and four times at 15 to 20 per cent. The dry kata reading varied on these different days between 3.62 and 3.86. In spite of the active ventilation the kata reading was low throughout. Experience has shown that a reading of 6, designated as optimum for Great Britain, is too high for class-room conditions in this country.

A summary of the results of these fifteen observations is given in Table 1 and Fig. 1. The figures and graphs represent not the actual number of individuals voting for the different grades of comfort, but the percentage of the total attendance for each day that so voted.

TABLE 1

DRY BULB TEMPERATURE IN ROOM, 69° TO 71° F.
DRY KATA 3.62 TO 3.86

Comfort report	Relative humidity 55 to 60 per cent.	Relative humidity 48 per cent.	Relative humidity 35 to 40 per cent.	Relative humidity 20 to 30 per cent.	Relative humidity 15 to 20 per cent.
Too cold (1)	1.7	4.2	5.6	1	5.1
Comfortably cool (2)	24.3	34.0	34.25	40.4	49.55
Comfortable (3)	59.3	49.0	51.3	53.0	41.7
Comfortably warm (4)	12.6	8.5	8.8	4.45	3.4
Too warm (5)	2.1	4.2	0	1.0	0

1. The record shows that in the experiments as a whole from 91 to 97 per cent. of the group found 70° F. comfortable, irrespective of the humidity. That is to say, they reported that the conditions were either comfortable, comfortably cool or comfortably warm. Much the larger portion, 83 to 93 per cent. made a selection between comfortable and comfortably cool. The composition of the group who voted 3, comfortable, on the different days varied considerably. For example, in the six experiments in which the physical conditions were kept constant at a dry bulb of 70° F. and a relative humidity of 55 to 60 per cent. only four voted "comfortable" consistently for the six days. The others on one or more occasions reported themselves as comfortably cool or comfortably warm.

2. It will be noted that as the humidity decreased the size of the group voting 2, comfortably cool, increased from 24 per cent. at humidity 55 to 60 to 49 per cent. at humidity 15 to 20, giving an indication of the cooling effect of the drier air when the dry bulb remains constant. On the other hand group 4, comfortably warm, shows an increase from 3.4 per cent. to 12.6 per cent. as the humidity increases.

3. The small groups who found the conditions too warm or too cold were composed for the most part of the same individuals. There were two or three in the class for whom 70° F. at any humidity was uncomfortably cool, and a few others for whom the same conditions were at times uncomfortably warm.

4. While the optimum humidity seemed to be 55 to 60 per cent. it may be concluded that in an auditorium kept at the standard temperature of 70° F. variations in humidity between the limits used, which are those that ordinarily prevail indoors in temperate climates under winter conditions, make but little difference in the sense of comfort and well being of the occupants. It is doubtful, therefore, whether there is any justification for the installation of expensive equipment for the control of humidity. For such conditions the dry bulb temperature is the important standard to maintain, together with provision for the renewal and adequate movement of the air.

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MODIFICATION OF THERAPEUTIC SERA WITH A VIEW OF AVOIDING COMPLICATIONS OF ALLERGIC NATURE[1]

THERAPEUTIC as well as prophylactic administration of various sera derived from immunized animals has proved of such great value that it is resorted to in a constantly increasing number of instances. However, a certain not insignificant hesitancy still exists among the practicing physicians due to the fact that occasionally parenteral introduction of therapeutic sera has been known to be accompanied by grave complications and even by the death of the recipient.

While Park[2] estimates that only one out of 20,000 of those receiving serum for the first time develops alarming symptoms and only 1 in 50,000 succumbs as a direct result of the treatment, one can readily understand the hesitancy of a physician who goes through the experience of losing his patient in spite of his taking all known precautions to ward off this calamity.

In this paper we are suggesting a procedure which promises to minimize if not eliminate entirely the risk involved in the practice of serum therapy.

With respect to possible response to parenteral introduction of therapeutic sera, the human race can be divided into four categories.

(1) A significant portion (about 10 per cent.) show no visible response whatever to injection of serum.

[1] Presented before the joint meeting of American Association of Pathologists and Bacteriologists and American Association of Immunologists at Cleveland, April 1–3, 1931. This investigation has been aided by a grant from Eli Lilly and Company.

[2] W. H. Park, *Am. J. Pub. Health*, 18, 354, 1928.

(2) The bulk of recipients of serum is composed of normal "individuals" who present more or less marked symptoms of the so-called "serum sickness," appearing usually within seven to twelve days after the parenteral introduction of therapeutic serum.

(3) A small number (a fraction of 1 per cent.) of individuals are so-called "naturally hypersensitive" to horse protein. These individuals have no knowledge of any previous exposure to parenteral introduction of horse protein, but they respond to injection of horse serum by an immediate violent reaction leading to collapse and sometimes death. The incidence of this sort of reaction is estimated to be about 1 in 20,000[2] of all those treated.

(4) Quite a large group of recipients of serum therapy is composed of individuals who originally belonged to the group of normally reacting individuals (group 2 above), but who, as a result of receiving parenteral injection of horse serum some time in the past, have become artificially sensitized to it and henceforth usually react to subsequent introduction of serum by developing "serum sickness" after a foreshortened (sometimes as short as three hours) period of incubation. A certain number of individuals in this group, however, may respond to injection by immediate acute symptoms entirely analogous to individuals in the group 3 above.

Due to continuous extensive use of therapeutic sera in connection with a variety of diseases this group is constantly on the increase. Moreover, the use of prophylactic immunization with toxin-antitoxin mixture further contributes to rapid increase of those artificially sensitized to horse protein.[3]

While the use of purified antibody preparations tends to diminish the frequency and the extent of sensitization, according to some investigators,[2] according to others[4] globulin fraction is an exquisite sensitizing antigen. Even the extremely small amounts of globulin introduced by the toxin-antitoxin immunization is sufficient not only to establish skin sensitization in a not inconsiderable percentage of cases,[5] but also in some instances injection of toxin-antitoxin seems capable of engendering a high degree of general hypersensitiveness resulting in severe symptoms following subsequent introduction of serum.[6]

In practice the frequency of complications incident to serum therapy is reduced somewhat by desensitization. However, while this procedure seems to be quite efficient when applied to animals, its efficiency in man is considerably less certain. In some cases a fair degree of tolerance to serum can be established after careful and prolonged desensitization. In other cases, particularly in individuals known to suffer from asthma or hay fever, desensitization is extremely dangerous if not impossible, because administration of even minute amounts of horse serum may be followed by grave symptoms or even death.[7]

The only procedure theoretically available for safe serum therapy of such individuals consists in employment of therapeutic sera derived from such animals to the protein of which the recipients show no hypersensitiveness. In practice this procedure usually can not be carried out because therapeutic sera are prepared in horses almost exclusively.

It is evident that if the protein of the therapeutic serum could be deprived of its species specificity the difficulty might be overcome.

The possibility of accomplishing this end was suggested by the early work of Obermeyer and Pick[8] and of Landsteiner,[9] who succeeded in destroying the species specificity of proteins and imparting to them a new chemical specificity by subjecting them to appropriate chemical treatment. Since these experiments were made only for the purpose of eliciting the relation between the antigenic specificity and chemical structure, the authors were not concerned with the extent of changes which protein underwent during this treatment. When the methods used by them were applied by us in the attempts to destroy the species specificity of therapeutic sera, it was soon found that their methods were too drastic. While sera usually lost their species specificity as a result of chemical coupling, the therapeutic properties of the sera were lost at the same time.

Fortunately by a proper modification of procedures, particularly with the view of avoiding extreme changes in temperature, hydrogen-ion concentration and rapid oxidation, we have succeeded in obtaining several compounds which seem to possess the desired properties.[10]

(1) Out of many procedures tried so far, in general coupling with diazotized aromatic amines has given the most promising results. Among the com-

[3] In this connection, Park's suggestion of using goats as donors of serum for the preparation of toxin-antitoxin mixture is an important step in the right direction.

[4] H. H. Dale and P. Hartley, *Biochem. J.*, 10, 408, 1916.

[5] S. B. Hooker, *J. Immun.*, 9, 7, 1924.

[6] J. E. Gordon and S. M. Criswell, *J. Prev. Med.*, 3, 21, 1929.

[7] R. W. Lamson, *J. Am. Med. Assn.*, 93, 1775, 1929; also *ibid.*, 82, 1091, 1924; R. A. Cooke, *J. Immun.*, 7, 119; 1922; J. G. M. Bullowa and M. Jacobi, *J. Am. Med. Assn.*, 46, 306, 1930.

[8] F. Obermeier and E. P. Pick, *Wien Klin. Woch.*, 19, 327, 1906.

[9] K. Landsteiner, *Biochem. Zeitschr.*, 58, 362, 1913; K. Landsteiner and H. Lampl, *Biochem. Zeitschr.*, 86, 343, 1918.

[10] J. Bronfenbrenner, Proc. Soc. Exp. Biol. and Med., 27, 734, 1930; similar observations were reported also by L. Reiner, SCIENCE, 72, 483, 1930.

pounds prepared, good results were obtained by coupling immune sera with diazonium salts of para-toluidin, para-anisidine, atoxyl, sulphanilic acid, anthranilic acid, naphthionic acid and amino R salt.

(2) The preparations obtained have lost their species specificity. They were not precipitated by the potent anti-horse precipitating serum. They did not cause anaphylaxis when injected intravenously into guinea-pigs highly sensitized to horse serum nor did the injection of these compounds protect the animals against subsequent death from injection of unmodified horse serum. They did not cause skin reactions in horse-asthmatics.

(3) Several of the preparations secured by the different couplings were found to be mutually heterologous—that is to say, they did not sensitize guinea-pigs to each other.

(4) Antigenic properties of these preparations were found to be in general less marked than those of native serum and thus there is a possibility that their use may not be followed by serum sickness in as large a percentage of cases as is usual with unmodified horse serum.

(5) While these serum preparations have thus completely lost their species specificity as result of coupling, they retained nevertheless to a fair degree their specific immune properties. Though in general the antibody content of these preparations was found to be lower than that of the original sera from which they were prepared, we hope that by further improvement of the chemical procedures the antibody content of the final product may be sufficiently increased to make this procedure practical.

(6) In so far as experiments on mice and guinea pigs have thus far indicated, these preparations are not toxic. Only when given intracardially in the amounts roughly approaching (weight for weight) the therapeutic doses in man have we seen any evidence of untoward symptoms. But even in the most marked cases these symptoms lasted only for a few minutes following the injection and in general suggested that they may have been caused by the rapidity of injection alone.

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A POSSIBLE RELATIONSHIP BETWEEN HEMOGLOBIN AND CHLOROPHYLL AS SHOWN BY THE USE OF LIVER EXTRACT

THAT there is a striking chemical similarity between chlorophyll, the characteristic green pigment of plants, and hemoglobin, the red-colored material of the blood of animals, has been called to the attention of biochemists since the early part of the century. Treatment of both materials with an acid and then an alkali results in the respective porphyrins—phyllo-porphyrin and hematoporphyrin—differing only slightly in the amount of oxygen contained. Furthermore from both of these substances can be obtained (Nentski and Marchlewski, 1901) the same substance, hemopyrrol.

In addition to these similarities in chemical analysis, it is not unreasonable to expect physiological resemblances. Both are pigments, and, according to Palladin, both are instrumental in the transfer of oxygen. This is the recognized function of hemoglobin, and Willstätter and others have assigned a somewhat similar function to chlorophyll in the photosynthetic process. Manoilov more recently (1922) produced evidence that the chemical tests which distinguish male from female blood are equally applicable to male and female chlorophyll in dioecious plants.

With these as precedents it was thought of possible interest to see if the same substances which influence the formation of hemoglobin in the blood would have any effect upon the formation of chlorophyll in plants. For this purpose liver extract was selected because of its interest in the study of pernicious anemia. Liver extract is a specific for pernicious anemia, but its method of action is still a disputed point. Does it check the disease by preventing the destruction of the hemoglobin, by aiding in its formation, or both? Also is the effect upon the pigment or upon the stroma of the red cells? The present tendency is to favor the idea that its effect is upon the destruction of the red cells rather than upon their formation, but no good method seems to have been devised to test the precise nature of these effects.

On the assumption that liver extract might have an analogous action on chlorophyll and that from such experiments hints might be obtained as to the action of the extract on hemoglobin, corn plants (also peas, but results were not so good) were grown in clean, moist sawdust until the roots were about 2 inches long and the first leaves were well unrolled. The plants were then carefully washed and transferred to 300 cc of Knop's nutrient solution, after which they were placed in the light for three days or until they should become accustomed to the new conditions of the nutrient solution.

To the solutions containing the test plants was then added 0.5 cc of a solution of liver extract made by dissolving a tube of Lilly's commercial extract (about 4.5 gm) in 25 cc of distilled water. The plants were then transferred to a dark room and left for from