the possibility of their reacting to these substances may constitute a serious problem.

Certain other problems are intimately related to this question. It is known, for example, that a number of cases of dermatitis from paraphenylenediamine and related compounds used in hair and fur dyes, photo developers, leather dyes, nylon stockings, etc. occasionally show flare-ups which cannot be explained on the basis of a new exposure to the causative agent. Our results suggest the possibility that the ingestion of certified azo-dyes, which have been shown to produce reactions in patients hypersensitive to paraphenylenediamine, may be responsible for these recurrences. Furthermore, it may be possible that certain eczematous eruptions now attributed to various foods themselves are actually due to the azo-dyes contained in these foods. A study of the influence of continuous exposure to these dyes on the causation and persistence of non-eczematous and possibly non-cutaneous allergies as, for example, asthma due to paraphenylenediamine and related compounds, would prove of great interest.

In evaluating the results shown in Table II it seems at first glance inexplicable that not all aminated azo-dyes used in foods, cosmetics and drugs produce irritations. While certain of the food dyes listed in Table II are seemingly harmless, even for patients highly sensitive to paraphenylenediamine, other dyes of closely related constitution elicit strong skin reactions in a high percentage of cases. The data gathered to date in various studies indicate that the presence or absence of a response to a given azo-dye in a case of cross-sensitization to compounds of quinone structure depends essentially upon the chemical structure of the dyes. Indeed, the capacity of an azo-dye to produce skin reactions in patients sensitive to paraphenylenediamine seems to be dependent in most cases upon the ease of its transformation into compounds of quinone structure and upon the ability of the quinone compound thus formed to couple with certain body constituents. We believe that only those azo-dyes capable of undergoing these changes have sensitizing power and elicit reactions in an appreciable number of cases.[4]

Conclusions. Skin tests with certain certified food dyes in patients sensitive to paraphenylenediamine suggest that eczematous hypersensitivity to paraphenylenediamine may not only cross over to azo-dyes used for the dyeing of leather and fabrics, or in ointments, but also to certain azo-dyes certified by the Food, Drug and Cosmetic Act of 1938 for use in foods, drugs and cosmetics. The implications of these findings are discussed.

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Effect of Pneumonectomy and of Lung Extract on Experimental Renal Hypertension.*

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Katz and Steinitz[1] have demonstrated in dogs that pulmonary arterial pressure is not altered in experimental renal hypertension. This may be explained by the inability of the pulmonary arterioles to respond adequately to the renal pressor mechanism, inasmuch as Brenner[2] found that the walls of these vessels average 5.7% of the external

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[1] Katz, L. M., and Steinitz, F. S., *Am. J. Physiol.*, 1940, **128**, 433.

[2] Brenner, O., *Arch. Int. Med.*, 1935, **56**, 211, 457, 724, 976, 1189.

diameter, compared with 36% for the systemic arterioles. Certain experimental data, however, demonstrate that the pulmonary arterioles do respond to pressor agents. Friedberg *et al.*[3] showed that the intravenous injection of angiotonin produced a rise in pressure in the pulmonary artery of the dog occurring almost simultaneously with the systemic rise. With renin, the pulmonary pressure rise lagged behind the systemic. Binet and Bergeton[4] observed a vasoconstrictor action of renin on the vessels of the isolated dog lung, and found that renin is inactivated by passage through a heart-lung preparation. Braun-Menendez *et al.*,[5] however, observed no appreciable diminution in renin activity after 2 hours of perfusion through a heart-lung preparation. These findings suggest either that renin and angiotonin are not involved in hypertension of renal origin, or that in chronic renal hypertension the pressor mechanism may operate differently in the pulmonary as compared with the systemic circulation.

Design of experiments. The pulmonary normotension in experimental renal hypertension may be due to the elaboration by the lung of an antihypertensive substance or to the lung's inactivation of a pressor agent produced by the kidney. This may occur to an extent sufficient to prevent the development of pulmonary hypertension, yet not to inhibit the production of an elevated pressure in the systemic circuit.

To test for an antihypertensive agent in lung tissue, 2 dogs were injected with lung extract for 2 months, then were subjected to a unilateral renal artery constriction and a contralateral nephrectomy. Injections were continued throughout the operation period and for 2 months following. Good evidence exists that prophylaxis can be obtained by a similar injection procedure with certain renal extracts.[6] The technique used in constricting the renal arteries has been found to result in the development of hypertension in a high percentage of control dogs.

To investigate the effect of a reduction in lung substance, pneumonectomy was performed on 4 dogs with moderate renal hypertension. Two of these dogs were later subjected to contralateral lobectomy. It was felt that any possible pressor inactivating effect of the lungs might thereby be reduced to a degree sufficient to permit the hypertensive substance elaborated by the kidney to raise the systemic pressure to a still higher level. Two normotensive dogs were pneumonectomized as controls. Unilateral renal artery constriction and contralateral nephrectomy were later done on these controls.

Procedures. Arterial pressures were obtained on the animals by direct femoral puncture at least twice a week.[7] The renal arteries were clamped according to our modification of the Goldblatt technique[8] which produces hypertension in practically 100% of dogs. The pneumonectomies and lobectomies were performed according to the technique of Joannides.[9]

The lung extract was prepared from dog lungs removed immediately after death. The lungs were frozen and ground in a meat chopper. The tissue was then defatted over 48 hours by 2 changes of cold acetone and for another 24 hours by cold ether. It was then dried under vacuum at room temperature in a drying column and finely divided in a coffee grinder. Fresh extracts of this lung powder were made with a .5% $NaHCO_3$ in physiological salt solution. One cc of the final extract was equivalent to one gram of fresh tissue. Streptomycin and penicillin were added as preservative. The animals were injected intramuscularly 6 days a week with a dose of 1.5 cc per kg of body weight.

[3] Friedberg, L., Katz, L. N., and Steinitz, F. S., *J. Pharmacol. and Exp. Therap.*, 1943, **77**, 80.

[4] Binet, L., and Bergeton, D., *C. R. Soc. de Biol.*, 1942, **136**, 134.

[5] Braun-Menendez *et al.*, *Renal Hypertension* (translated by L. Dexter), C. C. Thomas, Springfield, Ill., 1946, p. 207.

[6] Wakerlin, G. E., Johnson, C. A., Smith, E. L., Moss, W. G., and Weir, J. R., *Am. J. Physiol.*, 1942, **137**, 515.

[7] Dameshek, W., and Loman, J., *Am. J. Physiol.*, 1932, **101**, 140.

[8] Wakerlin, G. E., unpublished data.

[9] Joannides, Minas, *Arch. Surg.*, 1928, **17**, 91.

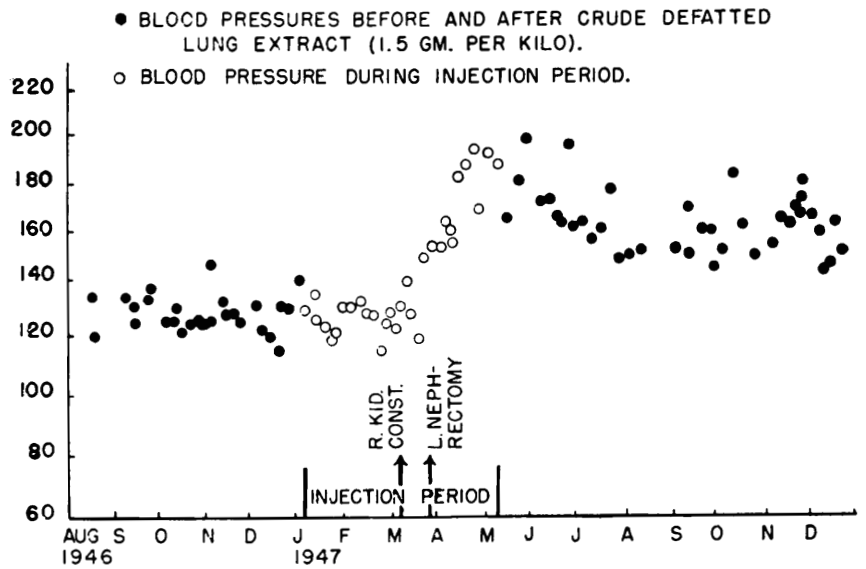

FIG. 1.

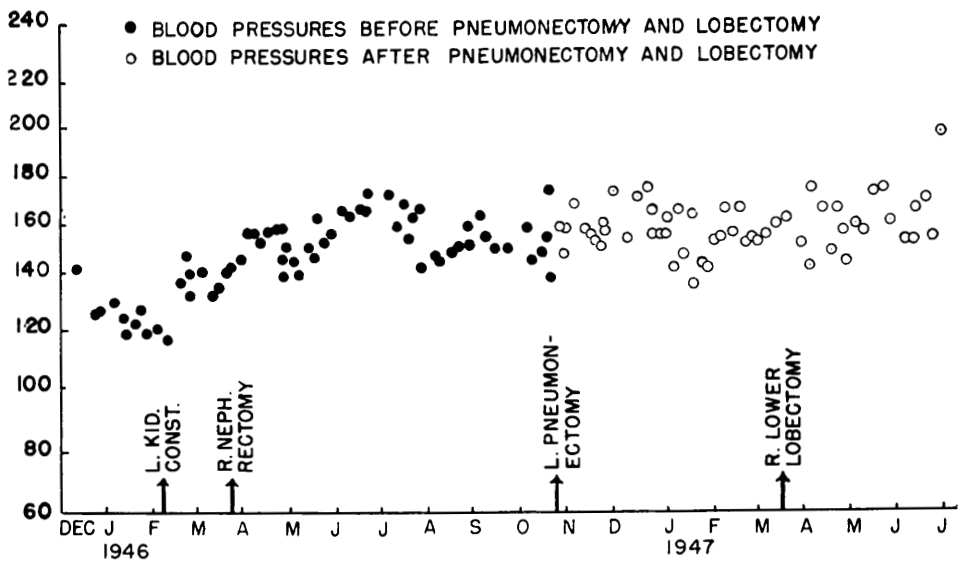

FIG. 2.

Results. 1. The lung extract failed to prevent the development of hypertension in the 2 injected dogs following constriction of the renal artery and contralateral nephrectomy (Fig. 1). All ten of the control dogs developed hypertension, 2 of them dying of malignant hypertension. 2. Pneumonectomies performed on 2 of the 4 moderately hypertensive dogs did not alter in any way their pressure over a period of 4 months. 3. Pneumonectomy and contralateral lobectomy on the other 2 hypertensive dogs likewise did not alter their pressure over a period of 6 months (Fig. 2). 4. The normotensions of 2 dogs were not influenced by pneumonectomy, nor did the absence of a lung alter the hypertension produced by subsequent renal artery clamping and contralateral nephrectomy.

Discussion. The results demonstrate that the lung extract used had no prophylactic

antihypertensive effect. Moreover, a preliminary experiment with the dog lung extract in rats likewise indicated no prophylaxis against experimental renal hypertension.[10] However, antihypertensive substances not obtained by this method of extraction may be present in lung.

A reduction in the amount of functioning lung tissue was shown to be without effect on the systemic blood pressure of moderately hypertensive animals. No regeneration of lung tissue was found in these dogs on sacrifice, and it seems likely that sufficient tissue was removed to demonstrate some effect if the lung plays an active antipressor role in experimental renal hypertension.

Summary. 1. Daily intramuscular injections of lung extract for two months preceding and following clamping of the renal artery and contralateral nephrectomy failed to prevent the development of hypertension in two dogs. 2. Pneumonectomy performed on 2 renal hypertensive dogs and pneumonectomy plus contralateral lobectomy on 2 other hypertensive animals did not alter their pressure levels. 3. The pressures of 2 normotensive dogs were not influenced by pneumonectomy, nor were the hypertensions subsequently produced by renal artery constriction and contralateral nephrectomy. 4. The results of these experiments suggest, but do not prove, that the lungs do not elaborate an antihypertensive substance and do not inactivate the pressor agent of experimental renal hypertension. 5. Further work is necessary to explain the pulmonary normotension of renal hypertensive dogs.

[10] Klatch, B. Z., unpublished data.

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Relationship Between the pH of the Duodenal Content and Pancreatic Secretion.*

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Bayliss and Starling[1] demonstrated the mechanism whereby acid introduced into the intestine provoked a flow of pancreatic secretion. With increasing interest in the role of the endocrine glands in the regulation of bodily function it has been widely assumed that the secretin mechanism largely determined the volume of pancreatic secretion.[2] Farrell and Ivy,[3] who feel the secretin mechanism is the most important, found that a denervated pancreas failed to secrete as much as expected. McClure,[4] on the basis of his determination of enzyme in the duodenal content, stated that "stimulation of the external enzymic function of the pancreas is dependent on some factor or factors unrelated to acidity of intestinal contents." Thomas

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[1] Bayliss, W. M., and Starling, E. H., *Am. J. Physiol.*, 1902, **28**, 325.

[2] *Howell's Text Book of Physiology*, 15th Edition, 1946, p. 1064, W. B. Saunders Co., Philadelphia; *Physiology in Health and Disease*, C. S. Wiggers, 4th Edition, 1947, p. 809, Lea and Febiger, Philadelphia.

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