 days. 2.) Acetic Acid Topical Application Model. Application of 100% acetic acid upon the serosal surface of the rat produced penetrating duodenal ulcers as well as gastric ulcers a low perforation rate. The duodenal ulcers healed completely within 60-80 days after preparation although the gastric ulcers (fundic and antrum) persisted at 80 days following operation. These experimental ulcer models appear to lend themselves to the screening of therapeutic drugs for peptic ulcers of the stomach or duodenum, and to the investigation of the mechanisms of chronic ulcer. - Authors' summary.


In this study of the incidence and severity of cholelithiasis in monkeys fed different diets, it is concluded that the squirrel monkey is a valuable model for the formation of gallstones composed of cholesterol. Squirrel monkeys fed a semipurified diet to induce atherosclerosis showed a high incidence of gallstones, which began to appear 3 months after the start of the atherogenic diet. The incidence in animals maintained on this diet for over 9 months was 83%. The gallstones consisted essentially of pure cholesterol and increased in size, number, and total mass of stones during the period of feeding. The cholesterol:phospholipid ratio in bile was highest in the group and in the individuals with stones. Monkeys fed a natural diet had very low ratios and were free of gallstones. - Authors' summary modified.


Chronic periodontitis is the major cause of tooth loss in human adults. The consistent presence of a dense infiltrate of plasma cells and lymphocytes in the affected tissues is the basis of the widely held hypersensitivity concept of pathogenesis of the disease. The marmoset exhibits an advanced
form of the disease, with all of the features of tissue destruction seen in man but in the virtual absence of an infiltrate of plasma cells and lymphocytes. - Authors' summary.


Periodontal disease resembling that described for man was observed in a mini mouse sized mammal, the least shrew (Cryptotis parva). This condition developed spontaneously under laboratory conditions and appeared to be related to the diet. Several different species of bacteria were isolated. E. coli was found to be pathogenic, but it was suggested that it was an opportunist. The least shrew was suggested as a new model for the study of periodontal disease. - Authors' summary.


A model for studying the pathophysiology of diarrhea has been developed by inducing salmonella enterocolitis in rats. In vivo intestinal net water and electrolyte transport rates were determined in infected rats with and without diarrhea and were compared with control animals. The only significant alteration in net water and electrolyte transport between control animals and infected animals without diarrhea was a diminution of ileal absorption and a reversal of ileal HCO3 transport from secretion to absorption. In the infected animals with diarrhea, jejunal and large intestinal transport was not significantly different from that in infected animals without diarrhea. However, in all animals with diarrhea there was ileal secretion of H2O, Na, K, and Cl. Thus ileal secretion appeared to be a major physiological determinant of diarrhea in this disease model. Among the possible mechanisms to explain the net blood to lumen transport, the most likely are either (1) a passive transudation of fluid and electrolyte secondary to increased hydrostatic pressure in the lamina propria or (2) active electrolyte secretion by the mucosa. - Authors' summary.


This paper describes an experimental model of peritoneal adhesions in the rat, based on two relatively minor accidents that may occur during abdominal surgery in man: drying of the serosa, and bleeding. Drying alone had little effect; drying plus bleeding consistently produced adhesions to the dried area. Fresh blood alone produced adhesions between the three membranous structures [omentum and pelvic fat bodies (PFBs)]. The formation of persistent adhesions required whole blood. Preformed clots above a critical size induced adhesions even without previous serosal injury; they were usually...
captured by the omentum and PFBs. If all three membranous structures were
excised, the clots caused visceral adhesions. The protective role of the
omentum, its structure, and the mechanism of omental adhesions, are
discussed. These findings are relevant to the pathogenesis of postoperative
adhesions in man. - Authors' abstract.

18. Sarles, H. (Unite de Recherches de Pathologie Digestive, Marseille,
France), G. Lebreuil, F. Tass, C. Figarella, F. Clemente, M. A.

Acute ethanol intoxication was studied in 38 Wistar rats, 18 on a balanced
diet and 20 on a high fat diet, fed by gavage on 47% ethanol in a dosage
of from 3 to 12 g/kg body weight daily for periods ranging from three to
16 days. No macroscopic changes in pancreas or liver were found in any of
these animals. Histological changes (venous congestion of the pancreas,
the liver, and the kidneys) were found in rats given 4 g or more per kilogram.
The only difference between the findings in rats given a balanced diet and
those given a high fat diet was the development of fatty livers in the latter
group. Chronic ethanol intoxication was studied in 45 Wistar rats, on a
balanced diet, which were given 20% ethanol freely for 20 to 30 months.
More than half the animals developed pancreatic lesions very similar to
those of human chronic pancreatitis. The pathological changes, in foci
surrounded by normal pancreatic tissue, were a reduction in acini, duct
multiplication (probably by neogenesis), protein concentrations than samples
taken from two control animals. Protein precipitates appeared spontaneously
in the pancreatic juice of the animals exposed to ethanol, but not in that
of the controls. These findings are very similar to those in alcoholic
pancreatitis in man, which has thus been reproduced for the first time in
experimental animals. Beta-cell adenomata of the islets of Langerhans were
observed in four of the rats exposed to ethanol. - Authors' summary.

19. Stwart, H. L. (Registry of Experimental Cancers, National Cancer
Institute, National Institutes of Health, Bethesda, Maryland 20014).

The role of agents, alone or in combination, which produce adenocarcinoma
of the stomach in experimental animals is reviewed. These include 3-methyl-
cholanthrene; N,N'-2,7-fluorenyleneisacetamide; N,N'-2-fluorenylacetamide;
irradiation; aflatoxins; elaiomycin; N-methyl-N'-nitro-N-nitrosoguanidine; 7,
12-dimethylbenzanthracene; and N-methyl-N-nitroso-N-acetylurea. Incidence,
criteria for diagnosis, and different routes of administration in mice, rats,
guinea pigs, and hamsters are discussed. The observations in experimental
animals are related to the problem of human cancer. - Author's abstract.

20. Watt, J. (Department of Pathology, University, Liverpool, England),
and R. Marcus. 1971. Carrageenan-induced ulceration of the large

A 5% aqueous solution of degraded carrageenan derived from the red
seaweed Eucheuma spinosum was fed to guinea pigs in their drinking water
over a period of 20-45 days. Occult blood in the feces and multiple ulcers
in the cecum, colon and rectum occurred in 100% of animals by the 30th day.
The clinical and ethological features bear a close resemblance to human ulcerative colitis. The method provides a simple experimental model for the study of various aspects of the pathology of ulcerative lesions in the large intestine and the effects of therapeutic agents. - Authors' abstract.


The Gunn rat (Rattus norvegicus) is a mutant of the Wistar strain in which jaundice appears as a recessive trait. This rat strain served as a useful animal model for comparative research on bilirubin excretion, jaundice, kernicterus, bilirubin nephropathy, and perinatal toxicology. - Authors' summary.

CARDIOVASCULAR SYSTEM


The distribution and morphology of diet-induced atherosclerosis were studied in adult rhesus monkeys. Diffuse intimal thickening and atheroma formation were generally greater in the coronary and peripheral arteries than in the aorta. The atheromatous lesions resembled those seen in hyperlipidemic man in the prominence of arteritic change, medial damage, the frequent presence of foam cells, and in the common involvement of the aortic and mitral valves. The advanced changes in the hindlimb vessels suggest the potential usefulness of this primate in investigations of the pathophysiology of atheromatous peripheral arteries. - Authors' abstract.


The acute and chronic effects of infection with Coxsackie virus B 
are described for the mural endocardium and valves of 170 mice for selected periods from 1-210 days after a single i.p. inoculation of Coxsackie B 
. Significant microscopic changes were seen in the valves in 50 percent of the infected animals and in the mural endocardium in 48 percent of the animals. The time sequence and histology of the changes are described, beginning with the earliest changes noted on the 2nd day after inoculation. Fibrosis or scarring of the valves and mural endocardium are demonstrated in those animals allowed to survive after the 3-5th weeks of infection. Coxsackie B 
was recovered from the hearts up to 8 days after inoculation and Coxsackie virus specific antigen was demonstrated up to 7 weeks after inoculation. The findings are discussed with reference to chronic "rheumatic" valvular disease in man. - Authors' summary.

Round heart (RH) disease in turkeys was studied by cardiac catheterization and was found to have the following features: low normal cardiac output, low systemic arterial pressure, and increased filling pressures. These observations were similar to those of congestive cardiomyopathies in man. This disease in turkeys could provide an experimental model for the study of human cardiomyopathies. - *Authors' summary.*


The purpose of this study was to develop a model in swine for advanced coronary atherosclerosis and myocardial infarction. The approach was to combine a number of techniques that were thought to induce the development of atherosclerosis, including high-fat, high-cholesterol diets plus propylthiouracil and X-irradiation to the precordial region. The dose of X-irradiation that was used produced no significant changes by itself, but seemed only to enhance the effect of atherogenic diets. Among 28 swine fed the severe atherogenic diet and X-irradiated twice, 24 developed myocardial infarcts. All had advanced coronary atherosclerosis. Many died "suddenly" in the sense that no clinical signs of illness were observed prior to death. Coronary angiography was done on some swine and direct measurements of coronary blood flow on a few others. Coronary atherosclerosis and myocardial infarction were also produced in a few swine without propylthiouracil using a combination of a high-fat, high-cholesterol diet and X-irradiation. - *Authors' abstract.*


Squirrel monkeys with induced insulin deficiency, hypothyroidism, and hypertension, as well as controls were fed a diet containing 1 mg of cholesterol per calorie for over 3 years. The hypothyroid and insulin-deficient monkeys had significantly greater concentrations of serum cholesterol and \( \beta \)-lipoprotein than did the controls, while the controls and hypertensive monkeys did not differ in these regards. The insulin-deficient, hypothyroid, and hypertensive groups all had more extensive coronary arterial and aortic atherosclerosis than did the controls. Atherosclerosis was especially severe in the insulin-deficient monkeys. The level of systolic blood pressure, the concentration of serum cholesterol, and the concentration of serum \( \beta \)-lipoprotein were significantly and positively correlated with coronary arterial and aortic atherosclerosis. The rate of disappearance of intravenously administered glucose was inversely related to serum cholesterol concentration.
and the indices of atherosclerosis. The squirrel monkey may be a good animal in which to study the mechanisms by which these disorders affect atherosclerosis, since these syndromes appear to affect atherosclerosis in this animal similarly as in man. - Authors' abstract.


Round heart disease in the turkey has been studied by light and electron microscopy. Myocarditis, characterized by focal muscle cell degeneration and mononuclear infiltratus, was present in turkeys from 1 day after hatching through 8 weeks of age. Myocardial injury was most severe from age 5 to 12 days. Virus-like particles, 60-90 µ in diameter, resembling the avian leukemia viruses, were present in the myocardial cells of all turkeys with myocarditis. Dilation and hypertrophy, predominantly of the left ventricle developed after the second week of life. Collagen accumulation beneath the endocardium was evident by electron microscopy in 1- and 2-day-old birds. This progressed to marked endocardial fibroelastosis after 1 month and was often associated with involvement of the mitral valve and its papillary muscles and chordae tendineae. Maturing and adult turkeys demonstrated congestive heart failure with congestion of the lungs and liver, pleural effusions and ascites. Because of the similarity of gross and microscopic findings, round heart disease in turkeys may serve as an experimental model for primary endocardial fibroelastosis in humans. - Authors' summary.


Sephadex particles (20-80 µ in size) were injected into the abdominal aorta of 134 male Sprague-Dawley rats near the renal arteries. In 31 rats, the right kidney was then removed. The Sephadex particles lodged in glomerular capillaries, afferent glomerular arterioles and interlobular arteries, creating renal infarcts, some of which were grossly visible. Shortly after injection arterial blood pressure rose significantly in most animals. The hypertension in uninephrectomized rats was not demonstrably different from that in rats with two kidneys. Severity and duration of hypertension (up to 8 months) were positively correlated with the number of Sephadex particles in renal vessels, and there was also a positive correlation between the degree of hypertension and serum urea nitrogen levels, and between degree of hypertension and degree of cardiac hypertrophy. The vascular permeability in acutely hypertensive rats was abnormal, as judged from penetration of iron-dextran into vessel walls. This experimental model resembles atheromatous microembolic renovascular disease, which may play a significant role in the pathogenesis of unexplained hypertension in patients with advanced aortic atherosclerosis. - Author's abstract.

The purpose of this paper was to document the changes seen in miniature pigs following total cardiopulmonary bypass and to present the results of several studies aimed at elucidating the etiology of this syndrome. It was observed that total cardiopulmonary bypass in miniature pigs for a period of 2 hours or longer was consistently followed by death, in spite of the fact that physiologic parameters throughout the period of bypass were normal. The postperfusion syndrome seen in the pig following bypass was similar to that seen in dog and man, but it developed after a much shorter period of bypass. Pulmonary hypertension was uniformly present. The pulmonary pathology seen in pigs following cardiopulmonary bypass appeared to parallel that observed in dog and man; however, the lesions in the pig developed sooner and were more severe. Low flow rates, acidosis, homologous blood, microemboli, loss of pulmonary compliance, and oxygen toxicity appear to have been eliminated as being prime factors in causing the postperfusion syndrome in the pig. The cause of this syndrome has not been identified, but it is believed to be directly or indirectly related to the exposure of blood to the pump-oxygenator system. A factor released or produced by this exposure is thought to be involved in the production of increased pulmonary vascular resistance, followed by a pattern of pulmonary pathologic changes suggesting a change in capillary permeability. The authors conclude that the miniature pig may well prove to be a useful model for the study of pulmonary hypertension and of the pathophysiologic changes associated with the postperfusion syndrome. - Authors' summary modified.


Spontaneous arteritis resembling the chronic form of the human disease polyarteritis nodosa occurred in up to 60% of outbred PN mice. The lesions were similar in histology and distribution to peri-arteritis nodosa as described by other investigators, the marked round cell infiltration occurring in 80% of mice at 18 months being the main difference from the human disease. Perivascular cuffing of renal vessels invariably preceded the arteritis, the frequency of which did not appear to be influenced by lymphoma, chronic virus pneumonia or amyloidosis. There was a significant association with antinuclear antibodies and a low incidence of red cell antibody, but no evidence of hemolytic anemia. The possibility that this disease is due to a chronic virus infection is discussed. - Authors' abstract modified.

The guinea pig was found to be a useful experimental model for the study of otitis externa. Infection of the external ear canal could be induced by methods which would result in human disease. The clinical appearance of the diseased ear canal was similar to that in man. Prolonged exposure to water resulted in a shift from gram-positive normal bacterial flora to abnormal gram-negative flora and in disease. Data presented suggest that the presence of a normal bacterial flora is of significance in reducing the incidence of otitis externa. Removal of ear canal lipids did not result in disease, although this procedure predisposed the ear to infection following contamination. The data support the concept of a multiplex etiology for otitis externa. -Authors' abstract.

ENDOCRINE SYSTEM


The diabetic hyperosmolar syndrome occurs predominantly in maturity-onset diabetics and is characterized by extreme hyperglycemia, hyperosmolality of plasma, and absence of ketoacidosis. A syndrome bearing a marked resemblance to the human disease can be produced in rats. The three prerequisites for the development of the experimental syndrome are: (1) moderate nonketotic diabetes (induced by either streptozotocin or alloxan); (2) treatment with hydrocortisone acetate; and (3) water deprivation. Plasma glucose concentrations in cortisol-treated, water-deprived diabetic rats ranged from 838 to 1,488 mg/100 ml and were significantly higher than those of control diabetic or ketoacidotic animals. Neither cortisol treatment alone nor water deprivation alone was adequate to raise plasma glucose concentration above that of control diabetic rats. The blood pH, acetoacetate, and B-hydroxybutyrate of cortisol-treated, water-deprived diabetic rats did not differ significantly from the diabetic control values, but all three of these parameters were different from those of ketoacidotic rats. Neither cortisol treatment, nor water deprivation, nor a combination of the two treatments significantly affected these parameters in nondiabetic rats. By analogy with the experimental syndrome, it is suggested that administration of corticosteroids may play a role in the development of the human hyperosmolar syndrome in some patients. Furthermore, the fact that water deprivation was necessary for the production of the experimental syndrome suggests that the extreme dehydration seen in the human hyperosmolar syndrome is not merely a consequence of hyperglycemia, but also a factor in the development of the extreme hyperglycemia. -Authors' summary.


Although few species of reptiles have been used as experimental animals in biochemistry or physiology, several are known to be superior in some respects to the traditional laboratory mammals. Their metabolic reactions
are slow and prolonged, and often the response to various stimuli is exaggerated. Low metabolic rates permit careful observations of metabolic reactions for days, and pathways that could not be observed in intact mammals are clearly revealed in several reptiles. - Authors' summary.


A naturally occurring case of diabetes mellitus in a rhesus monkey was described. The diabetes, characterized initially by cachexia and polydipsia, responded to insulin therapy but was poorly managed due to lack of proper dietary control. The literature on simian diabetes mellitus, which suggests that this species may be useful as an experimental model, was reviewed. - Authors' summary.


The feasibility of making monkeys diabetic by the infusion of low concentrations of the drug streptozotocin directly to the pancreas has been demonstrated. Pig-tailed macaques have been used most extensively in developing the diabetic model. The diabetes, similar to all human juvenile and some maturity-onset types, is apparently free of side effects that are introduced when this drug, or other chemicals, is given in higher concentrations into the general systemic circulation. This allows the diabetic-like state to be studied in experimental animals free of side effects unrelated to diabetes. Such a model can be used for studying not only the long-range effects of the numerous alterations in metabolism associated with diabetes but also the diabetes-related development of arteriosclerosis, microangiopathies, and other symptoms of this disease. - Author's summary modified.


Naturally occurring, histologically evidenced chronic thyroiditis has been found in 40 of 494 (8.1 per cent) marmosets examined. Susceptibility to chronic thyroiditis in this primate appears to be generically related. Chronic thyroiditis was noted in 33 of 209 (11.0 per cent) members of the genus Callithrix and in 7 of 285 (2.5 per cent) animals of the genus Saguinus. Approximately 60 per cent of the colony-born females, 28 per cent of the colony-born males, 12 per cent of the wild-caught females and 9 per cent of the wild-caught males of the genus Callithrix had chronic thyroiditis. In one runted Callithrix argentata the histological changes in the thyroid mimicked those of Hashimoto's disease. The pronounced vulnerability of marmosets of the genus Callithrix to chronic thyroiditis provides a new primate model for the study of the natural history of this disease. - Authors' abstract.
Naturally occurring canine thyroiditis was characterized in the present study by immunodiffusion, passive hemagglutination, complement fixation, immunofluorescence and skin tests. Canine thyroglobulin and thyroid gland extract were used as sources of antigen in all tests. Thyroid histology was examined in all instances. The study mainly concerned 11 beagles, which were classified as thyroiditis colony dogs. Precipitation antibodies were not detectable, while low titers of PHA and varying titers of CF antibodies were present in the sera of the thyroiditis colony dogs. Among the serologic procedures employed, only the fluorescent antibody (FA) tests were consistently positive. The skin test was generally positive in the less progressive stages of the disease. The dog thyroid extract rather than purified thyroglobulin was required for PHA antibody detection. This latter observation, together with the FA staining patterns obtained, implied involvement of the second colloid antigen. Overall evidence from present and past studies suggested that the development of the canine disorder is similar in many respects to human thyroiditis. - Authors' abstract.

It has been shown in rhesus monkeys that amygdalar stimulation leads to increased 17-hydroxycorticosteroids (17-OHCS) concentrations and this finding has been confirmed in a variety of animals, including man. In earlier reports the response was only temporary, lasting less than two hours, either due to the experimental design or because the response faded despite continuing stimulation. In this study the amygdala of rhesus monkeys was selected as the site for stimulation and by using bilateral stimulation and different parameters, the investigators succeeded in achieving prolonged stimulation during the entire experimental period. Thus, amygdalar stimulation resulted in elevation of plasma 17-OHCS concentrations for prolonged stimulus periods. This preparation may provide a suitable animal model for the study of Cushing's disease. - M.J.A.

A corneal degeneration has been described in an inbred mouse line, the KK congenitally diabetic strain. The lesion begins in early life, is progressive with age, tends to be bilateral, and is confined mainly to the anterior part of the corneal centre. The lesions appear to be due to an inherited
degeneration, but it is not known if they are the result of diabetes or of a separate genetic aberration. The condition is not due to exposure trauma such as that found in mutant mice which are born with slit lids or open eyelids. Histological study has revealed the presence of abundant calcium in the corneal lesions. Recent findings of tissue calcium deposition in the KK mouse heart and kidney after deficient dietary magnesium suggest that the corneal damage demonstrated in this study may also be related to dietary magnesium deficiency and raised dietary phosphorus in diabetic KK mice. The availability of an animal model with one form of corneal degeneration will provide ready access to viable tissues for biochemical and histopathological studies. - Authors' summary.


Anophthalmos is prevalent as an inherited trait in an actively reproducing stock of guinea pigs. Forty-three matings of bilaterally anophthalmic boars and sows produced 113 offspring, 93 (82.3%) of which were bilaterally anophthalmic. Nervous tissue changes included absence of the optic nerves and optic tracts, as well as hypoplasia of related oculovisual structures (lateral geniculate bodies and superior colliculi) within the brain. The optic canals and orbits of the bony skull were small. Anophthalmic guinea pigs demonstrated normal breeding behavior and reproduced satisfactorily. Birth weights and growth curves were comparable to normal values, and longevity was unaffected. It is anticipated that this stock of guinea pigs will provide the scientific community with a new laboratory animal model. - Author's summary.

HEMATOPOIETIC SYSTEM


Anti-I cold agglutinins, purified from the serum of patients with chronic cold haemagglutinin disease, were injected intravenously into adult rabbits, which are known to have I antigen on their red cells. This caused acute intravascular haemolysis, with haemoglobinaemia, haemoglobinuria and anaemia. Anti-coagulation with heparin or Arvin had no influence on the effect of cold agglutinin injection, but massive doses of heparin, thought to interfere with complement binding by the cold agglutinin, did prevent the haemolysis, thrombocytopenia and neutropenia. A rabbit, given daily injections of cold agglutinin, developed significant intravascular haemolysis only with the first injection. However, a chronic extravascular haemolysis occurred with marked spherocytosis, reticulocytosis and shortening of the red cell survival. The effects of injection of human anti-I cold agglutinins into rabbits are analogous to certain aspects of the human disease and this rabbit model may be useful in further studies of in vivo complement binding and removal of complement coated cells. - Authors' summary.

The presence of an hereditary hemolytic anemia in the X strain of rabbits is reported. This condition is rapidly fatal to both sexes with a mean survival time of 4.75 months. In rare protracted cases it is associated with thymic hyperplasia and thymoma. Because autosomal recessive inheritance is indicated the symbol ha has been assigned to the gene responsible for development of the hemolytic anemia. The possibility exists that it is identical with the gene (ls) conferring susceptibility to lymphosarcoma in strain Wi rabbits, since all affected animals in both strains have the same common ancestry in strain X. A common gene responsible for all conditions may have phenotypic expressions which are dependent on the host genotype. Breeding experiments are in progress to test this hypothesis. In summary, the authors report the hereditary basis for hemolytic anemia in strain X rabbits and discuss the pathological finding. This represents a new model for study of anemia and is caused by a single autosomal recessive gene. It is believed that the hemolytic anemia in strain X rabbits is similar to that of NZB mice and represents as in man and the dog, an immunopathy: (a) it has a hereditary basis, the autosomal recessive gene, ha conferring susceptibility, (b) it has been associated with an abnormal lymphoid system and thymoma development in a few protracted cases, and (c) preliminary data indicate that the homozygous (ha/ha) rabbits are Coombs positive. - Authors' abstract modified.


These initial 24 cases of an outbreak of malignant lymphoma occurred during an interval of 25 months at the National Center for Primate Biology. The incidence of lymphoma was disproportionately high in adult female Macaca mulatta with widespread, diverse organ involvement. Inoculation of tumor cells into one immunosuppressed neonate rhesus resulted in widespread tumor growth in 3 months at sites other than those of inoculation. Preliminary studies of pathogenesis indicate the need for further evaluation of several viral isolates, epidemiologic studies of proximity of affected animals, the potential role in some of the animals of repeated exposure to roentgen radia-tion, and/or prior infection with malarial parasites. A number of the features of this lymphoma resemble Burkitt's tumor in man. - Authors' abstract modified.


The investigators developed a canine model which shows promise for
studies of certain aspects of the pathogenesis of myelomonocytic leukaemia (MML) as related to changes that develop in a single animal. This report concerns the transplantation of cells from a dog with MML. Lesions observed in the hematopoietic organs of the recipients closely resembled those in the original donor dog, but were more pronounced. The population of neoplastic cells in the recipients consistently had more primitive cell types than the donor population. A further prominent feature was the occurrence, in all recipients, of large retroperitoneal masses of chloromatous tumour tissue in the sublumbar region, comprising up to 10% of the host's body weight. Cytogenetic evaluation of the recipient puppies, by analysis of the males sex chromosomes, showed conclusively that the tumour tissues consisted of the original female donor cells. Most of the cells examined from all the recipient puppies contained a very small, abnormal, acrocentric autosome which may be a disease-specific marker comparable with the Philadelphia chromosome that is characteristic of chronic granulocytic leukaemia in man. Thus, the authors have demonstrated, by the transplantation of malignant cells, the feasibility of using the dog as a model for the study of myelogenous leukaemia. - M.J.A.

MUSCULOSKELETAL SYSTEM


Degenerative arthritis has been produced consistently in adult rabbits by the injection of the proteolytic plant enzyme papain into the hip joint. Arthritic changes were recognizable radiographically after six weeks. A progression of changes occurred, from loss of acid mucopolysaccharide staining in the matrix, fibrillation, fissuring and erosion of articular cartilage with death of chondrocytes in the weight-bearing areas, to secondary bony changes of subchondral sclerosis, occasional cysts and osteo formation. Synovial inflammation occurred with accumulation of cartilage and bone debris in the inferior capsule and later capsular thickening. It is suggested that this arthritis is sufficiently similar to human osteoarthritis to be useful as a model for further studies of the pathogenesis of the disease and the effects of different methods of treatment. - Author's summary.


Mycoplasma arthritidis strains PC 6(T-R), ATCC 19611, ATCC 13988, and ATCC 14124, were each screened for their arthritogenic virulence in Sprague-Dawley female rats. Only strain ATCC 14124 would cause arthritis. The incidence of infection with unconcentrated cultures of this strain was 100 per cent after intravenous injection. Injection into the foot pad or peritoneum was generally ineffective. The incubation time of the culture was not critical above 24 hours, cultures from 24 to 77 hours all causing arthritis in 100 per cent of the infected rats. Details of the storage, culture, and identification of the mycoplasma strains are given. The animal model is considered to be suitable for the chemotherapeutic evaluation of drugs and the study of mycoplasmal arthritis. - Authors' summary.

Eight-week-old pigs fed a protein-rich diet ad libitum developed an abnormal intestinal microbial flora within 1 week. The main feature was a significant increase in the number of atypical Clostridium perfringens, type A. In the first week after the change of diet, the pigs showed disturbances of movement and swollen peripheral joints. The ESR was concomitantly elevated and later on hypergamma globulinemia with increased antibody titres to Cl. perfringens antigens were noted. Joint deformities were observed after some months. The joint lesions consisted of synovitis with a cell-rich exudate. The lesions of the synovial tissue were characterized by proliferation of the synovial lining cells with villous hypertrophy and highly vascularized granulation tissue containing accumulations of lymphoid cells. Pannus formation and erosion of joint cartilage were seen in some animals. Bacteriological examination, including search for mycoplasmas, was negative. Subcutaneous nodules of rheumatoid nature were also found. Signs of proliferative gianemulonephritis were demonstrated in most of the animals. Different pathogenic aspects are discussed with regard to the direct influence of Cl. perfringens antigens on the joint tissues, circulating antigen-antibody complexes and cell-bound antibodies. As the same abnormal intestinal flora and immunological reaction to intestinal Cl. perfringens have been found in human rheumatoid disease, this diet-induced pig arthritis of remarkably similar clinical and histological characteristics is of special interest. - Authors' summary.


Experimental allergic myositis (EAM) closely resembling human polymyositis was produced in rats by a single injection into two inguinal lymph nodes with either homogenates or purified subcellular fractions of homologous muscle in Freund's complete adjuvant. EAM is not necessarily accompanied by clinically evident arthritis and is manifest by elevated serum enzymes, and widespread but focal necrosis and phagocytosis of muscle fibers. EAM was transferred to normal animals of the same strain by infusion of washed lymphocytes from affected animals. - Authors' abstract.


An experimental model for bone healing that yielded a consistent pattern at each chronological period was described. This rabbit model was useful in studies of the effect of various systemic and mechanical factors on osteogenesis and remodeling. The osteoblastic blastema arose mainly from the periosteum. Cartilage was not found at any stage of the healing and this rules out the indispensibility of this tissue as a bone inducer. The study
confirms that osteoclasts are not the only source of bone resorption. Incorporation of the callus with the cortex appeared to involve the creation of new osteon formed partly by the callus and partly by the original bone. - Authors' summary modified.


The occurrence of a recessive mutation that affects the skeletal system in mice provides a model for studying genetic control of growth organization at the tissue, cell, and molecular levels. In this study the occurrence of a new mutation, designated chondroplasia, and affecting cartilage and bone in mice, is reported. The gene is lethal, shows autosomal recessive inheritance, and has high penetrance. It is not allelic to shorthead and probably not to phocomelia or achondroplasia. It results in a foreshortened face, cleft palate, defective trachea, and shortened long bone with flared metaphyses. Chondrocytes of epiphyseal cartilage from the mutant are not aligned in columns, and there is a decrease in the usual straining of the cartilage matrix. Electron microscope observations show large, wide collagen fibrils with "native" banding in the matrix of mutant cartilage, which are not present in normal cartilage. Possible explanations for the expression of this genetic disorder of cartilage development are put forward. The occurrence of this mutation in mice that affects chondrogenesis thus provides a model which adds new insight into the biology of normal cartilage and bone. - Authors' abstract modified.

NERVOUS SYSTEM


Each animal in 6 groups of 4 macaques (Macaca fascicularis) was given either 0 (controls), 0.5, 1.5, 4.5, 13.5, or 40.5 mg of chromatographically pure aflatoxin B1 [from Aspergillus flavus]/kg of body weight. Death occurred in 1 animal receiving 4.5 mg/kg and in all animals receiving 13.5 mg/kg or more. Cough, vomiting, diarrhea, and coma were characteristic clinical findings. Significant changes in serum chemistry values included: hypoglycemia, increased nonesterified fatty acids and transaminases, and decreased phospholipids. Cerebral edema with neuronal degeneration, bile duct hyperplasia, hepatic cell necrosis, lymphocytolysis, and marked fatty degeneration of the liver, heart, and kidneys were found at autopsy. There is a striking similarity between this reaction in the macaque and Reye's syndrome or encephalopathy and fatty degeneration of the viscera in children. - Authors' abstract modified.

Gunn rats are a Wistar substrain in which an enzymatic defect leading to neonatal jaundice and brain damage is inherited as a recessive trait. In 3 experiments, the behavior of homozygous (jj), brain-damaged animals of the Gunn strain was compared to that of asymptomatic littermate controls (JC). Despite the locomotor impairment (ataxia) present in the jj rats, their open field and activity-cage activity levels equalled or exceeded that of controls. In a swimming maze, the jj rats made more errors than JC subjects in learning to escape from water. Because the hyperactivity and learning impairment observed in the jj Gunn rat results from physiological events which closely parallel those found in humans, it is believed that the systematic examination of the behavior of these animals will contribute significantly to the comparative study of mental retardation. - Authors' abstract.


The clinical features of coonhound paralysis are very similar to those reported in the human Guillain-Barré syndrome. In man, however, the onset is preceded by an infection which often involves the upper respiratory tract. The initial symptom is usually weakness of the lower extremities which extends rapidly to the upper extremities and facial muscles. Pathologic changes in coonhound paralysis also resemble those found in the Guillain-Barré syndrome both in type and location. Changes in roots and nerves include perivenular leukocytic infiltration, degeneration of myelin sheaths, both Wallerian and segmental types; swelling and fragmentation axis cylinders, and chromatolysis of ventral horn cells. - Authors' comments.


A drug-induced lipidosis of the central nervous system of chickens is reported. Membranous cytoplasmic neuronal inclusions similar to those seen in Tay-Sach's disease in man and in spontaneous or drug-induced disease in swine were seen by electron microscopy. Fat was demonstrated in frozen sections. - Authors' summary.


A new technique, involving final purification on a continuous CsCl
gradient, was utilized for the isolation of cerebral myelin from adult (4-
to 6-month-old) quaking mice, littermate controls and young (10-day-young
mice was 5-10 per cent of that from adult controls. After delipidation,
myelin proteins were separated by polyacrylamide gel electrophoresis in buffers
containing sodium dodecylsulphate. Two gel systems were utilized: (1) a high-
resolution discontinuous electrophoresis system; and (2) a continuous system
utilizing gels cross linked with ethlecdiacrylate (EDA). The gels from the
discontinuous system were stained with Fast Green and quantified by densitometry.
The base lability of the EDA-linked gels permitted direct chemical determination
of protein in specific bands. Myelin from brains of normal adult mice contained,
as major components, one proteolipid and two basic proteins. There were
also a number of high-molecular-weight proteins which represented a significant
distribution of proteins but the high-molecular-weight fraction comprised
a much greater percentage of the total protein. The ratio of basic to proteo-
lipid protein in preparations from quaking mice was considerably higher than
that in the myelin from control mice. The distribution pattern of the myelin
proteins from 10-day-old mice was quantitatively similar to that of quaking
mice. Altogether the evidence supports the hypothesis that the quaking mutant
provides a model of an immature nervous system with respect to myelination. -
Authors' abstract.

56. Herschkowitz, N. (Department of Pediatrics, University of Bern,
Switzerland), F. Vassella, and A. Bischoff. 1971. Myelin
differences in the central and peripheral nervous system in the

The 'Jimpy' mouse is a sex-linked recessive mutant, characterized
clinically by the onset of tremor, tonic seizures, and death. Since myelin
in the central nervous system is derived from the cell membranes of the oligoden-
drocytes and the myelin of the peripheral nervous system is formed by the
Schwann cells, the structure and metabolism of the two systems in this mutant
mouse have been compared. The results indicate that the mutation in the
'Jimpy' mouse affects the central myelin only and, according to the authors'
criteria, the peripheral myelin is not affected. Their results are consistent
with the hypothesis that there exist different genetic controls for myelination
in the oligodendrocytes and in the Schwann cells. This makes the 'Jimpy'
mouse a useful mutant for the investigation of the regulation of myelin
metabolism. - M.J.A.

57. Lehrich, J. R. (Wistar Institute, Philadelphia, Pennsylvania 19104),
95:51-56.

The viral agents of subacute sclerosing panencephalitis (SSPE), either
present in brain biopsies of patients or isolated from their brain tissue
maintained in culture, have been found to be pathogenic for ferrets, with
encephalitis becoming manifest after a prolonged incubation period. Because
of the difficulties involved in handling ferrets, and the excessive cost
of their maintenance, a search for another experimental host became necessary -
an animal at least as susceptible as the ferret to SSPE infection, but easier
to handle and less costly to maintain. The present study shows that the Syrian hamster meets these criteria. Hamsters inoculated intracerebrally with cultured brain cells derived from biopsies of subacute sclerosing panencephalitis (SSPE) patients and with cell-free suspensions of the SSPE viral agents developed clinical signs of encephalitis and died 9 to 18 days after inoculation. Histological lesions of encephalitis were present in animals dying 14 or more days after inoculation. Two ferrets inoculated intracerebrally with brain tissue from one of the sick hamsters developed encephalitis. Infectious viral agents reisolated from brains of sick hamsters resembled the agents in the original inoculum in their infectivity and in their immunological and ultrastructural characteristics. The SSPE agents proved to be much more neurotropic than measles virus. Only one suckling hamster died of the 36 inoculated intracerebrally with measles virus as compared to 25 deaths among the 32 suckling hamsters inoculated with equivalent quantities of the SSPE agents. The encephalitis produced in hamsters by the SSPE infectious agents provides a useful in vivo system for the study of these agents.

Authors’ summary modified.


In mice a primary amebic meningoencephalitis which appears almost identical with the disease seen in humans is produced by intranasal inoculation with strains of Naegleria isolated from fatal human cases. This report deals with electron microscopic studies of the murine model. The infection was induced by nasal instillation of Naegleria strains isolated from human cases who died during the summers of 1967 and 1968. Animals were sacrificed at 5 to 7 days after inoculation, at which time, they were moribund. As in human cases, hemorrhagic meningoencephalitis was found throughout the nervous system, with the olfactory lobes and the base of the frontal lobes most markedly involved. Gray and white matter were both affected. Degenerative changes were characterized by dense collections of axoplasmic organelles, by swelling of axoplasm, and by pouching and bursting of myelin sheaths. Macrophages and leukocytes, including eosinophils, participated in the host response. Trophozoites were located between neurons and glia and adjacent to blood vessels. Ultrastructural characteristics of the amebas resembled those reported in Naegleria isolated from other human cases. Amebas displayed evidence of vigorous motility and feeding. Degenerating erythrocytes, portions of leukocytes, myelin figures, and occasionally, apparently degenerating axons were seen within amebas. The incubation period, path of entry into brain, areas of brain affected, involvement of both gray and white matter, hemorrhagic nature of the meningoencephalitis, and presence of eosinophils in the host response are all features observed in human cases of infection with Naegleria. These similarities suggest that the murine model is excellent for furthering our understanding of the disease. - Authors’ abstract.

A spontaneous case of lipidosis occurred in a 5 month old domestic cat. Microscopically, cytoplasmic vacuolation of nerve cell bodies in the central nervous system, retina, and ganglia was seen. Similar vacuolation was observed in cells of the reticuloendothelial system of the liver, spleen, and lymph nodes. The nature of this material was not determined by histochemical staining, but biochemical studies revealed an increase in sphingomyelin in affected tissues. Lamellar, membranous cytoplasmic inclusions were demonstrated in neurons and splenic cells by electron microscopy. In summary, the clinical history, histologic, histochemical, and biochemical findings in this case closely resembled a similar case of lipidosis described in the Siamese cat. The distribution of lesions, together with the morphologic and biochemical studies, indicate that this disease is similar in some respects to Niemann-Pick disease in man. This feline model may be of considerable value in future studies of lipid storage disease in man. — Authors' abstract modified.


Cerebral microembolism with carbon microspheres was studied by simultaneous radioactive tracer determination of the red blood cell, albumin, iodoantipyrine, and pertechnetate spaces in the rat brain. Brain edema was evident beginning at four hours after embolization and was associated with decreased cerebral blood volume. Early edema was not accompanied by abnormal capillary permeability to macromolecules; however, the albumin space was increased at later times. Increases in the whole brain and the more heavily embolized right hemisphere pertechnetate spaces developed prior to similar changes in the albumin space. The iodoantipyrine space did not reliably reflect total brain water possibly due to rapid hepatic deiodination of this molecule. In summary, the authors have applied a method for the simultaneous determination of multiple brain spaces to an experimental model of cerebral microembolism. They have identified a pattern in the alterations of these spaces accompanying acute ischemic cerebral edema. The results suggest that both method and model will be of further value in investigating the pathophysiology of ischemic brain injury. Furthermore, it may be possible to develop a similar method to appraise brain swelling in patients. — Authors' abstract modified.


Repeated intravenous administration of methylnitrosourea (5 mg. per kg. per week for 36 weeks) resulted in the production of neurogenic neoplasms in 97 per cent of the experimental rats. The sex and strain of rat were found to influence animal survival time and tumor incidence. Male Sprague-Dawley rats had the shortest median survival time (265 days) and the highest incidence of grossly detectable brain tumors (100 per cent). Fischer rats of either sex developed more peripheral nerve tumors and fewer brain tumors than did Sprague-Dawley rats. Subcortical white matter and periventricular...
regions represented predilection sites for experimental tumor development. A progression from focal oligodendrogial proliferation to grossly visible brain tumors was evident. Smaller neoplasms tended to be well differentiated, while large tumors were often anaplastic. Electron microscopy confirmed the neuroectodermal origin of methyl nitrosourea-induced neoplasms and aided the identification of poorly differentiated cells. Using light and electron microscopy, the experimental tumors were classified as astrocytomas, oligodendrogliomas, mixed gliomas, anaplastic gliomas, gliosarcomas, and differentiated and anaplastic neurinomas. Characteristic glial filaments and microtubules were demonstrated in gliomas and gliomatous portions of gliosarcomas. Sarcomatous regions in gliosarcomas occasionally formed collagen. Neoplastic Schwann cells appeared to be the main participant in neurinomas, since a complete or partial basement membrane was associated with most tumor cells. The experimental production of neurogenic neoplasms with methyl nitrosourea represents an excellent model for research in neurooncology. A high incidence of autochthonous tumors of the central or peripheral nervous systems can readily be induced following intravenous administration of the resorptive carcinogen, eliminating the complication of surgical trauma. - Authors' abstract.

REPRODUCTIVE SYSTEM


Experiments leading to the development of a model to study meconium aspiration of the newborn are described. The final model consisted of the undelivered progeny of a hysterotomized pregnant dog under spinal anesthetic. The puppies were subjected to tracheal intubation and meconium injection before clamping the umbilical cords. This model may be used to provide objective evidence of the value of parenteral steroids administration in instances of meconium aspiration in the newborn. - Authors' abstract.


Teratomas have been induced in Japanese quail (Coturnix coturnix japonica) by intra-testicular injections of 3% zinc chloride solution during a period of testicular growth artificially stimulated by increased photoperiod. These tumours resemble those previously induced by similar methods in domestic fowl and have histological features in common with spontaneous testicular teratomas in man. - Author's summary.
64. Hoover, E. A. (Department of Veterinary Pathology, The Ohio State University, 1925 Coffey Road, Columbus, Ohio), and R. A. Griesmer. 1971. Experimental feline herpesvirus infection in the pregnant cat. Am. J. Path. 65:173-188.

Intravenous inoculation of pregnant cats with feline herpesvirus produced minimal illness but resulted in abortion, intrauterine fetal death and congenital fetal infection. Placental lesions included multiple infarcts in the placental labyrinth, thrombosis of maternal vessels in the endometrium and placenta, and multifocal necrosis of the giant-cell trophoblast and endometrial epithelium in the junctional zone of the placenta associated with eosinophilic intranuclear inclusion bodies. The virus was isolated from all the placentas and uteri but from none of the fetuses aborted 6-9 days after maternal intravenous inoculation. Viral antigen was demonstrated in the uterine vessels and in the junctional zone of the placenta at this time. On postinoculation day 26, viral antigen was demonstrated in the chorioallantoic membrane on the fetal side of the placenta and in the liver of a congenitally infected fetus. Although all 4 pregnant cats inoculated intranasally with feline herpesvirus aborted, neither virus, viral antigen nor significant lesions were detected in the uteri, placentas or fetuses. Abortion after intranasal inoculation was interpreted as a nonspecific reaction secondary to the severe, debilitating upper respiratory disease that occurred. It is concluded that experimental feline herpesvirus infection in the pregnant cat constitutes a promising model for study of the interaction of indigenous herpesviruses with the uterus, placenta and fetus. - Authors' abstract modified.


Urethral exudate from human males with gonococcal urethritis was transferred to the urethras of three male chimpanzees. The chimpanzees developed gonococcal urethritis, as demonstrated by the presence of a purulent urethral exudate containing gram-negative intracellular diplococci and the recovery of Neisseria gonorrhoeae on bacteriological culture media. The gonococcal urethritis was then transferred from chimpanzee to chimpanzee. One chimpanzee developed gonococcal conjunctivitis, presumably by autoinoculation. All animals developed complement-fixing antibodies to N. gonorrhoeae in their sera. It appears, therefore, that an animal model of gonococcal urethritis has been established. - Authors' summary.


Cyclic ultrastructural changes in the baboon's endometrium have been analyzed quantitatively by stereologic measurements of organelles in electron micrographs. Around the time of ovulation, the total volumes of endoplasmic reticulum and mitochondria increase greatly. At the same
time, individual mitochondria increase in size and nucleoli become more complex. Although the cyclic ultrastructural changes in the baboon's endometrium are similar to those in man, two features unique to the baboon are: a specialized form of endoplasmic reticulum with a multivesicular structure and extremely prominent junctional complexes. The ultrastructural similarity of the endometrium of the baboon and that of man suggests that this monkey may be a suitable physiologic model for the study of human reproduction. - Authors' abstract.


Polydipsia, polyuria, polyphagia, and glucosuria followed the administration of streptozotocin to 6 nonpregnant and 15 pregnant monkeys (Macaca mulatta) in the first trimester of pregnancy. The diabetogenic action of the drug was also reflected in an induced but variable deterioration in maternal intravenous glucose tolerance and a marked attenuation of maternal plasma insulin responsiveness to intravenous glycemic stimuli. The products of conception were examined in 29 pregnancies. The neonates and the placentas of the streptozotocin-treated pregnant animals were significantly heavier than average for the period of gestation, polyhydramnios was consistently present, and there was an increase in the incidence of third trimester stillbirths. These and other data provide evidence that maternal glucose intolerance during pregnancy is associated with enhanced fetal and neonatal pancreatic islet cell responsiveness to glucose and mixed amino acids. Although the specific mechanism(s) that alters both the sensitivity and responsiveness of the normal pancreatic fetal islet to insulinogenic stimuli remains unclear, the data do indicate that insulin-independent maternal hyperglycemia and hyperaminoacidemia separately or in combination could contribute to the fetal hyperinsulinemia of pregnancies complicated by diabetes mellitus. Moreover, the overall experiences with these streptozotocin-treated animals suggest that a subhuman primate model may be available to examine directly the antenatal pathophysiology of abnormal carbohydrate metabolism. - Authors' abstract.

RESPIRATORY SYSTEM


A review of the current literature on experimental models used in respiratory carcinogenesis studies indicates that the method of repeated intratracheal injection of large doses of polycyclic hydrocarbons, with which a high incidence of bronchogenic carcinomas can be induced in rats and hamsters, has apparently not been attempted in mice. This communication
reports the induction of squamous cell carcinomas in the respiratory tract of (C57Bl x C3H) F1 (BC3F1) and DBA/2 mice by repeated intratracheal injections of 3-methylcholanthrene (MCA). The tumors showed frank invasion and metastasis and were readily transplantable to isogenic recipients. Only 3 of 50 DBA/2 mice developed squamous cell carcinomas at 7 months, after 4 weekly injections of 0.5 mg MCA. In BC3F1 mice given 6 weekly injections of 0.5 MCA, a tumor incidence of 86% with an induction time of 10-28 weeks was observed. The short induction time (the first carcinoma appeared 4 weeks after the 6th carcinogen injection) makes this tumor system particularly attractive. These findings suggest that the mouse should be reconsidered as an experimental animal for respiratory carcinogenesis studies. The exact origin of the observed respiratory tract carcinomas still needs to be determined. - Authors' summary modified.

69. Richerson, H. B. (Allergy and Applied Immunology Section, Department of Internal Medicine, and the Departments of Radiology and Pathology, University of Iowa College of Medicine, Iowa City, Iowa 52240), F. Cheng, and St. C. Bauserman. 1971. Acute experimental hypersensitivity pneumonitis in rabbits. Am. Rev. Resp. Dis. 104:568-575.

An animal model of hypersensitivity pneumonitis is described. Rabbits were sensitized with ovalbumin in complete Freund adjuvant. Three weeks after immunization, the animals were placed in an aerosol chamber and challenged with ovalbumin in 0.15 M sodium chloride aerosolized by ultrasonic nebulization. The amount of antigen retained after challenge was studied using ovalbumin-125I and was found to be approximately 0.2 per cent of the total aerosolized antigen. Histologically, lesions in the lungs were seen by 24 hours and had essentially cleared at six days. Abnormalities included thickening of alveolar septa and increases in mononuclear cells, lymphocytes, phagocytic macrophages, and eosinophilic granulocytes within alveolar walls and spaces. Distribution of these lesions was patchy, involving most conspicuously the alveolar ducts distal to the termination of respiratory mucosa, thus illustrating an allergic alveolitis. Other histologic abnormalities included peribronchiolitis and vasculitis. No similar lesions were seen in unsensitized, challenged animals or in sensitized, unchallenged control animals. This model allows study of the pathogenesis of hypersensitivity pneumonitis and elaboration of the role played by the lung in various types of immune damage. - Authors' summary.

SKIN AND ADNEXA


Twenty Sinclair (S-1) miniature swine with pigmented skin lesions were killed and necropsied. Melanotic lesions were found regularly in the regional lymph nodes and occasionally in the brain, meninges, lungs, liver, urinary
bladder, heart, spleen, adrenals, ovaries, skeletal muscle, bone, stomach, and small intestine. Sinclair (S-1) miniature swine are a potential model for the study of melanin metabolism and melanomas. — Authors’ abstract.


Ectodermal dysplasias in cattle and horses resembles the human disorders aplasia cutis congenita, focal dermal hypoplasia and a variant of epidermolysis bullosa with congenital localized absence of skin. A severe form of congenital ichthyosis in cattle is mirrored in morphology and gravity by ichthyosis foetalis (harlequin foetus) of human beings, and a somewhat milder form in cattle has a human counterpart in ichthyosis congenita. In cattle, dysplasias of the cutaneous appendages (hair follicles, arrector pili muscles, sebaceous glands, sweat glands) are classified into the following types: ichthyotic hyperkeratosis (recessive); patterned congenital alopecia: follicular-glandular dysplasia (recessive); tardive symmetrical alopecia (recessive); streaked hairlessness (semi-dominant, sex-linked, lethal); woolly semi-hairlessness (recessive); follicular-glandular dysplasia, anodontia and macroglossia (sex-linked recessive); and hypotrichosis with anodontia. In several of these types there may be analogues in man. — Author’s abstract.


The intradermal as well as intraperitoneal injection of zirconium salts in CBA/J mice produced local foreign body type granulomas which regularly persisted for over eight months. Granulomas produced were similar to the experimental silica granuloma in man. However, none of the animals exhibited evidence of the late delayed immune type of epithelioid cell granulomatous hypersensitivity such as has been induced experimentally in man. Benign chondromas developed locally in the ear cartilage plate in half of the mice who had received zirconium injections in this area. The authors indicate that this is the first technique of experimentally producing chondromas. — Authors’ abstract modified.

URINARY SYSTEM


The early pathologic changes of the kidney with significant glomerular mesangial cell, tubular epithelial cell, and interstitial cell necrosis are described in mice infected with the encephalomyocarditis (EMC) virus.

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In addition, viral crystals are demonstrated electron microscopically in interstitial and tubular epithelial cells - findings never reported before. These studies show that the EMC virus can cause glomerulonephritis in mice. The mechanisms by which the virus damages the kidney may include an antigen-antibody reaction, a direct viral invasion of tissues of the kidney, and/or an autoimmune reaction established by the virus. Because EMC virus can readily damage the renal glomeruli of newborn mice, damage which may later develop into glomerulonephritis, the authors have postulated that viruses may also produce renal disease in man, including glomerulonephritis. Glomerulonephritis produced directly by viral invasion of glomeruli needs further investigation. Thus, mice infected with EMC virus are good models for the study of glomerulonephritis caused by direct viral invasion of the kidneys, especially since the EMC virus produces distinct crystals in the infected tissues, which can be readily identified electron microscopically. - Authors' abstract modified.


Necropsies in eleven strains of rabbits at The Jackson Laboratory reveal a high incidence of cortical renal cysts in strain III. These cysts are similar to the "simple cysts" in man. They occur primarily in adult life and affect the normal structure of the renal cortex, but do not appear to be associated with pathological changes in the overall functioning of the kidney. In the rabbit these are inherited and are due most probably to a single autosomal recessive gene with incomplete penetrance. We have assigned the symbol re (renal cysts) to this gene. This finding of cortical renal cysts in the rabbit provides a new model for the study of simple cysts in man. - Authors' summary.


A nephrotic syndrome has been induced in albino rats by feeding them with a diet containing N,N'-diacetylbenzidine. Glomerular lesions appeared rapidly and consisted of florid epithelial crescents, progressive sclerosis and obliteration of many glomeruli. In females, the severe proteinuria was rapidly followed by hypoproteinaemia, hyperlipaemia, generalised oedema and severe anaemia; renal insufficiency with urea retention ensued. In males, similar renal lesions developed more slowly and though the proteinuria was eventually as heavy as in females, they manifested no features of nephrosis. The experimental syndrome resembles morphologically a form of rapidly progressive human glomerulonephritis. - Author's summary.


Immunization of rats with homologous kidney suspension in Freund's
complete adjuvant plus Bordetella pertussis administered in an adjacent site resulted in severe autologous immune complex glomerular disease, as well as in several forms of tubular and interstitial damage, and in some instances in renal vein thrombosis. In comparison with previously described immunizing procedures employing renal tissue in Freund's adjuvant but without injections of B. pertussis proteinuria and the glomerular disease appeared earlier and were manifested by more conspicuous histologic changes, principally capillary wall thickening and mesangial cell hypercellularity. In addition, it was possible to induce the disease in Buffalo rats, which are resistant to the induction of nephritis using only Freund's adjuvant. The tubular lesions were detectable by in vivo accumulation of IgG and/or β1C. Four patterns were observed: (1) granular deposits of IgG and β1C along the basement membrane of proximal tubules, (2) accumulation of IgG and often β1C as well in the brush border of proximal tubules, (3 and 4) accumulation of IgG but not of β1C in basilar portions of tubules in the ascending thick limb of loops of Henle and in distal convoluted tubules. Animals with the last three patterns of staining displayed circulating autoantibodies which were capable of reacting in vitro with the corresponding segments of the nephron. In some animals, histologic evidence of tubular damage was apparent in the form of nuclear hyperchromatism, vacuolation or basophilia of cytoplasm, and loss of periodic acid-Schiff staining of brush borders. Interstitial infiltrates of mononuclear cells, principally lymphocytes, were found in many animals in the outer medulla and cortex, suggesting the participation of cell-mediated mechanisms in the renal disease. The same immunization procedure with liver or small bowel failed to produce renal lesions, providing evidence that the antigen responsible for autologous immune complex disease is not present in these tissues. This highly efficient, yet simple, method of inducing severe autologous immune complex nephritis, as well as renal tubular and interstitial lesions, provides a model which suggests probable mechanisms for similar immune deposits that occur in patients with lupus nephritis, rapidly progressive and membranoproliferative glomerulonephritis, and Sjogren's syndrome. - Authors' abstract modified.


Lesions with the morphologic characteristics of papillary transitional cell carcinomas of the urinary bladder were found in a talapoin monkey and a capuchin monkey infected with Schistosoma haematobium, and a papilloma of the ureter was found in an infected African baboon. Marked proliferation and squamous metaplasia of the bladder epithelium were seen in 2 squirrel monkeys and in 1 capuchin monkey. These lesions were seen 5-24 months after infection of the monkeys. Epithelial proliferation was topographically related to the presence of S. haematobium eggs in the lamina propria of the bladder. This and the absence of reports of spontaneous bladder cancer in monkeys suggest that the proliferative lesions were caused by the schistosome infection. The relatively small number of capuchin, talapoin, and squirrel monkeys at risk during the period in which tumors developed suggests that infected animals of these species may offer useful models for the study of bladder cancer. - Authors' summary.
An inherited kidney disease, which arose spontaneously in an inbred strain of mice, appears to be due to an autosomal recessive gene which has been given the name and symbol kidney disease, \(kd\). This gene is located in linkage group \(X\), and shows about 16.4% recombination with grizzled (gr). Clinically, the disease was first detectable at about 10 weeks of age by increased proteinuria. This was followed over several weeks by excessive drinking, dilute urine, loss of weight, anaemia, and death in uraemia usually at 5 to 7 months. Pathologically, areas of tubular atrophy alternated with areas of dilated tubules, often containing hyaline casts. The glomeruli were sclerotic in the areas of tubular atrophy and the cells of some of the atrophied tubules contained haemosiderin. Epithelial hyaline droplet change occurred in the earliest stages. In clinical, genetical, and pathological respects the mouse disease strongly resembled the human inherited kidney disease, nephronophthisis. - Authors' summary modified.
in rats is slightly smaller than in man. In addition in the 3rd and 4th month of the experiment periodic acid-Schiff (PAS) positive histiocytes constantly appeared at the periphery of the xanthogranulomatous pyelonephritis and mostly in small clusters. Despite these differences, the obstructive form of purative pyelonephritis is a suitable model for the study of the problem of xanthogranulomatous pyelonephritis. - Authors' abstract.


The production of polycystic renal disease in newborn rabbits by the use of a long-acting corticosteroid, fluprednisolone (Predef 2x [Greece]; Alphadrol; comparable US product) as reported earlier by other investigators has been confirmed and extended. Rabbits followed up to 3 months of age show disappearance of the cysts. Comparison with "glomerular" type human polycystic kidney shows important similarities. In summary, evidence is presented that the cardinal features of this experimental model are similar to that observed in two previously reported cases of human polycystic kidneys and to a third similar case subsequently observed. - Author's abstract modified.


A splenectomized aotus monkey infected with human quartan malaria (Plasmodium malariae) developed oedema and proteinuria. Histological examination revealed a generalized diffuse glomerulonephritis and immuno-fluorescent staining showed granular deposits of IgM in the glomeruli. The pathological picture resembled that shown by human patients with the quartan malaria nephrotic syndrome. The occurrence of the syndrome in a splenectomized aotus monkey suggests that it may be possible, using this model, to determine the immunological conditions that give rise to the nephrotic syndrome in human P. malariae infections. - Authors' summary modified.


An inbred strain of mice NZC was found to have a high incidence of spontaneous hydronephrosis with up to 56% of males and 81% of females showing some stage of the disease. Either unilateral or bilateral hydronephrosis was found in mice between 80 and 660 days of age, and in most cases did not appear to have had a marked effect on survival time. Blood urea nitrogen levels in these mice were slightly elevated. NZC F1 hybrid mice did not show the disease, nor did backcross progeny to normal parent strains. However, 43% of backcross progeny to the NZC parent showed hydronephrosis. These results indicate that a single autosomal recessive gene controls the inheritance of this renal disorder. The relation of this to other reported cases of hydronephrosis and to other genetic disorders

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in NZ mice is discussed. The results presented in this paper further extend the known cases where a genetically controlled process of hydronephrosis can occur without any obvious obstructive cause. These mice may accordingly be a most suitable laboratory model in which to further explore the detailed process whereby this condition can occur in both man and animals. - Author's summary modified.

AUTOIMMUNE DISEASES


The naturally occurring immunodeficiency syndrome of the hypopituitary Snell-Bagg dwarf mouse has been characterized. The immunopathological aspects of this syndrome derive primarily from an arrested ontogenetic development of the thymus. The alteration of the thymus function is caused by the failure of the pituitary to produce certain hormones, especially somatotropic hormone. The relation of this syndrome of the dwarf mouse to human immunodeficiency diseases and endocrinopathies is discussed. - Authors' summary.


By prolonged immunization of an inbred rat strain with isologous liver homogenate in Freund's complete adjuvant a low grade autoimmune 'cholangitis' with periductular fibrosis has been demonstrated. The lesion could be transferred to isogeneic animals by serial spleen cell injections and was associated with mild but variable delayed skin sensitivity to a supernatant fraction of the liver homogenate. It is thought to be due to a combined cellular and antibody-mediated immune response, directed against bile duct constituents. Pulmonary (peribronchial) lesions have also been described in the same animals and are considered to be of similar origin and to represent a cross reaction with tissue of similar embryological (entodermal) origin. This appears to be the first description of periductular hepatic fibrosis clearly resulting from an autoimmune reaction and may provide a model for further study of rather similar histological reactions known to occur in man. - Author's summary.


NZB and (NZB x NZW) F1 hybrid mice are a widely studied model of several, sometimes clinically related, human diseases of unknown etiology.
These diseases include idiopathic glomerulonephritis, systemic lupus erythematosus, related connective-tissue and autoimmune diseases, and malignant lymphoma. The present work on the animal model reveals interrelated viral (Gross leukemia virus), genetic, and immunologic determinants of disease. These studies may contribute to the further elucidation of the cause, nature, treatment, and prevention of one or more of the corresponding human diseases. - Author's abstract.


Agammaglobulinemic chickens, which have less than 0.5% of normal immunoglobulin levels, develop a hemolytic anemia with variable frequency. Autologous red blood cell (RBC) survival studies using DFP-3H-labeled cells demonstrated a survival of 15 days in agammaglobulinemic anemic chickens compared with 30 days in normal chickens. Homologous survival studies demonstrated normal survival of normal RBC in agammaglobulinemic anemic chickens and shortened survival of agammaglobulinemic anemic RBC (Ay-RBC) in three of four normal chickens. Ay-RBC could be specifically agglutinated by an antibody present in the normal serum of several species. Several lines of evidence indicate that chicken immunoglobulin is not on the Ay-RBC surface and hence not involved in the agglutination reactions observed. Infectious agents were not identified in the agammaglobulinemic anemic chickens. The absence of an autoantibody in this hemolytic anemia, which is similar to that described in other species as "autoimmune," was consistent with the concept that autoantibodies may not play a primary pathogenetic role in at least some phenomena generally characterized as autoimmune. The most likely etiologic factor in the hemolytic anemia was thought to be an unidentified infectious agent, although the contribution of the absence of immunoglobulin per se could not be adequately evaluated. The pertinence of the use of the agammaglobulinemic chicken as a model for "autoimmune" phenomena in immune deficient humans was discussed, and the necessity of proper controls in using anti-immunoglobulin sera in the investigation of hemolytic anemias was stressed. - Author's abstract.

BACTERIAL DISEASES


Ninety-one cynomolgus monkeys were exposed for up to 32 days to dusty air from a mill processing imported goat hair known to contain anthrax spores. Twenty-three monkeys contracted inhalation anthrax. The morphologic study of the infected monkeys supports the notion that, in most cases of inhalation anthrax, spores are carried to the mediastinal lymph nodes, where they germinate and produce a primary lymphatic infection. The large bacteria
quickly invade the bloodstream and cause fatal septicemia. The anthrax bacillus produces a toxin which often causes marked local vascular injury with edema, hemorrhage, and thrombosis. In anthrax septicemia the toxin causes generalized vascular injury with widespread capillary thrombosis, circulatory failure, shock, and death. The morphologic findings in this experimental model of Woolsorters' disease not only give evidence of the pathogenesis and pathophysiology of inhalation anthrax but also illustrate a basic disease mechanism of most bacterial infections. - Authors' abstract modified.

NUTRITIONAL - METABOLIC DISEASES


Although the most obvious characteristics of the rhino mouse are the absence of hair and the wrinkling of the skin, the basic metabolic defect may well be one of lipid metabolism. The deficient triglyceride storage, the massive accumulation of waxes, and the relatively large amount of lathosterol ester (with no accompanying members of the desmosterol synthesis route) all suggest some gross abnormality of lipid metabolism. The response of the rhino to vitamin A, including the striking sensitivity to toxicity, may also indicate abnormalities of lipid handling. Thus, the rhino mouse may be a useful tool for a variety of studies other than those based on its abnormal skin and its sensitivity to carcinogens. - Authors' abstract.


The urinary output of uric acid from the purebred Dalmation is similar in amount to that in man. Also, this breed of dog has a higher plasma uric acid level than other dogs and, like man, this hyperuricemia is accompanied more frequently with renal and bladder lithiasis. Allopurinol is effective therapy in both man and dog. Study of the fate of uric acid in the Dalmation shows that the liver does not oxidize the available uric acid completely although it is capable of doing so when liver homogenates are studied. Consequently, the hepatic cellular membrane appears impermeable, or partially so, to uric acid. The possibility of a general membrane transport problem similar to that encountered at the liver cell has not been confirmed with studies of red cells in the Dalmation. This dog shows some similarities to certain rare clinical human diseases with deafness, cardiac arrhythmias and renal tubule leak of uric acid, all of which offer ample opportunity for close and detailed examination as clinical models in biochemical, physiological, pathological and genetic studies. - Authors' abstract.
91. Levin, E. Y. (Johns Hopkins University School of Medicine, Baltimore, Maryland 21204), and V. Flyger. 1971. Uroporphyrinogen III cosynthetase activity in the fox squirrel (Sciurus niger). Science 174:59-60.

The activity of uroporphyrinogen III cosynthetase in hemolyses and tissue extracts from fox squirrels is much less than in similar preparations from gray squirrels. Low activity of this enzyme explains the production of large amounts of uroporphyrin I by the fox squirrel. Members of this species thus provide a small animal model for studies of congenital erythropoietic porphyria, a hereditary disease of man and cattle which is associated with a similar partial deficiency of uroporphyrinogen III cosynthetase. - Authors' abstract.

92. Nitzan, M. (Section of Endocrinology, Metabolism and Nutrition, Department of Medicine, Northwestern University Medical School, Chicago, Illinois), B. E. Metzger and J. F. Wilber. 1971. The effects of acute uremia on plasma glucose, insulin and growth hormone in the rat. Life Sci. 10:671-676.

The effects of acute uremic syndrome upon plasma glucose, insulin and growth hormone were evaluated in the fasted rat 24 hours following bilateral nephrectomy. Appropriate control studies were instituted to correct for the non-specific effects of surgical intervention. The mean levels of plasma glucose, IRI and GH, as well as insulin to glucose ratio were significantly higher in the uremic animals than in the sham-operated controls. The fasting hyperglycemia in the presence of high levels of circulating IRI observed in the nephrectomized rats suggest impaired responsiveness of the peripheral tissues to the action of insulin. Since similar findings have been reported in chronic renal failure in the human, it is suggested that the acutely uremic rat might be employed as an experimental model for further elucidating the underlying mechanisms of glucose intolerance in uremia. - Authors' abstract.


Young chimpanzees (Pan troglodytes) will accept ethanol in quantities sufficient to produce symptoms of withdrawal when ethanol is subsequently discontinued. Mild to severe symptoms of physical dependence, including grand mal seizures, are observed when ethanol is abruptly withdrawn after 6 to 10 weeks of chronic oral intake. In addition, the rate of disappearance of ethanol in blood increased during periods of chronic ingestion, an indication of developing metabolic tolerance. These results suggest that the young chimpanzee may be a suitable model for experimental studies of alcoholism. - Authors' abstract.

A number of chemical agents, including certain drugs and steroids, can produce biochemical disorders in various animal species (mice, rats, rabbits, guinea pigs, dogs) which resemble different types of hepatic porphyria in man. The main agents used to produce experimental porphyria are allylisopropylacetamide, dicarbethoxydihydrocollidine, griseofulvin, and hexachlorobenzene. The porphyrias produced by these agents are discussed in this paper. The experimental porphyrias also provide excellent systems for study of a complex control mechanism in mammalian liver. Thus, it has been shown that drugs, diet, hormones, and iron all affect the induction of the mitochondrial enzyme 6-amino-levulinic acid synthetase (ALA synthetase) which plays a major role in the control of heme biosynthesis. In addition, clinical observations provided the basis for the development of experimental porphyria which in turn has provided information that has had significant clinical application. A close interrelationship between clinical observations and basic research is seen in the history of the development and use of the experimental porphyrias. - Authors' abstract.


Caenorhabditis briggsae was used as a model to study aging of a metazoan under gnotobiotic conditions. At higher temperatures nematodes were shorter-lived and had a shorter generation time. Nematodes moved more slowly as they aged. Physiologic aging was marked by a decreased ability to withstand osmotic stress, a possible increase in the body's internal solute concentration, and increased sensitivity to formaldehyde. These results suggest that the ability to osmoregulate and the permeability of the body wall are altered during senescence. The interchordal hypodermis, as well as the chordal hypodermis, contained fairly abundant structures having biosynthetic activity. During aging mitochondria of the hypodermis degenerated, some areas of the thin hypodermal band thickened and lysosome-like bodies formed in the interchordal hypodermis. Changes in osmoregulatory and excretory mechanisms are probably associated with deterioration of the hypodermis organelles. - Authors' abstract.

ONCOLOGY


Specific features of metastases from a transplantable dimethylbenz(a)-anthracene-induced Syrian hamster sarcoma maintained in tissue culture for 123 generations were investigated. Tumor tissue was inoculated s.c. to 33 1-month-old Syrian hamsters (0.2 ml of a 25% suspension in physiological solution). The tumor strain elicited 100% transplantability and a fast growth rate after a latency period of 4-6 days. The neoplastic tissue consisted of large polymorphous cells with vacuolated nuclei and high mitotic activity; the stroma was poor and of rather fibrillar consistency. Metastases located in the axillary lymph nodes were observed in 29 (90.6%) of 32 tumor-bearing hamsters 10 days following inoculation. Bilateral metastases were found in the pararenal (50% incidence) and in the lumbar lymph nodes (53%
incidence) 15 days following inoculation. Twelve hamsters (37%) were found to have developed metastases in the lung and, later, 11 hamsters developed metastases in the inguinal, 11 in the cervical and 9 in the paratracheal lymph nodes. No metastases were seen in the liver, kidney or spleen. Three morphologically distinct stages could be established for the development of metastases at the respective sites: 1) a stage of subcapular growth of the tumor within the lymph node; 2) a stage of "break-through" of the tumor mass directed towards the central region of the lymph node with a gradual substitution of the lymphoid tissue by tumor tissue; 3) a stage of total substitution of the lymphoid tissue by tumor tissue whereby morphological integrity of the lymph node capsule is maintained. The transplantable Syrian hamster sarcoma is thought to provide an experimental model for lymphatic metastases. - Author's abstract.


Inbred LSH and MHA hamsters were compared with random bred LVG hamsters for susceptibility to induction of tumor by SV40, adenovirus 7, or adenovirus 12 viruses and for appearance of tumor after homologous transplantation. The LSH inbred strain proved superior to the MHA inbred line in terms of susceptibility to induction of tumor by SV40 and adenovirus 7 virus and showed a shorter latent period after transplant with homologous SV40 virus tumor. The LSH animals were also somewhat better than MHA hamsters from the point of view of husbandry. The susceptibilities of the inbred LSH and random bred LVG animals to induction of tumor by viruses were similar and the transplantation characteristics of tumors evolved in the two breeds of animals were approximately the same. The inbred LSH hamster provides a satisfactory model for induction of tumor by virus and for investigations of transplant tumor immunology employing a truly syngeneic system. - Authors' summary.

PARASITIC DISEASES


Parasitologic, serologic, pathologic, biochemical and clinical studies were conducted in 15 chimpanzees exposed to Schistosoma japonicum cercariae. Numerous viable eggs were passed in the feces after a prepatent period of 5 to 8 weeks. Worm recoveries at autopsy varied considerably, but no evidence was found of a reduction in worm burdens with infections up to 17 months duration. No consistent difference was observed in the percent recovery and location of worms in animals exposed only once or in those exposed repeatedly. Most eggs in tissues were found in the liver and large intestine, but numerous eggs were also present in the small intestine and lungs of heavily infected
animals. Nearly normal hepatic blood flow was maintained via the hepatic artery even in animals with completely obstructed intrahepatic portal branches. Well-developed porto-systemic collateral venous channels effectively decompressed the portal system. Hepatomegaly and severe portal fibrosis were common gross findings; variable degrees of pipe-stem fibrosis consistent with infection intensity were found. The development of pipe-stem fibrosis was particularly rapid and destructive, and hepatic lesions were more inflammatory and polymorphous with *S. japonicum* than has been reported with *Schistosoma mansoni*. Marked intestinal lesions were present in a variable and patchy segmental distribution. Glomerular lesions occurred in most chimpanzees with pipe-stem fibrosis, and the prothrombin time was abnormal in several of the more severely diseased animals. Marked hypoalbuminemia and hypergammaglobulinemia were frequent. Hypoglycemia and uremia appeared to be important factors in some infected animals. The chimpanzee was a particularly valuable model for studies on the pathogenesis of schistosomiasis japonica. - *Authors' abstract.*

**TERATOLOGY**


An in-depth study of congenital anomalies of swine was done to establish the usefulness of this species as a model for similar studies in man. The malformed swine were collected from cooperative farms in Missouri over a period of 4 1/2 years. The swine were examined for gross defects and classified according to the body system involved. An existing classification system for malformations in human beings was found to be generally satisfactory, but it was necessary to expand the system for certain categories, e.g., limb anomalies. - *Authors' summary.*

**MISCELLANEOUS**


The activity of phenylethanolamine N-methyltransferase in mice of the C57B1/Ka strain was determined after a 4°C stress. The enzyme activity increased 1.2-fold at the end of 3 hours and by 1.4-fold by the end of 6 hours of the stress. The results are in contrast to those from other species with intact animals in which the enzyme changes only after several days of chronic stress. Cycloheximide prevents the rise in enzyme activity, suggesting the increase may be due to protein synthesis. The increase may provide a model system for studying regulation of catecholamine biosynthetic enzymes. - *Authors' abstract.*
Inherited susceptibility to malignant hyperthermia has been recognized in Poland China swine. Clinical and laboratory studies were made to compare the syndrome with that observed in man and in other breeds of swine in South Africa and Europe. Malignant-hyperthermia-susceptible (MHS) swine were identified by increased ATP depletion in biopsied muscle studied in vitro. MHS and related swine had elevated serum creatine phosphokinase values compared with control swine (MHS swine x 2,435 IU/l; MHS-related swine x 1,260 IU/l; control swine x 144 IU/l). The syndrome was triggered by administration of halothane and of succinylcholine chloride. Resulting clinical responses, in order of appearance, were tachycardia, hyperventilation, skeletal muscle rigidity, hyperthermia, cardiac arrhythmias, and death. Blood chemical responses which occurred early in the syndrome included hypercapnia, acidosis, elevated plasma inorganic phosphorus, and lactacidemia. The malignant hyperthermia syndrome in this breed of swine appears similar to that in Landrace and Pietrain swine, and in man. The Poland China swine is an appropriate animal model for the study of this disease. - Authors' abstract.
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APPENDIX

The following reports of conferences and symposia contain papers that pertain to animal models or genetic stocks.

ILAR PUBLICATIONS

During the past five years, ILAR has sponsored five symposia on "Animal Models for Biomedical Research" to acquaint biomedical investigators with the unique animal models that exist for diverse biomedical needs. The proceedings of these symposia have been published by the National Academy of Sciences. The papers stress the specific genetic, physiologic, and pathologic traits or conditions in particular species or strains of animals that make them appropriate and unique research tools with which to gain insights into parallel human conditions or basic biomedical phenomena. (Available from the Printing and Publishing Office, National Academy of Sciences, 2101 Constitution Avenue, N.W., Washington, D.C. 20418.)


Wostmann, B. S. Germ-free versus non-germ-free animals in gerontological research. p. 52-61.


Clarkson, T. B. Summary: The laboratory animal in gerontological research. p. 104-108.


PART I ANIMALS WITH DISEASES OR ABNORMALITIES


PART II UNIQUELY USEFUL ANIMAL TYPES


Clarkson, T. B., B. C. Bullock, N. D. M. Lehner, and M. A. Feldner. The squirrel monkey as a laboratory animal. p. 64-87.

Barnes, R. D. Harmania mitis, a small marsupial for experimental biology. p. 88-100.

PART III THE SEARCH FOR ANIMAL MODELS


Patterson, D. F. Animal models of congenital heart disease (with special reference to patent ductus arteriosus in the dog). p. 131-156.

Prichard, R. W. Some human diseases for which animal models are needed. p. 157-167.
Animal models for biomedical research II. 1969.


Holmes, A. W., J. D. Ogden, and F. Deinhardt. Marmosets in microbiological research. p. 11-17.

Brewer, W. E. Aquatic animals as indicators of toxic materials in an ecosystem. p. 18-25.


***

Animal models for biomedical research III. 1970.


Ader, R. Psychological factors in comparative biomedical research. p. 91-102.

Nace, G. W. The use of amphibians in biomedical research. p. 103-124.


Hubbard, R. C. The use of marine mammals in biomedical research. p. 133-146.

***

Animal models for biomedical research IV. 1970.


Klontz, C. W. Fish as biomedical research models. p. 27-30.

Ablin, F. R. Chronic and degenerative diseases of man: The value of natural and experimentally induced diseases of animals. p. 31-46.


Morrison, P. Arctic and alpine rodent as models for biomedical research. p. 85-91.


Glenn, B. L. Feline porphyria: Comparative aspects with porphyria of other domestic animals and man. p. 135-148.


***

OTHER PUBLICATIONS


This symposium, held at the Smithsonian Institution, Washington, D.C., June 19-21, 1968, was the first international meeting convened specifically to consider tumors and tumorigenesis in lower animals. The material discussed at the symposium and presented in this publication suggests the potential value of studies in lower animal pathology to medical and environmental welfare.
FISHS, PREVERTEBRATES, AND ECHINODERMS
Sang, J. H. Biochemical basis of hereditary melanotic tumors in Drosophila. p. 291-301.

INSECTS

Hladen, E. Proliferation and dynamics of cell heredity in blastema cultures of Drosophila. p. 351-364.
Sutherland, D. J. Neve severance and tumor induction in Periplaneta americana (L.). p. 399-418.
Sutherland, D. J. Effects of certain carcinogens on Periplaneta americana (L.). p. 433-442.
Sutherland, D. J. Rectal tumefactions in the cockroach, Periplaneta americana (L.). p. 459-458.
Smirnoff, W. A. Formation of cysts as a defensive reaction in pupae and adults of Neodipirion swainii (L.). p. 475-479.

INVERTEBRATES OTHER THAN INSECTS AND ECHINODERMS
Couch, J. A. An unusual lesion in the mantle of the American oyster, Crassostrea virginica. p. 557-562.
the shells of *Crassostrea virginica*. p. 575-580.


Dunn, T. B. Comparative aspects of hematopoietic neoplasms of rodents. p. 43-47.


Nielsen, S. W. Spontaneous hematopoietic neoplasms of the domestic cat. p. 73-94.

Jones, T. C. Chromosomal analyses of feline lymphomas. p. 95.


Whang-Peng, J. Chromosome studies in various neoplasms of domestic animals. p. 117-151.


One of the aims of this symposium was to inform French research workers concerning a variety of pathological mutants in order to promote their use. Animal species are subject to an array of inherited diseases that represent spontaneous models of conditions that sometimes cannot be artificially reproduced. These models are particularly useful in biomedical research. They enable a number of investigations that are particularly useful in biomedical research. Analysis of spontaneous models of conditions that sometimes cannot be artificially reproduced. These models promote their use. Animal species are subject to an array of inherited diseases that represent muscular dystrophy.

This publication is a collection of papers related to diabetology, genetics, and physiology. It includes reports and discussions on spontaneous models of conditions that sometimes cannot be artificially reproduced. These models promote their use. Animal species are subject to an array of inherited diseases that represent muscular dystrophy.


This publication is a collection of papers.
from the Second Brook Lodge Workshop on Spontaneous Diabetes in Laboratory Animals held at Brook Lodge, Augusta, Michigan, November 6-8, 1969. Three years had gone by since the first Brook Lodge Workshop was held and published (Diabetologia 3: 63-286, 1967). Publication of the first Workshop served to define and consider the types of "inherited diabetes," and to explain why it seemed eminently appropriate to a number of investigators to obtain a fresh view of the problem of diabetes mellitus by making use of the occurrence, in small laboratory animals, of syndromes that exhibit many of the features of human diabetes. One of the main ends served by the first Workshop was that of establishing a common nomenclature acceptable to all participants, representing a majority of the laboratories then working in the field of animal "diabetes." (The second Workshop is a report, demonstrating quite clearly the stress where considerable progress has been made, and others where new information had not been forthcoming during the intervening three years.)


Orci, L., W. Stauffacher, M. Amherdt, E. Piclet, A. E. Renold, and Ch. Rouiller. The kidney of...
Methods of handling primates. The sections covered leukemia and oncogenic virus studies.


Orihel, T. C. Primates as models for parasitological research. p. 772-782.


Kinard, R. A program for inoculation of primates with potentially oncogenic viruses. p. 895-902.


Deinhardt, F. Use of marmosets in biomedical research. p. 918-925.


This collection of over 100 papers is an outgrowth of the Second Conference on Experimental Medicine and Surgery in Primates held in New York in September 1969. It is not a proceedings volume in the usual sense, in that the papers were reviewed and edited on the basis of their contribution to the total concept of the publication. It was the editors' intention that the volume describe the nature of medical primatology at this time. The Conference from which this book originated emphasized the results of medical research using nonhuman primates as experimental animals and the improvements in husbandry and methods of handling primates. The sections covered in this volume include: Man and Nonhuman Primates; Immunological Response; Cross-circulation between Man and Simians; Experimental Transplantation in Primate Animals; Comparative Biology, Genetics and Phylogenetics; The Nervous System, Man and Nonhuman Primates; The Nervous System, Perinatal Biology and Development; Behavioral Physiology; Reproduction, Perinatal Development Studies; Virology; Infectious Diseases; and Reports from Major Primate Laboratories and Current Programs. Papers of particular interest with regard to the Animal Models and Genetic Stocks Program are cited below.


Sorokin, S. P. The cells of the lungs. p. 3-44.


Berg, J. W. Epidemiology of the different histologic types of lung cancer. p. 93-104.


Nielson, S. W. Pulmonary neoplasia in domestic animals. p. 123-146.


Smith, W. E., L. Miller, and J. Churg. An experimental model for study of carcinogenesis in the respiratory tract. p. 299-316.


Wagner, J. C. The pathogenesis of tumors following the intrapleural infection of asbestos and silica. p. 347-358.


***


This monograph was stimulated by, and is partly based on, an international working conference on experimental ulcer that was held in conjunction with the Fourth World Congress of Gastroenterology in Copenhagen, Denmark, July 1970. This conference brought together approximately 50 leading medical scientists, representing 19 nations, concerned with research in peptic ulcer. This interdisciplinary group was comprised of gastroenterologists, physiologists, pharmacologists, pathologists, and surgeons. The present monograph contains the contributions of many of the participants of the Conference, as well as those of many experts in the field of peptic ulcer research who were unable to participate in the Copenhagen gathering. The purpose of the book is to convey to the medical scientific community at large current reviews and experimental findings relating to the ulcer problem and to record some of the transactions of the working conference. The monograph is intended for those in many disciplines, including medicine and gastroenterology, physiology, pharmacology, pathology, and psychology. The book contains many reviews with extensive bibliographies and many new and previously unpublished experimental findings in peptic ulcer research. It is hoped that the international working conference and the monograph will contribute to progress in understanding peptic ulcer.
PART I RECENT ADVANCES IN EXPERIMENTAL DUODENAL AND GASTRODUODENAL ULCER

Seronde, J., Jr. The Zucker ulcer: The duodenal ulcer of pantothenate deficiency. p. 3-12.


Eagleton, G. B., and J. Watt. The selective production of gastric and duodenal ulceration using histamine. p. 34-44.

Doteuchi, M. Gastrointestinal ulcers. Produced by reserpine and stress. p. 45-64.

Wynn-Williams, A. Peptic ulcer in the NZB mouse. p. 65-68.

PART II METHODS FOR ACUTE AND CHRONIC GASTRIC ULCERS

Brodie, D. A. Stress ulcer as an experimental model of peptic ulcer disease. p. 71-83.

Pfeiffer, C. J. Cold immersion, restraint stress - An ulcer model in the mouse for rapid, massive screening. p. 84-91.


PART III MUCO-SUBSTANCES AND BIOCHEMICAL ASPECTS OF EXPERIMENTAL ULCER


De Graef, J. Physiology and physiopathology of sulfated glycoproteins and sulfated polysaccharide secretion by the gastric mucosa in the dog. p. 155-161.


Schwartz, J. C. Gastric histamine in the pathogenesis of experimental ulcer. p. 190-198.

Abdel-Gall, A. A. M. Effect of parabiosis on phenylbutazone ulcerations in adrenalectomized rats. p. 199-203.

PART IV VASCULAR AND ANATOMIC CONSIDERATIONS IN PEPTIC ULCER

Wynn-Williams, A. Peptic ulcer in the NZB mouse. p. 207-220.

Guth, P. The role of the microcirculation and the mast cell in stress ulcer. p. 221-236.


Oi, M., T. Toriumi, O. Miho, and M. Kijima. Location of experimental ulcers as compared with that of human peptic ulcer. p. 244-259.


PART V EXTRA-GASTRIC FACTORS IN EXPERIMENTAL GASTRIC ULCERS


PART VI CLINICAL AND PHARMACEUTICAL PERSPECTIVES


***


This report is the summary of the proceedings of a conference on breast cancer in animals and man held at the 10th International Cancer Congress in Houston, Texas, in May 1970. Participants in the conference included scientists from the United States, Japan, India, and Europe who discussed new developments in studies on human breast cancer and contributed to the exchange of recent information on breast cancer in animals and man. The article summarized each of the papers listed below.

Session 1

Hall, W. T. "Parturient montes nascitur ridiculus mus," or Experiments that came out, but not as expected. p. 335-337.


Lavrin, D. Investigation of the C3Hf/Bi (Zb) strain for the absence of NIV and attempts to infect it with MTV. p. 356.

Session 2

Liebelt, A. G. Hyperplastic nodules and breast cancer in several strains of inbred mice of the Kirschbaum Memorial Laboratory. p. 357.

Medina, D. Some preliminary observations on cell culture of pre-neoplastic mouse mammary gland. p. 357-358.

Mühlbock, O. Genetics of the susceptibility of the mouse mammary gland to MTV. p. 358.

Nandi, S. Differences between M-MTV and R-MTV. p. 358-359.

Session 3

Ranadive, K. J. Highlights of observations of the inbred ICRC mouse susceptible to spontaneous breast cancer and leukemia. p. 359.

Slemmer, G. Pre-malignant mammary tissue of mice: Antigenicity, cellular composition, and progression to malignancy. p. 359-360.


Hilgcrs, J. Mouse antibodies to MTV. p. 360.

Sibal, L. Methods for the detection of MTV antigens. p. 360-361.

Heppner, G. H. Attempts at selective manipulation of humoral and cellular immunity to mouse mammary tumors. p. 361.


Session 4


Session 5

Heston, W. E. Inability to predict mammary tumorigenesis in strain A mice from presence of mammary tumor virus or antigen in the milk. p. 365-366.

Smith, G. Preliminary studies on the ultrastructural localization of MTV antigens in chronically infected cells with peroxidase-labeled antibody. p. 366.

Calafat, J. Differences between B particles from some mouse strains. p. 366-367.


Session 6

Heston, W. E. Inability to predict mammary tumorigenesis in strain A mice from presence of mammary tumor virus or antigen in the milk. p. 365-366.

Smith, G. Preliminary studies on the ultrastructural localization of MTV antigens in chronically infected cells with peroxidase-labeled antibody. p. 366.

Calafat, J. Differences between B particles from some mouse strains. p. 366-367.


Session 7


Bucciarelli, E. Virus particles in BALB/cF(RIII) and related mouse strains. p. 368.

Hageman, P. Separation and properties of B and C particles. p. 369.


Session 8


Priori, E. Studies on human breast cancers using the fixed immunofluorescence test. p. 373.

***


The materials in this publication have been drawn extensively from the presentations and remarks made January 9-11, 1970, at the New Orleans Conference on the Rodent as a Model System for Research in Aging. The most significant aspects of the conference are highlighted in selected summaries prepared by the participants. The information presented in the monograph serves partially to delineate the needs of the investigator in research on aging as they relate to the development of animal model systems; the environmental concerns that must be an integral part of long-term studies; and the genetic and statistical considerations that must be exercised in the selection and development of the animal model system in aging. The various papers characterize the needs of research on aging for the critical selection, care, and maintenance of animal model systems for research in the field and emphasize that research on aging is heavily dependent on the knowledgeable selection, development, and controlled rearing of animal model systems that survive to natural senescence.

SECTION I THE RODENT AS A MODEL SYSTEM OF AGING

Johnson, H. A. The relevance of the rodent as a model system of aging in man. p. 3-6.


Walburg, H. E., Jr. Microbiological definition and relevant microbiological considerations in rearing, maintenance and care of the laboratory rodent for research in aging. p. 23-29.

SECTION III GENETICS AND LABORATORY RODENT MODEL SYSTEMS IN AGING RESEARCH

Russell, E. S. Genetic considerations in the selection of rodent species and strains in aging. p. 33-53.


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This looseleaf handbook contains 16 annual model studies originally printed in the Journal of American Pathology and the Comparative Pathology Bulletin during the past three years. Subsequent sets of animal model papers will be prepared for future inclusion in the handbook, continuing the collection of animal models for the comparative study of disease.


Cornelius, C. E. Congenital hyperbilirubinemia, Dubin-Johnson syndrome (Corriedale sheep).


Rowlands, D. T., Jr. Bacterial endocarditis (opossum, Didelphis virginiana).

Jones, T. C. Sex chromosome anomaly, Klinefelter's syndrome (male tortoiseshell cat).

Glenn, B. L. Porphyria: Erythropoietic and hepatic types (cat).


Cornelius, C. E. Congenital hyperbilirubinemia, Gilbert's syndrome (Southdown sheep).

Fletcher, T. F. and H. J. Kurtz. Globoid cell leukodystrophy (dog).

Stevens, L. C. Teratoma, embryonal carcinoma, teratocarcinoma (mice).

Zook, B. C. Lead poisoning (simian primates).


Shenefelt, R. E. Gross congenital anomalies (several species).

Oppenheimer, K. N. and J. B. Brayton. Needed:
An animal model for cystic fibrosis.

Osburn, B. I. Hydranencephaly and porencephaly (sheep).

Kitchen, H., R. E. Murray, and B. Y. Cockrell. Spina bifida, sacral dysgenesis and myelocele (Manx cats).
DATE:

May we announce the existence of your colony in our quarterly publication, the ILAR News?

<table>
<thead>
<tr>
<th>SPECIES MAINTAINED (Genus, species, &amp; common name)</th>
<th>STRAIN OR BREED (Include synonyms &amp; symbols)</th>
<th>COLONY BREEDING SYSTEM (Random, inbred, include coefficient of breeding, etc.)</th>
<th>STOCK ORIGIN (Former owner or natural habitat)</th>
</tr>
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<tbody>
<tr>
<td>TOPIC(S) FOR WHICH THE ANIMALS MAY SERVE AS A MODEL</td>
<td>DESCRIPTION OF THE ANIMALS’ CHARACTERISTICS (e.g., gross, histologic &amp; ultrastructural anatomy; physiologic, metabolic &amp; behavioral features; incidence, severity, and complications of disease; etc.) and KEY REFERENCES characterizing the animal</td>
<td>COMMENTS: (Availability of stock to other investigators, special husbandry requirements, etc.)</td>
<td>(Continue on reverse side if needed)</td>
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</tbody>
</table>
In an effort to determine the usefulness of this publication, ILAR is asking biomedical investigators to complete and return this questionnaire. Please send to: Animal Models and Genetic Stocks Program, Institute of Laboratory Animal Resources, National Academy of Sciences, 2101 Constitution Avenue, Washington, D.C. 20418.

**QUESTIONNAIRE**

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<tr>
<th>Investigator's name</th>
<th>Institution</th>
<th>Department</th>
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1. Investigator's specific area of interest

2. Means by which the publication was obtained

3. Was this publication useful to you? Did you find the appendix of value? Please make comments.

4. Would you like to continue having *Selected Abstracts on Animal Models for Biomedical Research* available on an annual basis? Did you receive the first edition of *Abstracts*? Please indicate if you desire a copy.

5. Suggestions for future issues, other remarks, etc.

6. General comments regarding Animal Models and Genetic Stocks Program

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