Approximately one third of laboratory animal workers have occupational allergy to animal danders, and a third of these have symptomatic asthma. Sensitization generally occurs with the first 3 years of employment, and risk factors include atopic background, as well as job description as it relates to the intensity of exposure. A symptomatic worker can reduce allergen exposure with personal protective devices. A laboratory can further reduce exposure with generally available equipment, such as laminar flow caging, and procedures, such as frequent wet washing of vivaria and careful maintenance of ventilation systems. It is advisable to institute periodic medical screening of all laboratory animal workers with questionnaires and allergy skin testing in addition to providing them with training programs to reduce personal exposure. (J Allergy Clin Immunol 1998;102:99-112.)

Laboratory workers who are in regular contact with furred animals commonly develop sensitivity to those animals. As such, laboratory animal allergy represents a major occupational illness to the thousands of technicians, animal caretakers, physicians, and scientists whose work requires such exposure. Allergy to rats and mice is the most common clinical problem, primarily because these animals are the most widely used in medical research. Estimates of the prevalence of laboratory animal allergy have varied considerably in different studies, at least in part because of differences in the diagnostic techniques that have been used. For rats, prevalence rates have ranged from 12% to 31%.[1-5] The prevalence of mouse allergy is overall very similar, ranging from 10% to 32%.[2,4-6]

In addition to rats and mice, allergic reactions will occur upon regular exposure to virtually all furred animals. Although allergy to other animals in the workplace is less common overall than allergy to rats and mice, this is primarily because these other animals are used less often, not because they are inherently less allergenic. Allergy to guinea pigs, rabbits, hamsters,

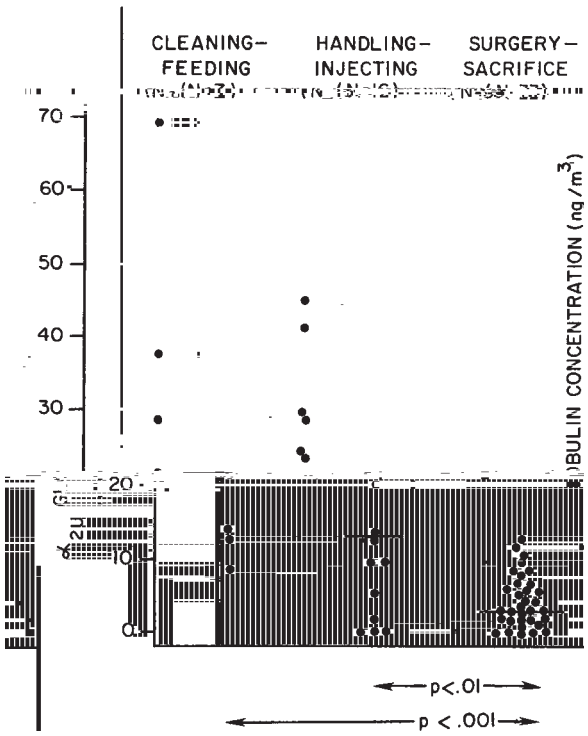
and aerodynamic properties. Although rodent allergens can certainly be present in household environments, they have been studied primarily in laboratory settings. Cat and dog allergens, on the other hand, have been characterized best in home environments. Information on total airborne allergen levels and particle size distribution are available for most of the allergens, although variations in sampling devices and assay methods make data from different centers difficult to compare. In addition, the clinical relevance of these levels has only been explored in detail for rat and cat allergens. These factors make the interpretation of airborne levels quite difficult, especially when making decisions about occupational risk and the efficacy of various interventions.

In general, animal allergens tend to be carried on relatively small particles. These particles can remain airborne for extended periods and are easily respirable. Airborne mouse allergen has been shown to reside on particles ranging from 3.3 to 10 μm in one study[33] and from 6 to 18 μm in another study.[8] Ohman et al.[33] also found a particle size distribution ranging from 0.43 to 3.3 μm in rooms that did not contain mice.

Airborne mouse allergen levels in the Ohman study ranged from 16.6 to 563 ng/m^3 in rooms with mice and from 1.2 to 2.7 ng/m^3 in rooms without mice, with the highest levels being associated with direct mouse contact. In another study levels ranged from 1.8 to 825 ng/m^3 and varied with both the number of mice and the degree of work activity in the rooms.[34] An additional study demonstrated higher allergen levels in rooms with male mice compared with rooms with female mice (Mus m 1, 13,050 pg/m^3 versus 317 pg/m^3, respectively).[35]

Airborne rat allergens are carried on particles ranging from less than 1 μm to more than 20 μm, with the majority of allergen on particles less than 7 μm in diameter.[36,37] It has been shown that a significant proportion of the airborne allergen remains airborne 15 to 35 minutes after disturbance. Levels of airborne rat allergen have been studied in a variety of settings, and it is clear that exposure is highly dependent on the type of activity being performed, with cleaning and feeding being associated with the highest levels of exposure (Fig. 1).[38,39]

Studies have also been performed in individuals allergic to rats to determine the levels of exposure that would be expected to induce symptoms. In one study of 12 volunteers allergic to rats, all subjects experienced nasal symptoms, and five experienced a decrease in FEV_1 of greater than 10% during a 1-hour exposure with airborne Rat n 1 levels ranging from less than 1.5 to 310 ng/m^3.[39] In a follow-up study exposures to high allergen levels (cage cleaning, mean Rat n 1 = 166 ng/m^3) were compared with exposures to low allergen levels (quiet sitting in a rat vivarium, mean Rat n 1 = 9.6 ng/m^3) in 17 subjects.[6] A clear dose response was demonstrated, with both upper and lower airway responses being dependent on airborne allergen levels.



. 1. Task-related airborne rat allergen (Rat n 1) concentrations in a laboratory facility. (From Eggleston PA, Newill CA, Ansari AA, Pustelnik A, Lou SR, Marsh DG, et al. Task related variation in airborne concentrations of laboratory animal allergens: studies with Rat n 1. J Allergy Clin Immunol 1989;184:L347-52).

However, because of variations in response, it was not possible to determine a threshold or *safe* allergy level for an asthmatic response.[6]

Much less information is available about other laboratory animal allergens. Airborne guinea pig allergens have been measured with RAST inhibition that demonstrated urine and pelt allergen levels of 17 and 90 ng/m^3, respectively.[19] Forty percent of the guinea pig allergen was found on particles less than 0.8 μm in diameter, which remain airborne for long periods and are capable of depositing in small airways.

Cat and dog allergens have been best studied in nonlaboratory settings. Cat allergen has been shown to be carried on particles that range from less than 1 μm to greater than 20 μm in diameter. Although estimates have varied, it is clear that at least 15% of airborne cat allergen is carried on particles less than 5 μm in diameter.[40,41] Less data are available on dog allergen, but preliminary evidence suggests that it is distributed very much like cat allergen, with about 20% of airborne allergen being carried on particles less than 5 μm in diameter.[42]

The risk factors for laboratory animal allergy relate to individual susceptibility and environmental expo-

. Relationship of skin tests and RAST to laboratory animal allergens to work-related symptoms

. Relationship of atopic status to reported work-related symptoms, skin tests, and serologic tests to laboratory animal allergens

	*		(%)		(%)			(%)
Cockcroft et al.[51]	Yes	70	21 (30)	70	21 (30)	17	—	—
	No	109	4 (4)	109	8 (7)	4	—	—
Platts-Mills et al.[48]	Yes	71	17 (24)	71	32 (45)	—	71	30 (42)
	No	108	14 (13)	108	10 (9)	—	108	10 (9)
Beeson et al.[45]	Yes	110	10 (9)	—	—	—	—	—
	No	202	3 (1)	—	—	—	—	—
Slovak and Hill[44]	Yes	35	20 (57)	35	13 (37)	—	—	—
	No	111	28 (25)	111	6 (5)	—	—	—
Venables et al.[46]	Yes	56	27 (48)	56	13 (23)	19	56	17 (30)
	No	73	29 (40)	73	4 (5)	12	73	14 (19)
Agrup et al.[49]	Yes	22	16 (73)	22	13 (59)	—	—	—
	No	38	14 (37)	38	6 (16)	—	—	—
Cullinan et al.[3]	Yes	88	36 (41)	88	19 (22)	—	—	—
	No	150	34 (23)	150	2 (1)	—	—	—
Aoyama et al.[4]	Yes	2090	772 (37)	—	—	—	—	—
	No	3551	532 (15)	—	—	—	—	—
Gross[50]	Yes	86	34 (40)	—	—	—	—	—
	No	313	25 (8)	—	—	—	—	—
Total	Yes	2628	953 (36)	342	111 (32)		127	47 (37)
	No	4655	683 (15)	589	36 (6)		181	24 (13)

*Defined as a history of seasonal symptoms plus one or more positive skin prick test responses to inhalant allergens.

sure. Individual susceptibility has been examined carefully in multiple epidemiologic studies. At this time, methods to predict risk are well established and can be easily applied in workplace settings. Environmental exposure assessment, on the other hand, is more difficult, and the techniques are both less widely available and less clearly supported by research data.

Individual susceptibility has a genetic basis. The term *atopy* was coined in 1923 by Coca and Cooke[43] to describe the combination of a genetic predisposition to produce a prolonged IgE antibody response to environmental allergens and the resulting chronic conditions of allergic rhinitis, asthma, and eczema. The atopic status of a worker may be determined by asking for a history of allergic rhinitis, asthma, or atopic eczema either as chronic conditions that are not related to work or that have been related to previous jobs with animal exposure. Because atopy is familial, a family history of similar diseases in first-order relatives (parents, siblings, and children) also indicates an increased predisposition to atopy. Detection of IgE antibody to environmental allergens, either by using immediate wheal and flare skin tests or serologic tests for specific IgE, is a strong indicator of atopy; however, this may or may not be associated with an elevated total IgE.

What of the relationship of work-related symptoms and the presence of positive skin test or in vitro test responses for specific IgE antibodies? As shown in Table II, the relationship is relatively close. In seven studies[6,44-49] the concordance between skin tests and symptoms was 81% (790 of 971). However, 57% of persons with positive skin test responses did not report symptoms, whereas 62% of persons with symptoms had positive skin test responses. Thus the positive pre-

. Relationship of job description to symptoms of lab animal allergy, skin test responses, and RAST results

			(%)	(%)	(%)	(%)
Platts-Mills et al.[48]	Handlers	54	—	7 (13)	9 (19)	31 (58)
	Users	125	—	15 (12)	8 (6)	37 (30)
	Unexposed	34	—	0 (0)	0 (0)	6 (18)
Cockcroft et al.[51]	Handlers	52	17 (33)	—	—	—
	Users	127	32 (25)	—	—	—
	Unexposed	29	0 (0)	—	—	—
Schumacher et al.[6]	Handlers	33	12 (36)	—	—	—
	Users	98	25 (26)	—	—	—
	Unexposed	40	2 (5)	—	—	—
Venables et al.[46]	Handlers	42	19 (45)	—	—	—
	Users	80	32 (40)	—	—	—
	Unexposed	16	9 (56)	—	—	—
Slovak and Hill[44]	Handlers	19	8 (42)	—	—	—
	Users	101	34 (34)	—	—	—
	Unexposed	26	6 (23)		—	—
Total	Handlers	148	56 (38)	7 (13)	9 (19)	31 (58)
	Users	404	123 (30)	15 (12)	8 (6)	37 (30)
	Unexposed	116	17 (15)	0 (0)	0 (0)	6 (18)

. Relationship of duration of exposure and presence of IgE- and IgG-specific antibodies to murine antigens

			(%)	(%)
Schumacher et al.[6]	5	47	1 (2)	0 (0)
	16	63	14 (22)	55 (87)
	30	50	12 (24)	45 (90)

dictive accuracy of a positive skin test response was 43%. Ninety-two percent of workers with a negative skin test response reported no symptoms, giving a negative predictive accuracy of 92%. RAST and symptoms agreed in 93% of cases. The frequency of positive skin test responses varies widely among these reports, and it can be questioned whether each investigator used an active allergen extract for testing. For example, compare Beeson et al.,[45] who found that only 6% of workers had a positive skin test response, with Slovak and Hill,[44] who found a rate of 55%.

The importance of a history of atopy as a risk factor for laboratory animal allergy has been examined in nine studies (see Table III). In these reports atopy is defined either by a positive skin prick test response to at least one of a panel of common inhalant allergens other than laboratory animal allergen,[3,44-46] by a history of allergic rhinitis or asthma,[4,50] or by a combination of history and skin test responses.[48,49,51] Despite different criteria for atopy and the fact that several of the studies[4,48,49,51] evaluated had selected populations, the frequency of atopy averaged 36% in agreement with that found in the general population.[52,55] A history of work-related symptoms and objective evidence (positive skin test responses and RAST results) were equally useful in predicting symptoms reported by 36% of atopic workers and 15% of nonatopic workers (odds ratio, 3.35). The relationship of atopy to positive skin test responses and RAST results to laboratory animal allergens was similar, with odds ratios of 6.86 and 3.93, respectively. It is also obvious that both the frequency of laboratory animal allergy, whether defined by symptoms, skin tests, or RAST, varied widely between the various studies. For example, Venables et al.[46] found a high prevalence (48%) and a marginal relationship to atopy, whereas Cockcroft et al.[51] found a prevalence of 30% and a strong relationship to atopy. These variations were likely due to differently worded questions and different skin testing and RAST techniques, but the variability of the findings together with the modest association between atopy and laboratory animal allergy has led some to conclude that preemployment screening for individual susceptibility is of limited value. Alternatively, a study by Rothman et al.[54] suggests that atopic workers are at increased risk for laboratory animal allergy. Screening for atopy is helpful in alerting potential workers to the risk of animal exposure and educating them to take protective measures to prevent the development of laboratory animal allergy.

Environmental animal allergen exposure may be assessed by job description, by the percentage of time with direct exposure to animals, and by the specific tasks performed with the animals.

A useful categorization of job description, which was proposed by Cockcroft et al.,[51] is shown in Table IV. Handlers include workers who are responsible for cage cleaning and for the feeding and care of the animals. Users include persons involved in experimental use of the animals, such as technicians, students, and

. Preventative measures and interventions

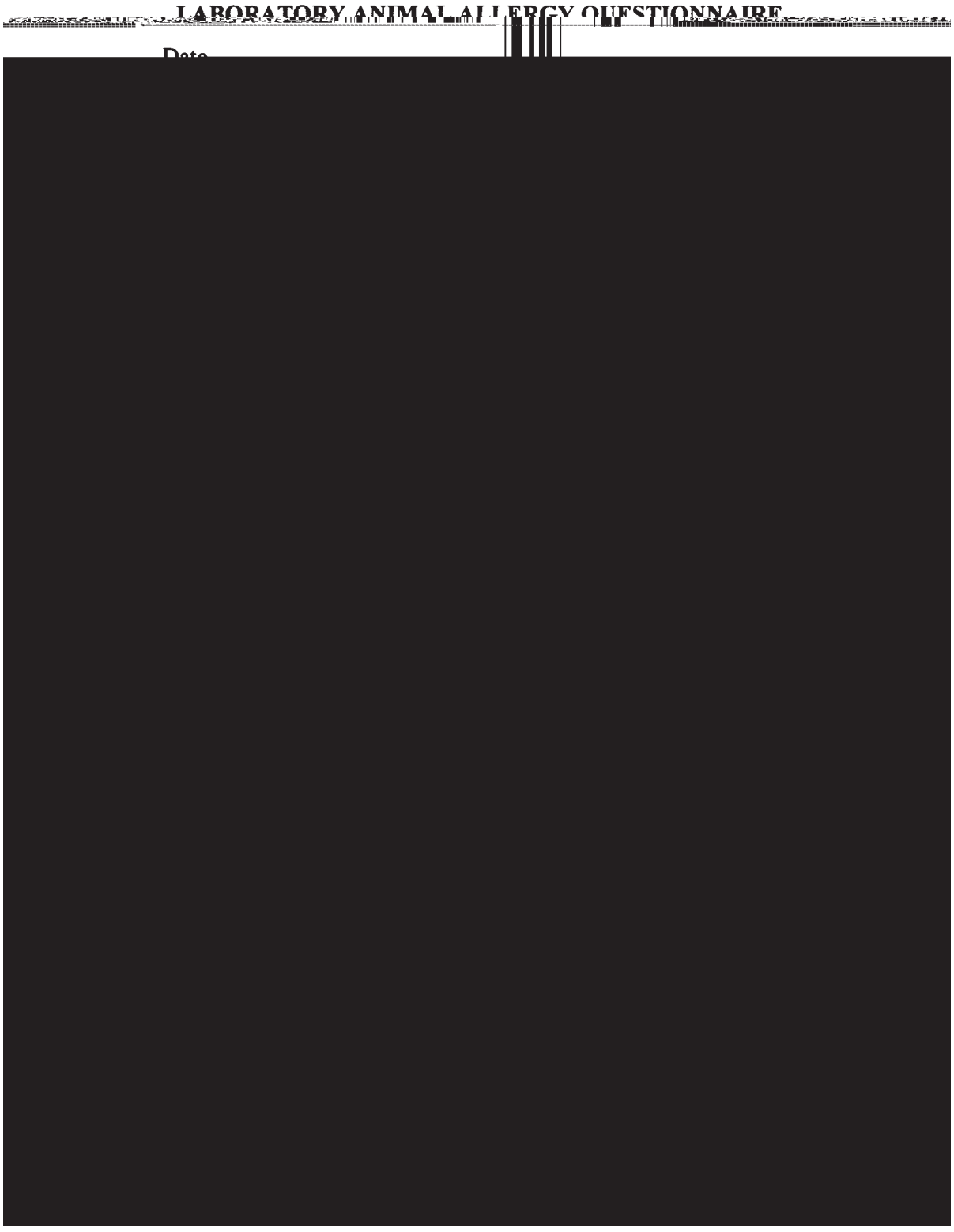
I. Screening and surveillance programs	
1. Questionnaires	Determine presence of nonwork-

investigators; these are persons who are in contact with the animals on a more intermittent basis. Unexposed workers include secretaries and administrators who have no direct contact with the animals but who have an office in the same building.

This classification predicts that those with the greatest exposure to the animals will be the most likely to become sensitized and to have symptoms related to work exposure. As seen in Table IV, this prediction is generally supported by epidemiologic studies. Compared with the rate of symptoms in unexposed workers, handlers (odds ratio, 3.56) and users (odds ratio, 2.31) have an increased frequency of symptoms. On the other hand, it is also important to note that many people who are not exposed have symptoms. Work-related symptoms were reported by up to 56% of workers with no direct contact with the animals.[46] A recent epidemiologic study of Dutch laboratory workers used a combination of area allergen assays and workers diaries of activities in these rooms to classify exposure. Statistical modeling allowed the investigators to demonstrate a clear relationship between sensitization to rat aller-

is dependent on the rate of allergen production, which is a function of animal density (numbers of animals present), and the rate of allergen removal from the air, which is a function of ventilation. To achieve a substantial reduction in allergen exposure in an area heavily populated with laboratory animals, frequent contact with the animals by lab-

Laboratory animal allergy is a common occupational hazard. Symptoms range from mild skin irritation to severe asthma. Many of the important allergens causing sensitivity have been identified and purified. The allergens are often carried on small airborne particles that remain suspended for extended periods, which makes them easily respirable. Methods to quantitate exposure have been developed, and certain tasks such as cage cleaning or surgery are associated with higher


LABORATORY ANIMAL ALLERGY QUESTIONNAIRE
Date

acility? ☐ Yes ☐ No 2 Did you work with laboratory animals prior to employment at this

If yes, how long? ____ years What type of animals?

any of the following tasks while working with animals: Do you use or wea

ses	☐ Yes	☐ No	Protective Eye Glas
	☐ Yes	☐ No	Mask/Respirator
	☐ Yes	☐ No	Lab Coat
	☐ Yes	☐ No	Gloves

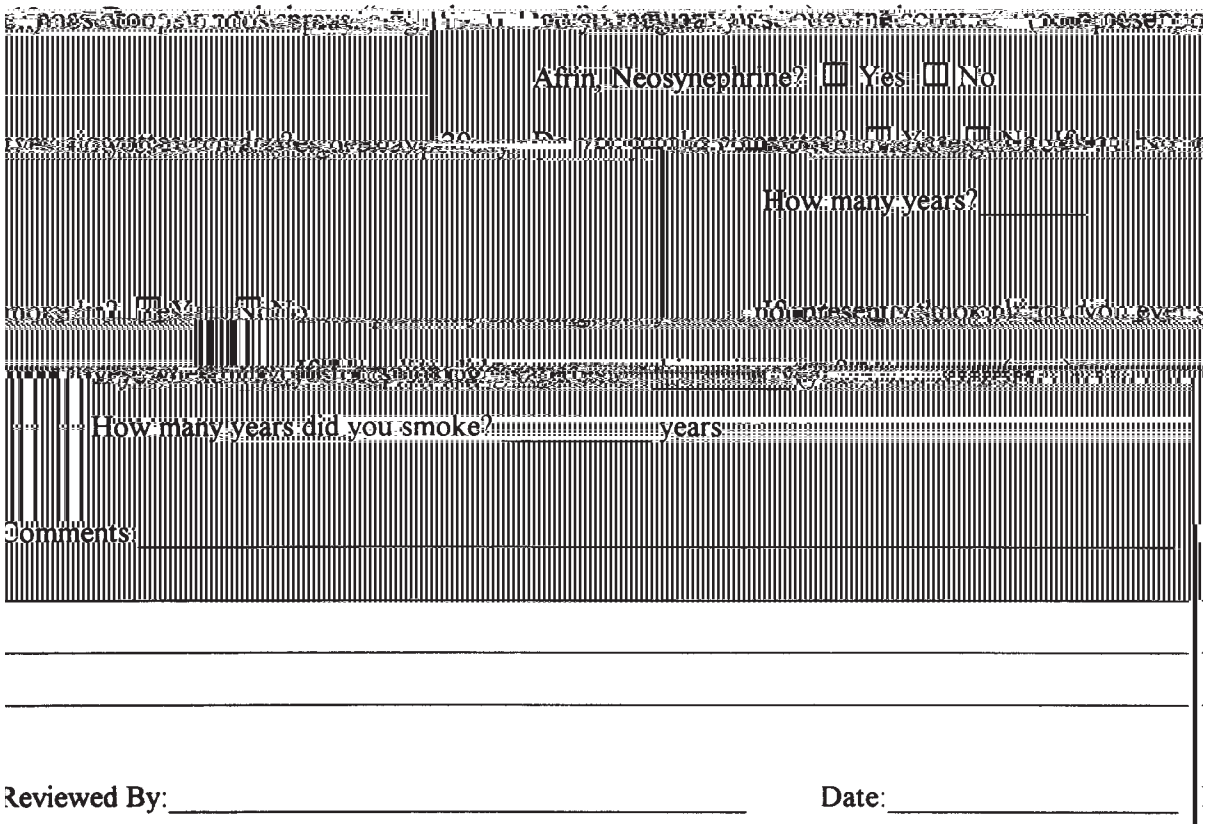
INFORMATION HOME ENVIRONMEN

[redacted]

If yes, please list illnesses:_____

_____

18. Do you take blood pressure medication(s)? ☐ Yes ☐ No



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Reviewed By:_____ Date:_____