93%; Ni_3Se_2, 91%; NiAsS, 88%; NiS_2, 86%; Ni_5As_2, 85%; Ni dust, 65%; NiSb, 59%; NiTe, 54%; NiSe, 50%; $Ni_{11}As_8$, 50%; amorphous NiS, 12%; $NiCrO_4$, 6%; NiAs, 0%; NiFe alloy, 0%; $NiTiO_3$, 0%, vehicle controls (N = 84), 0%. Distant metastases were found in 109 of 180 sarcoma-bearing rats (61%). The histological classification of the nickel-induced sarcomas included rhabdomyosarcoma, 52%, fibrosarcoma, 18%, undifferentiated sarcoma, 13%, osteosarcoma, 8%, and miscellaneous sarcomas, 9%. Relative carcinogenic activities of the compounds were not significantly correlated with dissolution half-times in rat serum or phagocytic indices by rat peritoneal macrophages *in vitro*. The relative carcinogenic activities were correlated ($P < 0.001$) with potencies of the compounds to stimulate erythropoiesis in rats after intrarenal injection. The mechanism of nickel carcinogenesis may involve binding of nickel to nucleoproteins, with inhibition of nucleic acid synthesis, formation of DNA–protein cross-links, impaired fidelity of DNA replication, and induction of chromosomal aberrations, including sister–chromatid exchanges and karyotypic anomalies. Manganese antagonism of nickel carcinogenesis may indicate competition of Mn(II) and Ni(II) for binding to specific loci on nucleoproteins or DNA polymerases.

Z3

Nutritional Aspects of Zn Deficiency

G. MAROZZI, F. CHIARAMONTE, T. DANTONIO and P. G. DEL CASTELLO

Istituto di Scienze dell'Alimentazione e Dietetica, Ospedale S. Spirito, RM/17 Rome, Italy

Zinc, which as been recognized as essential to man, has received considerable attention in recent years for its metabolic role. Zinc is an essential component of an number of enzyme systems and influences the structural configuration of certain nonenzyme organic ligands.

Several experimental studies have emphasized that many systems may be adversely affected by zinc deficiency, particularly if the deficiency occurs when cells of the particular system are rapidly dividing, growing, or synthesizing proteins.

Features of nutritional zinc deficiency in animals and men include anorexia, growth retardation, impaired keratogenesis, skin lesions, hypogonadism, hypogeusia, lethargy and behavioral changes.

Zinc-responsive growth failure and delayed sexual maturation were described in adolescent males from the Middle East. Furthermore, zinc deficiency has been reported in people maintained on long-term parenteral nutrition or suffering from alcoholism, chronic renal disease or malabsorption syndromes.

Recognition of the critical role of zinc in human nutrition has recently led to the hypothesis that in elderly persons, some degenerative changes result with advancing years from insufficient intake of protein foods that are the best dietary sources of this metal ion.

Z4

The Role of Aluminum in Experimental Osteomalacia. Preliminary Results: Aluminum Content and Bone Mineralization

E. BONUCCI

I° Istituto di Anatomia e Istologia Patologica, Cattedra V, Università degli Studi di Roma, Rome, Italy

S. COSTANTINI

Istituto Superiore di Sanità – Roma, Laboratorio di Tossicologia Applicata, Rome, Italy

A. IOPPOLO

Istituto Superiore di Sanità – Roma, Servizio Stabulari, Rome, Italy

In order to clarify the role of aluminum in the production of dialysis osteomalacia, an experimental study on rats has been carried out. Four groups of fifteen rats each have been treated daily with intraperitoneal injections of aluminum chloride for periods of up to three and half months.

Acute, sub-acute and chronic intoxication have developed in the treated rats.

The aluminum presence in the bony tissue has been determined both quantitatively and morphologically by means of atomic absorption spectrophotometry and specific histochemical studies. In this way we have studied the preferential localization of the aluminum in the bony tissue with reference to the mineralization processes.

Z5

A Pharmacological Analysis of Aluminium Effects on the Central Nervous System

A. LOIZZO, S. CAROLI and E. ORTOLANI

Istituto Superiore di Sanità, Rome, Italy

The possible causes of dementia are many, and most cases are associated with degenerative disease of the central nervous system; therefore, analysis of neurotransmitter systems may provide valuable information on the selectivity of the degenerative process. This report will deal with an experimental approach

to dementia, through quantitative analysis of electroencephalographic (EEG) effects induced by aluminium on laboratory animals.

In a first series of experiments we found that single oral doses of aluminium hydroxide induced in mice a dose-dependent diminution of the EEG power of 7.5 to 12 c/s frequency band, and a parallel dose-dependent increase of aluminium content in the brain, as early as 45 minutes after administration. It indicated that aluminium hydroxide is readily absorbed through an empty stomach or duodenum and is able to induce alterations of background EEG rhythms at doses equivalent to the ones used in human therapy. These and other data suggest that the EEG disturbances of background type, which are observed during the early stage in dialysis encephalopathy in man, may be due at least in part to a pharmacological and therefore reversible effect induced by an increased aluminium level in the brain. This effect was therefore investigated in a second series of experiments. Aluminium was found to induce, even in minute doses, profound effects on the hippocampal EEG of the rabbit after acute intracerebro-ventricular administration, consisting of long-lasting EEG desynchronization and, at higher doses, of EEG epileptiform pattern. These effects could be at least in part reversed or prevented by i.v. administration of drugs effective on the cholinergic and/or endorphinic systems.

These results, although preliminary in nature, may contribute to the elucidation of the pathogenesis of experimental 'dementia' models in animals.