The types of cases admitted were crushed chest, neurological disorders, barbiturate poisoning, post-operative respiratory failure, and chronic pulmonary disease with carbon dioxide narcosis.

Of the first 100 admissions, 76 patients recovered. The patients were all seriously ill, and most would have died if not treated by assisted ventilation. In many patients the primary condition was reversible, and the institution of adequate ventilation caused striking improvement and eventually a return to normal life.

Since the presentation of this paper, the management of the patient with respiratory insufficiency has been extensively described by H. B. Fairley and R. A. Chambers in the *Canadian Anaesthetists' Society Journal*, 7: 447, 1960.

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ALLERGY TO RAW COFFEE – AN OCCUPATIONAL DISEASE*

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ONE OF US (M.K.), on becoming associated with a coffee manufacturing plant on a part-time consulting basis, was surprised to learn that reactions, probably allergic in type, were occurring in a proportion of the workers.

The plant nursing personnel were aware that the symptoms complained of by affected workers were predominantly those due to air-borne material and involved the eyes, nose and lungs. The sole source of such material was the coffee which is brought into the plant as raw green beans. Bags containing the beans are emptied manually and the chaff is separated from the bean mechanically. Considerable very fine, dusty powder is released into the air during this process, and many of the workers had noted appearance or aggravation of their symptoms when working in this area. The green beans are conveyed to the roasting pans, roasted, packed and sealed. Little or no discomfort had been noted in the packing or dispatching areas. With this preliminary knowledge, the raw coffee was considered to be the likely allergen.

A few case reports of occupational coffee bean allergy have appeared in the literature, but no large series of cases has previously been reported.[1-3] Figley and Rawling[1] in their report of seven cases found that the burlap bags used to transport the coffee beans were contaminated with castor bean. On the basis of positive skin tests to castor bean and of Schultz-Dale studies, they came to the conclusion that the castor bean allergen was responsible for the symptoms in their patients. This possibility has been excluded in our study by careful inquiry into the methods of shipping the beans from South America. New bags are used, and at no time during transportation do the coffee beans or the bags come in contact with castor beans or fertilizer made from castor beans.

METHOD OF STUDY

Aqueous extracts of raw chaff, raw beans, roasted chaff and roasted beans were prepared in the Allergy Laboratory of the Montreal General Hospital and standardized by the method of Cooke and Stull[4] to contain 1, 10, 100 and 1000 protein nitrogen units (P.N.U.) per millilitre. Phenol 0.4% was included as a preservative. Intradermal testing on the arm, using 0.025 ml. of each extract, was carried out. All testing was carried out by the nurses, and after 15 minutes the size of any wheal was read by the physician, using a plastic rule with graduated circles of 4, 8, 10, 12 and 20 mm. diameter. If wheals with pseudopods occurred, no further testing was carried out with that particular extract. In the absence of pseudopods all subjects were tested with the four extracts at the four different strengths.

The personnel to be tested were subsequently divided into three groups but were selected initially as a whole by the nurses from the general worker population. These groups were: (1) 17 subjects who had had absolutely no contact with coffee manufacturing in the plant—these were usually new employees or office personnel; (2) 39 subjects suspected by the nurses to have allergic symptoms; (3) 56 subjects working in the plant and usually, but not always, having had contact with the raw and prepared coffee but who had no symptoms. This latter group included 17 subjects whose contact with the coffee processing had been extremely brief.

Immediately before skin testing, the plant physician, who until that time had not met any of the workers and was unaware of their individual complaints, took a brief history directed at eliciting allergic symptoms to coffee and including a previous history of asthma, hay fever, hives, bronchitis, sinusitis and eczema in the subject or his immediate family. Each person was then arbitrarily classified as allergic to coffee, not allergic, or not allergic and with no contact with coffee. This initial, entirely

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TABLE I.—SYMPTOMS OF COFFEE ALLERGY IN ORDER OF FREQUENCY

Symptom	Number of Subjects Showing Each Symptom: Group 2 — 39 subjects allergic by history	Group 3 — 56 subjects not allergic by history
Nasal congestion and discharge	29	—
Dermatitis	19	2
Dyspnea	18	—
Asthma	16	—
Sore eyes with lacrimation	14	—

clinical grouping led to the subdivision of the personnel as described above. Immediately after such categorization, the skin testing was performed. Both males and females were studied. All were adults of various ages and none were taking any medication at the time of testing.

Results

The symptoms in Groups 2 and 3 are shown in Table I. Subjects in Group 1 who had never been in contact with raw or roasted coffee had no symptoms.

TABLE II.—FREQUENCY OF WHEALS WITH PSEUDOPODS IN EACH OF THE THREE GROUPS TESTED

Group	No. in group	No. with pseudopods	%
I. No contact	17	0	0
II. Allergic by history	39	27	69
III. Not allergic by history	56	8	14

The presence of a wheal with pseudopods was considered a significantly positive reaction at any testing strength employed. Some individuals gave such reactions with the 1 P.N.U. extracts, though most in whom they appeared required the 10 P.N.U. or more to elicit pseudopods. Their frequency is shown in Table II.

TABLE III.—NUMBER OF SUBJECTS SHOWING WHEALS WITH PSEUDOPODS

Extract tested	Group 2 — 39 subjects allergic by history		Group 3 — 56 subjects not allergic by history	
Raw chaff	26	69%	7	12%
Raw bean	18	46%	1	2%
Roasted chaff	3	8%	0	—
Roasted bean	1	2%	0	—

Table III shows that the positive reactions were almost limited to the raw chaff and raw bean extracts and were predominantly found in the allergic group. Almost all pseudopods from the raw bean, roasted bean and roasted chaff were in subjects having positive reactions to raw chaff. To confirm that the reaction to raw bean was not due to contaminating raw chaff, several beans were carefully separated by dissection from their outer coverings and an aqueous extract was prepared. This extract, when tested by passive transfer against the serum of an individual who was known to react on direct skin test to the regular raw bean extract, again gave a positive reaction.

The significance of the fact that a worker or any close member of his family suffered from asthma, hay fever, sinusitis, eczema, hives or bronchitis unrelated to contact with coffee was studied. Of subjects who were allergic to coffee by history, and who also had wheals with pseudopods on skin testing, 20 out of 27, or 74%, had a positive personal or family history. In contrast, of 65 subjects who neither had an allergic history to coffee nor pseudopods on testing, the personal or family history for the above conditions was positive in only 31, or 48%. The importance of the previous personal or family history was brought out further by analysis of the reactions in individual cases as shown in Table IV. Although the groups are small, they do suggest that an individual who has suffered from asthma, bronchitis or, to a lesser extent hay fever, is very likely to develop allergic symptoms to coffee. This is less likely if only the family history is positive. The presence of two of these three factors in his personal history, or one in his personal and one in his family history, results in an almost 100% incidence of coffee allergy.

DISCUSSION

The results of this investigation have confirmed the presence of allergy to raw coffee in a selected group of workers. As the total worker personnel approximates 400, at least 10% have developed allergic symptoms. This is a minimum, as not all the workers were questioned or skin-tested, and in addition, some have had negligible contact with the raw coffee area. Although sensitization to both raw chaff and green bean has been demonstrated, there is little likelihood of dust being produced from the bean itself. It is probable that one or more common antigens are shared by both the raw chaff and raw bean, thus giving positive skin tests to both, although only the chaff dust was responsible for the sensitization. In view of the incidence of symptoms, the chaff is clearly a potent allergen. It is of interest that none of the allergic personnel,

TABLE IV.

	Asthma		*Bronchitis*		*Hay fever*		*Sinusitis*		*Hives*		*Eczema*	
Number of subjects in all groups with a personal history of	7		10		7		14		5		6	
Number of above who are allergic to coffee by history	6	85%	9	90%	5	71%	7	50%	2	40%	1	17%
Number of subjects in all groups with a family history of	13		13		9		3		4		5	
Number of above who are allergic to coffee by history	7	54%	9	69%	1	11%	1	33%	3	75%	2	40%

with one possible exception, had any symptoms associated with taking coffee as a beverage. The negative skin tests to the roasted bean indicates that the antigenic structure was changed during the roasting and the finished product would be similarly altered and rendered non-allergenic.

Methods of reducing the content of chaff dust in the air are at present under study, as is the possibility of desensitizing those personnel with the more severe symptoms. Employment in the future of workers who do not have any previous history of asthma, hay fever or bronchitis will also reduce the incidence of clinical allergy. Further work is at present in progress to define the chemical moieties in the chaff responsible for its antigenicity.

SUMMARY

Allergic reactions to the chaff of the raw coffee bean have been demonstrated. These mainly take the form of coryza, dermatitis, lacrimation and bronchial obstruction, and are due to contact with chaff dust in the air and respiratory passages. Methods of control are under study.

We wish to thank Mrs. Judith H. Rollins, who prepared the extracts used for skin testing.

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THE CONTROL OF PULMONARY VENTILATION IN PHYSIOLOGICAL HYPERPNEA*

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THE IDENTIFICATION of the factors responsible for the control of pulmonary ventilation has been a subject of interest to physiologists for at least one hundred years. Research in this field has contributed a great deal to our knowledge of respiratory physiology. Most of the evidence upon which this knowledge is based is concrete and indisputable, although some of it is circumstantial and indirect. However, a great deal of speculation has been, and is, accepted as fact; and some illogical conclusions have been deduced from experimental data. Much of the literature on the subject is contradictory;[41] and it is unfortunate that after 50 years of intensive investigation, our knowledge of this important subject is still far from complete.

THE CLASSICAL THEORY AND ITS DISCREPANCIES

It is generally stated that the control of pulmonary ventilation under normal physiological conditions is carried out through the action of carbon dioxide on the respiratory centre. This theory, although still unproved, was firmly established by Haldane,[100-104] who demonstrated beyond doubt that carbon dioxide (CO_2) is a powerful respiratory stimulant. Since the time of Haldane's classical work, the evaluation of experimental data and the evolution of thought have tended to support the hypothesis that the tension of carbon dioxide in the arterial blood ($paCO_2$) is the major factor controlling the volume of pulmonary ventilation.[12, 46, 56, 57, 95, 101, 189] It has been shown that the arterial tension of oxygen (paO_2) and the pH of the arterial blood may play a role in the increase in volume of pulmonary ventilation under certain abnormal conditions;[102, 142, 150] and it has been suggested that they play a significant role in the normal physiological state.[13, 83, 84, 95, 120, 189] For the past 30 years assessment of the role of the classical stimuli, pCO_2, pO_2 and pH, has dominated the thinking of the majority of physiologists; and there has been considerable controversy concerning the importance of each.[6, 12, 32, 45, 46, 83, 84] It has been recognized by a few that the theory is deficient in many respects,[41] but much of the literature tends to emphasize the desirability of integrating experimental data with the classical hypothesis. Although minor modifications have been proposed, the basic tenets of the classical theory are still generally accepted despite many observations which tend to discredit it. The evidence in favour of this theory has been reviewed recently by Gray,[95] who has quantitated the ventilatory response to artificially induced changes in these three stimuli. His thesis is that the normal physiological stimulus of the respiratory centre is the arterial tension of carbon dioxide, aided by changes in pH when these occur, and by hypoxia on occasion. He has derived an equation which quantitates and predicts the respiratory response to these stimuli when changes are induced in them either singly or in combination. Minor modifications of Gray's equations have been proposed,[45, 47, 135] but little attention has been directed to an assessment of the adequacy of the theory as a whole.

Most of the investigative work on the problem of identifying the factors which control pulmonary ventilation has been concerned with the respiratory response to artificially induced changes in $paCO_2$, paO_2 and arterial pH in resting subjects. An induced change in one of these stimuli certainly evokes a respiratory response, but the assumption that these

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