Lampl; Landsteiner and Jacobs; Landsteiner; Jacobs; Breinl and Haurowitz; Heidelberger and Kendall; Erlenmeyer and Berger; Berger and Erlenmeyer; Eagle and Vickers; Mutsaars and Grégoire; Marrack; and Klopstock and Selter).

Animals injected with these azoproteins developed immune bodies (precipitins and complement fixing antibodies) against the particular haptenic group and chemically related substances (group-immunity). Erlenmeyer and Berger reported that an immune serum against an amino-antipyrin-protein complex reacted with aniline, acetylphenylhydrazine, histamine, histidine, and those pyrazolon compounds containing the $C_6H_5—N=N—C—H_3$ group, which is responsible for the antipyretic effect displayed by aminoantipyrine. An antiserum against the diazo-compound of beta-aminopyridine yielded positive immune reactions with beta-aminopyridine, pyridine, alpha-picolin, beta-picolin, collidin, nicotinic acid, coramine, quinoline, and nicotine. Jacobs found that antisera against the azoproteins of aniline and toluidine did not interact with polycyclic hydrocarbons, such as diphenyls, naphthylamines, and anthramines, while naphthylamine antisera reacted with various polycyclic antigens. These group immune reactions are of importance not only from the viewpoint of providing an explanation for the well-known observation of polyallergy, but also from the consideration that a noncarcinogenic hydrocarbon may elicit an allergic status to a chemically related, carcinogenic substance and vice versa.

The second method by which proteins can be conjugated with aromatic compounds was developed by Hopkins and Wormall in 1934. These investigators used the phenyl-isocyanate method for producing with the ureido-linkage ($R—\underset{\underset{O}{\|}}{C}—NHC_6H_5$) allergenic, hydrocarbon-protein complexes. In the production of these compounds, the aromatic isocyanates react mainly with the epsilon amino-group of the lysine molecules and occasionally with the tyrosine molecule of the proteins, forming carbamidoacids. This technique has been employed extensively by Creech and Franks; and Fieser and Creech for the coupling of various carcinogenic hydrocarbons and numerous, non-carcinogenic, cyclic compounds with proteins in their investigation of the immunizing properties exerted by these complexes against hydrocarbon carcinogenesis.

These allergens are of special interest in connection with the occupational cancer problem, as they suggest a possible route by which water insoluble carcinogens may be converted into water soluble ones, and because of Boyland and Levi's observation concerning the excretion of certain polynuclear aromatic hydrocarbons fed to animals, in part, in conjugation with aminoacids (Fieser and Creech). A possible interaction of aminoacids with carcinogenic hydrocarbons in the organism seems more likely by the experiments of White and White, who found that sulfhydryl containing aminoacids counteract the growth inhibiting action of toxic doses of carcinogenic hydrocarbons upon young animals.

It is of significance from an allergic view-point that ureido-antigens give