Communications

p = NS.) If the patient population were doubled and this trend continued, the difference would be statistically significant.

Despite the possible bias introduced by patient selection and the limited number of patients, articles such as that of Wilson et al demonstrate the potential importance of clinical presentation subgrouping and should be encouraged.

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Erratum

To the Editor:

I wish to inform you of an error in my part in my article in the July, 1982 supplement to Chest. On page 165, footnote, the velocity (V) was omitted from the Poiseuille equation, which should read:

\[ \Delta P = \frac{V^2 l}{\pi r^4} \]

where V is velocity of flow. All other symbols are correct as printed.

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Calcium Homeostasis in Asthma

To the Editor:

The recent editorial, "Calcium channel antagonists in coronary artery spasm and bronchial spasm" by Robert G. Townley, (Ches and may 1982; 82:401) posed a variety of interesting issues. Inferring among them was the potential role of calcium homeostasis in coronary asthma. In 1979, we reported an increased sensitivity to extracellular calcium (Ca\(^{++}\)) in airways smooth muscle following in vitro anaphylaxis in the guinea pig. This post-anaphylactic acquired sensitivity to (Ca\(^{++}\)) was based upon the finding of an increase in resting isometric smooth muscle tension assessed in a Ca\(^{++}\)-free medium to which (Ca\(^{++}\)) was cumulatively restored. Preliminary experiments indicated that incubation in putative "anaphylactic" mediators was not the cause. While the responsible cellular homeostatic mechanism is not defined, this work suggested: normal airway smooth muscle + anaphylaxis → acquired Ca\(^{++}\) defect (eg membrane) → sensitivity to (Ca\(^{++}\)) → increased basal muscle tone.

Since that time, other published observations have supported this concept. Measuring calcium efflux rate constants by the method of Hurwitz and Joiner, 1 Rodger and Martorana found tracheal muscle from ovalbumin-sensitized guinea pigs to exhibit a definite change in the utilization and binding affinities of activator calcium. Similarly, employing Ca\(^{++}\) release from microsomal fractions of sensitized guinea pig lungs, Hedman reported a small but statistically significant difference in Ca\(^{++}\) microsomal binding in comparison to control animals.

Collectively, these observations should be viewed as preliminary findings. They do nevertheless suggest some acquired defect or disturbance in Ca\(^{++}\) membrane flux or intracellular Ca\(^{++}\) homeostasis in airway smooth muscle following immunologic activation since it appears well established that transcellular fluxes of calcium are critical in influencing basal cellular metabolism and cellular response to membrane stimulation. It may be of more than passing interest that such primary disturbance of cellular calcium metabolism is also speculated to be an important factor in the pathogenesis of human and animal hypertension, implying a basic similarity in these two smooth muscle disorders. In asthma, a liability in Ca\(^{++}\) homeostasis could account for an alteration in the threshold to specific agonist contractile processes, as well as the effect of nonspecific processes which presumably must also increase free myoplasmic calcium to the contractile-regulatory processes in smooth muscle. Concurrently myorelaxation may also be affected. We believe the concept of a calcium-modulating defect could be fundamental to the genesis of human asthma.

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To the Editor:

The essential issue raised by Dr. Weiss is the role of calcium homeostasis in bronchial asthma. A primary mechanism common to all of the neurotransmitters and physical factors that elicits smooth muscle contraction in variant angina or asthma is an increased free calcium in the cytoplasm. Thus, all muscle contracts and relaxes in association with increases and decreases of intracellular free calcium. In this regard, various neurotransmitters that can evoke coronary or bronchial spasm could do so through a common mechanism of activating receptor-operated calcium channels, whether these channels be activated by histamine, serotonin or acetylcholine receptor-operated calcium channels. Thus, such a mechanism would result in increased intracellular cytoplasmic calcium which initiates the contraction response. The cytoplasmic concentration of free calcium appears to be the primary intracellular signal controlling smooth muscle tissue tone.

However, the observation reported by Dr. Weiss that some acquired defect or disturbance in calcium membrane flux or cellular calcium homeostasis in airway smooth muscle following immunologic activation is still highly speculative. Dr. Weiss has reported that calcium hypersensitivity occurs in airway smooth muscle following anaphylaxis. Thus, it is interesting to speculate that the
sensitization of the airways in the asthmatic patient could somehow result in a defect in calcium membrane flux or intracellular calcium homeostasis in the airway smooth muscle. This, however, would not explain nonatopic asthma and would be difficult to correlate with asthma and the persistent airway reactivity to mediators such as acetylcholine and histamine during periods when individuals with asthma are not exposed to specific antigens or allergens. Nevertheless, increased airway reactivity to methacholine has been reported following sensitization to Acanthocephalus in monkeys and dogs as reported by Patterson et al. and Kepron et al. More importantly, increased airway reactivity to histamine or methacholine does occur following antigen challenges that are associated with late bronchial responses.

Since much of the information derived with respect to smooth muscle pharmacology may be relevant to calcium ion movement and mast cell mediator release, the relationship between airway hyperreactivity and mast cell sensitization deserves further investigation. In this regard, the requirement of calcium for the anaphylactic release of chemical mediators from target cells such as mast cells or basophils is well established.

Since calcium is a common mediator for the various neurotransmitters and physical factors that evoke the bronchial constriction and mast cell mediator release, a defect at the level of cellular calcium regulation may be linked to the etiology of bronchial hyperreactivity in asthma.

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Concealed Ventricular Parasystole Exposed by Abrupt Cessation of Pacing

To the Editor:

I should like to comment on the article by Drs. Castellanos and Castillo in the September, 1982 issue of Chest. The evidence these authors present to support their thesis that they are dealing with a concealed parasystolic ventricular pacemaker is both inferential and very soft. The one bit of hard and convincing data that should be presented is missing. In this article, the authors describe the appearance of an alleged parasystole upon cessation of artificial electronic ventricular stimulation. To be completely convincing, they should have once again stimulated the patient electrically and then allowed the so-called parasystolic pacemaker to come out again after stopping stimulation. If we could observe the idioventricular pacemaker to march through the stimulated area and come out again when the stimulated area was stopped, and if we could observe the idioventricular pacemaker to maintain a parasystolic interval even though it would not appear because of an exit block during ventricular stimulation, then we could agree with the authors that there was indeed a parasystolic rhythm. To hide behind the conclusion that this so-called parasystole represents an "intermittent arrhythmia" is a cop-out. This is like saying that any ectopic arrhythmia that intermittently appears alongside another type of dominant cardiac rhythm represents an intermittent parasystole that is constantly being reset by non-parasystolic QRS complexes.

The definition of a ventricular parasystolic pacemaker, whether concealed or not, as shown by Katz and Pick and others, is now and has always been associated with three criteria: first and foremost, there is a constant RR interval of the parasystolic pacemaker that can be measured out at a regular rate irrespective of the dominant rhythm even though, at times, the parasystolic QRS complex may be concealed because there is an exit block due to a refractory period of the dominant rhythm. The second criterion is one of non-fixed coupling with the dominant rhythm. The third criterion is the presence of fusion beats. Fusion beats, at times, might not be present if both the parasystolic and dominant rhythms arise close to the same point in the heart. One should still look for two out of the three criteria prior to concluding the presence of parasystole. In this particular case, however, only one of the three criteria is present, namely: non-fixed coupling.

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To the Editor:

Dr. Breall’s points are well taken. We did observe that the parasystolic cycle length remained unchanged during the periods of pacing. What we wanted to emphasize, as done by Nau et al., was that the exit block in "concealed" parasystole is different from the usual types of exit conduction disturbances occurring in ventricular parasystole. The latter, usually type 2 (Mobitz) or type 1 (Wenckebach), do not depend so much on concealed penetration, in the ventricular parasystolic junction, of entering impulses. Thus considered "concealed" parasystole is but a variant of continuous parasystole with exit block. Presently, the diagnosis of parasystole has been extended to include a variety of arrhythmias which do not fit "classical" parasystole. These authors have observed that the zone of protection could be traversed by subthreshold, electronic depolarization (not by full action potentials) to produce: a) "modulated" parasystole (time-dependent variations in parasystolic cycle length); b) "trained" ("captured") parasystole; c) "reentrant" ("reflected") parasystole with fixed, and variable, coupling intervals; and d) "pacemaker annihilation" ("extinction") of parasystolic activity. These findings may be construed to indicate that the spectrum of parasystolic activity is much wider than what is classically accepted.

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