

Environmentally Triggered Cardiac Disease

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Abstract: Twelve highly selected patients with nonarteriosclerotic cardiac arrhythmias and/or chest pain refractory to medication and having symptoms related to smooth muscle sensitization were studied in a rigidly controlled, relatively fume- and particle-free environment. The majority of signs and symptoms cleared in 10 patients without medication while under environmental control, and in 10 of the 12 patients all arrhythmias were reproduced with controlled, repeated individual-blind and double-blind incitant challenges. Blood abnormalities occurred in the complement and T-lymphocyte systems.

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Environmentally triggering agents for arrhythmias of nonatherosclerotic heart disease, excluding infectious agents, have rarely been reported. However, isolated case reports of arrhythmias triggered by massive environmental exposure to food¹ or chemicals² have appeared. Randolph's meticulous description of the environmental maladaptation syndrome³ and the author's involvement with several cases of apparent triggering of arrhythmias by environmental incitants has led to an in-depth study of the subject.

MATERIALS AND METHODS

Part I discusses case reports that aroused the author's suspicions.

Part II shows a controlled study of nonatherosclerotic heart patients with associated symptomatology related to smooth muscle sensitization who had unexplained and uncontrolled arrhythmias and chest pains.

Part I

Suspicions as to the clinical importance of chemical air pollution on the cardiovascular system were first aroused when the author observed a 38-year-old physician who had a broad spectrum of symptoms related to smooth muscle sensitization, which included gastrointestinal involvement resulting in bloating, gas, belching, and cramping after each exposure to the fumes from an X-ray developer. He also experienced urinary urgency, chest tightness and peripheral arterial spasm. When he was forced to stay in the area of the developer, the symptoms progressed from mild uneasiness to shortness of breath and frequent premature ventricular contractions (pvc's). Withdrawal from this environment resulted in cessation of the arrhythmias while on at least 20 separate occasions re-exposure resulted in the pvc's.

Suspicions of a more than casual relationship between environmental incitants and the triggering of arrhythmias were further aroused when the author had an opportunity to resuscitate a 68-year-old male truck driver in ventricular fibrillation. The patient was hypotensive for two days, requiring vasopressors. When he was out of shock, of vasopressors, and satisfactorily recovering, he was fed. Immediately after eating, the patient developed bloating accompanied by pvc's and a blood pressure drop. After this happened on three different occasions, with each instance appearing life threatening, an ecological history was obtained. This revealed that during the patient's lifetime, every time he ate milk or eggs, the aforementioned sequence of events occurred. At age seven the patient had been in a coma for two weeks and, upon awakening, he was placed on an elimination diet consisting solely of potatoes, which resulted in recovery. Throughout life he went on this avoidance diet to clear symptoms whenever he experienced bloating and irregular heart beats. In addition, during his childhood a similar sequence of events would occur when the patient was exposed to gasoline fumes. This reaction caused some difficulties during the patient's trucking career, since frequently he would have to stop by the roadside and get away from the truck to allow his symptoms to clear. Avoidance of offending foods and inhaled chemicals subsequently allowed an uneventful recovery.

Further suspicions were aroused when a 32-year-old female was seen with uncontrolled ventricular arrhythmias refractory to drugs. This patient was clear after five days fasting in an environmentally controlled room. On subsequent individual transient exposure (15 seconds to two minutes) to ambient chemical fumes such as natural gas, chlorine or floor cleaner reproduction of arrhythmias occurred immediately.

Since there appeared to be a more than casual relationship between food and chemical susceptibility and the cardiac arrhythmias, a controlled study was initiated.

Part II

From this cardiovascular surgeon's practice 12 consecutive adult patients (ages 12-45) with unexplained and uncontrolled cardiac arrhythmias, having nonatherosclerotic cardiac disease and having multi-symptomatology related to smooth muscle sensitization, were studied. Arteriosclerosis was ruled out by the usual methods of electrocardiograms, exercise stress tests, and cardiac catheterization. Competent cardiologists saw the patients initially before instituting environmental control and agreed that the patients had arrhythmias of unknown etiology.

Detailed lifelong ecological histories were taken by Randolph's⁴ method in a search for other parts of the environmental maladaptation syndrome. Specific symptoms complexes and recurrent inflammations such as sinusitis, laryngitis, hoarseness, bronchitis, cystitis, spastic colon, enteritis, colitis, migraine or vascular headaches, myalgia, arthritis, arthralgia, depression, or phlebitis of unknown etiology were recorded. To establish cause and effect, an attempt was made to create an environment that was as free as possible from inhaled and ingested contaminants where triggering agents could be clearly defined. This was done in the following manner:

Rooms were specially constructed with walls made of glass and cement blocks. The blocks were painted with a low outgassing paint that was allowed to dry from six months to one year so as to eliminate any volatile petrochemicals. Floors were terrazzo or hard vinyl and were also allowed to age; ceilings were of mineral rock; lights were fluorescent ceiling fixtures with metal shades. Beds and furniture were all metal or hard wood and void of volatile plastics. Mattresses were of chemically less treated 100% cotton with all the plastic removed. All bed linens and curtains were chemical less contaminated 100% cotton that had been laundered in nondetergent vegetable or animal soap. The heat and air conditioning were local-electric, using air blown over steel coils containing water or copper coils with aluminum fins without a blower. Filters consisting of a series of activated charcoal, alumina-oxide impregnated with potassium permanganate and hepa paper were placed at the entrance to rapidly eliminate extraneous fumes, odors, and particles that might come through the doors. Offensive synthetic or natural odors were not allowed in the rooms. The rooms were as void as possible of volatile petrochemicals and dust, as judged by susceptible humans acting as monitors and as registered on the synthetic odor detector. Smoking was not allowed. Rooms were cleaned with borax, nonchlorinated cleaner, and water.

Food used for testing was grown, transported, stored, and prepared in the relative absence of petrochemicals in the manner of Randolph.⁵ Only natural fertilizers were used to grow the food and no insect sprays, herbicides, or preservatives were used. Storage was in glass jars or nonpetroleum-based cellophane bags. Preparation was in glass or stainless steel utensils heated by electricity; the eating utensils were glass or stainless steel. Drinking water was filtered with activated charcoal to remove chlorine and pesticide residues.

All patients during the course of diagnosis and treatment were kept in the rooms for at least a 16-day period. Patients were required to remove all hair sprays, cosmetics, perfumes, and polyester clothing before entering the room and to wear chemically less treated 100% cotton. Upon the patients entrance into the rooms all medications, including anticoagulants, steroids, and anti-arrhythmic drugs, were discontinued. Once the patients reached the symptom-free basal state, they could act as their own controls. No medications were given during the stay in the unit with the exception of oral or intravenous bicarbonate of soda and oxygen. Pulses, blood pressure, temperature, bruising, petechiae, and color changes were monitored every four hours. After the patients were in a basal state free of signs (including absence of most arrhythmias, had normal pulses and a rate below 80), able to sleep all night, and had lost their hunger, challenge with single chemically less contaminated source food (source food is an individual pure food whose biological origin is known, i.e., wheat, oats, cane sugar, beat sugar, chicken, duck, turkey, etc.) was begun. The food was selected individually and randomly. In order not to miss delayed reactions, no more than four source foods were tested in one 24-hr period; none was tested closer than four hours. As many as 60 individual source foods were tested sequentially during the period in environmental control. Pulses were recorded 5 minutes before and 5, 20, 40, and 60 minute intervals after meals; and electrocardiograms were taken with the onset of any arrhythmia. The time of onset and duration of reaction after the challenge was noted; and all signs and symptoms were recorded. Testing of the next food was not begun until all previous reactions had subsided.

After totally tolerated pure foods were identified, the patients were retested with the same foods purchased from the commercial market and cooked on gas stoves in synthetic cookware. During their production and processing, commercial foods are contaminated by synthetic sprays, herbicides, preservatives, artificial colorings and sweeteners, wax and plastic wrappings, and/or other additives. Individual and accumulative reactions from one to six consecutive meals were observed and recorded.

Testing of odors was done in the following manner: Each patient was given a times exposure of 15 seconds to 60 minutes to the flames of natural gas, odor of cigarette smoke, chlorine, perfume, pine-scented floor wash, ethyl alcohol, formaldehyde, phenol, and pesticides. In addition, the patient was challenged with the fumes of common odor-producing material which the individual breathed daily in the home and work environment, such as carpet, foam pillows, and polyester clothes. Each exposure was at a distance of 30 inches with a constant flow of the vapor. All odors tested were of a double-blind nature in that neither the examiner nor patient knew the content of the container until after the test. Saline was used as a control. The following laboratory tests were performed: Complete blood count by the Coulter Model S Method; sodium, potassium, chloride, carbon dioxide, blood urea nitrogen, serum protein, calcium, glucose, uric acid, alkaline phosphate, serum glutamic oxalo-acetic transaminase, lactic dehydrogenase and serum calcium by the SMA Method; protein electrophoresis by the Helena Cellulose Acetate Method; quantitative immunoglobulins (IgE, IgG, IgA, IgM), C₃, C₄, alpha 1, antitrypsin and C-reactive protein by the Behring

Radial Immuno-Diffusion Method; total hemolytic serum complements and serum complements fractions by the Hemolysis Sheep Cells Method; prothrombin time, partial thromboplastin time, platelets, and Lee White clotting time by the Dade Reagents method; phosphorus by the Hycel Method; fibrinogen and fibrinolysins clot lysis by the Biuret Quantitative Method; fibrin split products by the Burroughs-Wellcome Method; C₁ esterase inhibitor by the Behring IEP Method; B lymphocytes and T lymphocytes by the Sheep Cell Rosetting Method. All tests were performed upon the patient's entrance into the room and at the beginning and end of testing. C₃ and C₄ were done daily during the period of fasting.

RESULTS

As shown in Table I, there were numerous associated signs and symptoms related to the environmental maladaptation syndrome occurring during the patient's lifetime. Each patient averaged more than ten distinct recurrent signs and symptoms.

Pt.	
1	Shortness of breath, gastric constricture, loss of peripheral pulses, bruising, sinus, GI upset, head foggy, petechiae
2	Chest tight, nose itched and burned, dizzy, hoarseness
3	Leg aches, personality change, drowsy, nausea, vomiting, tingling headache, petechiae
4	GI upset
5	Malaise, mild GI upset
6	Blue hands and feet, nonpitting periorbital and peripheral edema, depression, confusion, headache, dysuria, GI upset, petechiae
7	Headache, depression
8	Sinus, vertigo, urinary frequency and urgency, bruising, cyanosis
9	Nose runs, neck tightness, periorbital edema, petechiae
10	Headache, swelling, hives
11	Headache
12	Headache, shortness of breath

Distinctive symptomatology related to the smooth muscle systems was evident in all patients. All had long histories of gastrointestinal, respiratory, and/or genitourinary problems in addition to their cardiac problem; most had at least recent histories of vascular involvement including petechiae, spontaneous bruising, and edema.

Once under environmental control, ten patients cleared their active symptoms, including their ongoing arrhythmias, in three to ten days. Frequently, symptoms were accentuated the first two to three days. Most patients underwent withdrawals just as patients with phlebitis⁶ and vasculitis⁷ described in previous reports. Each patient initially had hunger followed by complaints of Anervousness, Ajitters, and headaches. There were observable signs of agitation, trembling, and depression. Insomnia or disturbed sleep was the rule the first night, which was followed by assorted symptoms such as nausea, diarrhea, wheezing, and/or headaches. Initial accentuation of arrhythmias was common. Backaches, sometimes excruciating, usually signaled the termination of the symptoms. At this time all significant cardiac arrhythmias and other associated signs and symptoms were gone. The patient's feeling of well being was confirmed by observable signs of animation, walking or even riding a stationary bicycle without the initiation of arrhythmias. No patient had previously been able to do this.

After testing started it became quite obvious that extra-cardiac reactions fell into three categories. The first consisted of unmistakable signs such as rhinorrhea, nasal stuffiness, hoarseness, cough, wheezing, peripheral blanching, cyanosis, swelling or loss of pulses, bruising, polyuria, fever, increased pulse rate, blood pressure decreased or elevated, petechiae, bruising, and phlebitis. The second category consisted of equivocal signs, and the third category had no observed reactions. Two and three were grouped together for statistical purposes and considered as having no observed reactions.

Ten patients clearly had their arrhythmias reproduced on at least three separate occasions. Usually, there was a sequential progression of minor signs or symptoms such as rhinorrhea, mild confusion, nose or mouth irritations, nausea, vomiting, or an uneasy feeling preceding the arrhythmias. It is evident by the data shown in Table II that many susceptibilities existed in each patient. Also, it was observed that some individual incitants would produce only portions while others would produce all the patient's original signs and symptoms. These reactions were further substantiated by the benign asymptomatic course after ingestion or inhalation of nonreactive foods and food odors plus the reproducibility of signs by retesting of reacting foods. Of the reactions occurring within the first four hours, 95% started within the first five minutes after ingestion, leaving no doubt in the minds of observing personnel and patients that there was a

direct cause-and-effect relationship. The severe reactions lasted up to 48 hours with lesser effects lasting up to five days. The moderate reactions lasted four to eight hours while the mild ones were terminated within a four-hour period. One hundred percent of the associated signs and symptoms were reproduced.

Patient	Reaction to Food	HT	Reaction to Ingested Chemical	(Dbl-blind) Inhaled Challenge	HT	(Dbl-blind) Water Positive Reaction	HT
1	5/30	5	1 meal	12/15	7	1	0
2	14/30	0	1 meal	10/15	4	1	0
3	52/68	5	2 meals	7/15	1	2	1
4	17/83	17	not tested	10/10	10	13	12
5	1/30	1	negative	0/15	0	0	0
6	96/96	10	1 meal	10/15	4	5	0
7	68/68	11	1 meal	15/15	2	13	2
8	69/90	0	1 meal	35/40	2	3	0
9	80/120	10	1 meal	20/35	6	5	1
10	12/28	12	6 meals	2/8	2	0	0
11	0/16	0	0	0/16	0	0	0
12	0/18	0	0	0/12	0	0	0

Testing for ingested chemicals resulted in symptoms and signs after the initial meal in eight patients; two patients took from two to six meals to produce signs though symptoms were reproduced at least one meal earlier.

All reactions to inhaled chemicals were observed within the first 90 minutes, and their after effects lasted up to 48 hours, although most terminated within a four-hour period. Nine patients reacted to the fumes of the flame of the gas pilot, reproducing assorted signs and symptoms in all patients and reproducing the cardiac signs in six. The most striking example was of a 33-year-old female who had a 15-second exposure to the natural gas pilot. She developed immediate dizziness, staggering, then premature ventricular contractions followed by severe leg pain and bruises over both extremities followed by bigeminy. Recovery took 36 hours.

Double-blind exposures to the various inhaled chemicals are shown in Table III. One can see the widespread involvement of susceptibilities to these chemicals; however, not shown is the fact that the transient exposures produced arrhythmias in all patients at least on two different occasions.

Patient	Saline Control	Petroleum Alcohol	Phenol	Chlorine	Mixture Pesticides	Pine-Scented Floor Wash	Formaldehyde
1	-	+	+	+	+	+	+
2	-	+	+	+	-	+	+
3	-	-	+	+	+	+	-
4	-	-	+	+	-	+	+
5	-	+	+	+	+	+	-
6	-	+	+	-	+	+	+
7	-	+	+	-	-	+	+
8	-	+	+	+	+	+	+
9	-	+	+	+	+	+	-
10	-	+	+	+	+	+	+
11	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-

Laboratory Data X Tables IV and V

Tables IV and V show a tendency for the white blood count to be depressed. Immunoglobulins generally were within normal limits. Alterations in total serum hemolytic complements were seen in eight patients. Frequently, this was due to abnormalities in several of the components, C₃'s were abnormally lower in nine patients. C₄'s were altered in only four patients, all being slightly elevated. Bleeding studies were all normal. C-reactive proteins were positive in seven of eight positive reactors. Total eosinophil counts were generally low on admission and returned to normal with time in the controlled environment. However, two

patients had initial elevation. T-cell decrease was seen in seven out of seven patients measured though one was 58%, which was near the control norm. However, the total lymphocyte count was below 1,000, probably indicating an abnormality.

Controls		50-200 cumm	10-200 mg/dl	800-1800 mg/dl	90-450 mg/dl	60-280 mg/dl	
Patients	CRP	Eosinophil	IgE	IgG	IgA	IgM	WBC
1	+	55	110	960	180	244	3,500
2	+	66	40	1100	264	156	4,800
3	+	-	370	1240	255	226	5,100
4	+	33	50	1400	285	240	6,300
5	ND	67	35	1140	304	108	4,200
6	-	33	12	1210	213	300	3,800
7	+	28	70	1060	148	80	3,500
8	ND	800	40	1000	75	91	3,000
9	+	288	115	930	250	180	2,500
10	+	70	165	790	228	188	3,900
11	-	50	50	900	300	240	5,000
12	-	60	35	1100	250	190	5,500

Control	90-100%	80-120 mg/dl	20-40 mg/dl	20-40 mg/dl	E-rosettes 65-75%	1800 ∇ 200 cumm
Patients	THSC	C ₃	C ₄	B Lymph	T Lymph	Average Number T Absolute Count
1	80	72	36	45	41	500
2	80	50	52	ND	ND	ND
3	90	92	44	ND	ND	ND
4	40	64	30	32	58	800
5	90	62	28	ND	ND	ND
6	80	50	28	40	53	750
7	60	80	48	44	39	300
8	80	60	34	40	49	712
9	90	56	37	59	48	415
10	80	69	35	61	44	309
11	90	90	35	40	70	1800
12	90	100	38	35	68	2100

DISCUSSION

Abnormal cardiac responses due to environmental stimuli have been noted by several investigators in the past. Hare,⁸ in the early 1900s, described vasoactive phenomena in patients after food challenge and showed an increased heart rate in some. In 1925 Lichtwitz⁹ probably demonstrated the first causal relationship of food and a case of angina pectoris. In the next decade numerous case reports and small series showed a direct cause-and-effect relationship between food ingestion and arrhythmias.¹⁰⁻¹⁹ Harkavy²⁰ demonstrated that some angina could be triggered by cigarette smoke. Using a semi-controlled environment, Randolph²¹ has been able to demonstrate the whole spectrum of arrhythmias in patients challenged with synthetic chemicals.

Recently, much has been written about the ill effects produced by aerosols and fluorocarbons. This may have been stimulated by Taylor's²² report of a cardiac death in a 16-year-old boy due to sniffing of the aerosol. The harmful effects of fluorocarbons were reinforced by Spizer,²³ who reported an increase in arrhythmias with an increase in length of exposure to fluorocarbons.

Certainly, Nour-Elden's studies showing that the vascular tree had an increased affinity to phenol, coupled with Yevick's²⁵ demonstration of inflammatory and fibrotic changes in the cardiovascular system of sea animals exposed to oil spills, add substantiation to the adverse effects of excess pollution on the heart. With our environment steadily becoming more contaminated by synthetic chemicals, it is important to recognize their influence in inducing disease processes. If one is not aware of the environment's specific effects on the individual, relentless disease occurs without causal realization. This was graphically demonstrated in one patient who reacted to the 12 different inhaled chemicals used daily in her physician employer's office. Had she known of the cumulative and specific sensitizing effects on her cardiovascular system, she easily could have prevented years of malaise and 22 years of extremely expensive suffering. Similar long-term effects have been described by other observers (Morgan,²⁶ Randolph,²⁷ Sandberg²⁸). The impingement of the chemical environment is lessened markedly by the patient's long-term withdrawal through creating environmentally sound, chemically less contaminated home environments. Susceptibilities gradually subside and the patient is able to return to function in the outside world; however, a home oasis must always be preserved.

Ability of food to induce arrhythmias was extensive in this series. Usually, foods as inciting agents were not perceived until the patient had been in the relatively fume and particle free environment for several days. Apparently, there is an unmasking process derived from the food abstinence which allows the challenge reaction to become acute and definable. Failure to recognize the masking, or so-called adaption principle, probably explains so few published observations on multiple food incitants. Also, the absence of controlled fume and particle free environments adequate enough to restore the patient to a nonadapted state precluded adequate study of these complex cases.

Needless to say, once the patient learned which foods precipitated his symptoms, avoidance was undertaken voluntarily and meticulously. Certainly, after atherosclerosis is ruled out in patients with arrhythmias of unknown etiology, one should suspect the commonly ingested foods and work them out accordingly.

Water contamination is also a problem in this type of patient and did trigger arrhythmias. Certainly, one can speculate as to the causative agents in water. Chlorine is incriminated since it is absent in all filtered and spring waters and all patients reacted to challenge with chlorinated water. Pesticide residues and numerous chemical residues not taken out by water treatment plants could cause arrhythmias. Apparently, new chemical compounds are now being formed by the interaction of some chemicals in public water supplies, and these could account for unknown inciting agents. The question arises as to why some spring waters trigger arrhythmias. According to Glaze,²⁹ there are naturally occurring phenols resulting from decayed humus or acquired by absorption from running over coal deposits that are present in some spring waters. The tachycardia and sinus arrest seen in one of the patients that resulted from spring water ingestion also resulted from various dilutions of phenol under the tongue. This is circumstantial evidence supporting this concept.

Emphasis should be placed on the degree of specificity of the chemical triggering in these patients.

Initially, it appears that each patient is set off nonspecifically by any incitant, yet as one closely observes each patient it becomes apparent that all are generally susceptible to specific derivations of petroleum products and more specifically to one or more of the halogenated hydrocarbons. However, any given individual is more susceptible to certain incitants than others within this spectrum. The magnitude of response also appears to be dose related per individual. One individual cannot tolerate a transient exposure while another may take an hour's

exposure to get an adverse reaction. In a given individual, two types of responses occur. The first is a classic allergic type having memory and specificity triggered by varying small amounts of incitants. The second response is one of an overall nonspecific depressant effect which is cumulative and tends to lead to chronicity because it changes overall responses, both to other chemicals and foods, by masking acute responses. It adversely influences food compatibility. This cumulative chemical buildup was seen clinically in these patients as evidenced by the fact that long-term withdrawals of multiple incitants tended to decrease overall symptomatology with less food and chemical susceptibility while symptomatology increased as the overall chemical load increased.

As the effects of chemical build-up were lifted, it became evident that intra-organ as well as multiple organ sensitization occurred. It appears that myocardial and coronary artery sensitization are only one facet of the whole spectrum of smooth muscle involvement. No patient in this series had isolated heart involvement without symptoms related to other smooth muscle organs; however, in some patients the extra cardiac involvement was minimal. Also, most patients had some aspects of peripheral vasculitis, particularly petechiae, periorbital or peripheral non-pitting edema, spontaneous bruising and/or peripheral vasospasm. The varied types of arrhythmias in this series were further evidence of the effects of chemical build-up on different areas of the heart.

Specificity of intra-organ response was apparent in all patients since various areas in the heart in a given patient appeared to be more affected than others. One tends to think of the autonomic nervous system being influenced by environmental incitants and this was partially true in the patients studied in that some of the

sinus brady and tachycardias could be triggered by environmental stimuli. It was clear that two patients had sensitization of the atrium, or imbalance of the nervous impulses leading to it and that all cardiac effects were secondary to this. In themselves, these atrial arrhythmias did not appear to be life threatening other than through their indirect effects of lower organ perfusion due to the resultant brady or tachycardia. Rapid atrial arrhythmias certainly could be life threatening by acting as triggering agents for hypoxia, which, in the presence of underlying arteriosclerosis in any of the vital organs such as kidney, heart, or brain, could be devastating. This appeared to be so in patient number four who, when challenged with an ambient dose of the fumes of natural gas for one hour, developed a pulse of 200 with crushing chest pain and S-T depression on EKG. The reaction lasted for 12 hours while the residual hangover of generalized gastrointestinal upset and cardiac irritability lasted for another five days. This necessitated the patient being placed in oxygen during most of this period. Any time he was out of oxygen, tachyarrhythmias occurred. Regardless of whether or not these atrial arrhythmias were life threatening, their incapacitating effects were evident in the patients. Each felt as though he were going to die due to the symptoms of shortness of breath, pounding heart, chest pains, memory loss, or mental confusion. Because of these recurrent symptoms the patient's capacity to function, even marginally, was impaired. It was extremely important to remove these triggering agents in order to restore the patient to optimum function.

Patients with coronary artery spasm fell into two categories: those with only chest pain and those with EKG changes. Coronary angiograms showed spasm of the large vessels in each case with good distal runoff. Although the angiograms were not done under environmental control during a known food or chemical challenge, it is probable the patient was receiving an inadvertent chemical incitant: the angiographic rooms have a chemically contaminated environment due to their equipment.

Final word awaits angiographic studies under environmentally controlled conditions. Apparently, the detrimental effects of the myocardial ischemia in these patients is controlled by the basic collateral myocardial blood supply that each individual is born with and/or whether other myocardial disease is present. Again, the incapacitating effects of the transient ambient chemical incitants were present in patient number five who always took 24-65 hours to recover after being challenged. Since she worked around many chemicals to which she was sensitive, her heart was constantly being triggered and she was ill most of the time.

Ventricular arrhythmias are obviously more life threatening and are probably the result of a sensitized ventricular myocardium. Patients having these appeared to be in serious difficulty since they were also refractory or sensitive to all the anti-arrhythmia agents. However, it was clear that once under rigid environmental control the triggering agents were removed, thus reducing the total immune load and allowing the heart to recover rapidly. Although the patients were not always entirely arrhythmia free at the end of the fasting, they were clinically asymptomatic and their arrhythmias continued to improve the longer they were in a controlled environment. Initially, transient exposures still resulted in frightening, but always manageable, situations by withdrawal of incitants and oxygen. Over a period of time, one week to one year, all arrhythmias disappeared. It was always apparent, though, that massive exposure to the worst inciting agents for a long period of time, one or more days, would trigger the still sensitized, but for practical purposes, well heart. Patients in this series are contrasted to Stewart's³⁰ patient who survived two episodes of coronary shock only to die on the third because his environment was not controlled. He had underlying arteriosclerotic coronary disease but received high exposure to fumes of paint remover, which apparently triggered his coronary shock. Unfortunately, in this case the inciting agent, furniture paint remover, was not determined until after death.

The internal metabolic mechanism disruption is still not clearly defined in these patients. Once the inciting agent gets inside the body, it apparently triggers one or more segments of the basic homeostatic mechanism. In some cases the antigen antibody sequence apparently is activated which, when joined with complement, results in release of mediators which trigger the already primed smooth muscle. Other patients apparently had complement triggered directly via the alternate pathway.

Still other incitants probably directly activate the kinin system^{31,32} resulting in the smooth muscle triggering. We would expect that the one patient who had all laboratory studies near normal to have this system involved. Unfortunately, studies on this aspect have not been done as yet in cardiac patients but the multiplicity of incitants and responses in any one patient suggests involvement of the kinin system. Entry through the fibrinolytic and coagulation mechanism would also be possible but to date had not been demonstrated in these patients. If triggering is involved via these systems, we possibly did not demonstrate changes because they occurred at a local level and total peripheral blood studies were not altered enough to show a difference.

The presence of positive C-reactive proteins in some patients agrees with Papish's³³ findings in monocellular vasculitis. Unfortunately, due to inaccessibility of the specific area of involved heart muscle, it was impossible to do biopsies to see whether deposition occurred. In the patient with the spontaneous bruising as a terminal event of a sequential action after coronary spasm, the serum calcium was depleted along with the positive CRP, which would suggest deposition on the heart and in blood vessels. Previously deposition of C₃ and C-reactive protein in the vessel wall of those patients with spontaneous bruising has

been shown to occur. Hopefully, in the near future fluorescent studies will be available in our laboratory, enabling us to demonstrate this phenomenon and otherwise completely delineate the terminal event in this clearly defined sequential reaction. Since T-cell decrease occurred more areas are open to speculation. In this study it is obvious from the multitude of incitants and laboratory abnormalities that many facets of the body's homeostatic system are not functioning properly, thus preventing the person from being able to handle the daily environmental insults. This was immediately evident by the large numbers of foods and individual chemicals that any one patient could not tolerate. Though the basic internal mechanism derangement is unclear it is evident that the unmasking processes after chronic adaptation (or maladaptation) is the central issue in these type patients. New techniques will have to be designed to define properly the basic underlying mechanism derangement.

SUMMARY

Twelve consecutive, highly selected patients with nonarteriosclerotic cardiac arrhythmias and/or chest pain refractory to medication, having various associated symptomatology relating to smooth muscle sensitization, were studied in a rigidly controlled, relatively fume- and particle-free environment. The majority of signs and symptoms were cleared in ten patients without medication while under environmental control and all arrhythmias were reproduced with controlled, repeated, individual blind and double-blind, incitant challenges in ten out of twelve patients. The incitants were common foods and chemicals to which the individual has been exposed frequently. Double-blind challenges with ambient doses of inhaled chemicals also reproduced the spectrum of arrhythmias. This myocardial involvement appeared to be part of a more generalized sensitization of smooth muscle. The distorted homeostatic mechanism included abnormal positive C-reactive protein, serum complements and T-B cell interactions in individual patients.

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REFERENCES

1. Harkavy J: *Vascular Allergy and Its Systemic Manifestations*. Washington: Butterworths, 1963, page 92.
2. Taylor GS and Hern WS: Cardiac arrhythmias to aerosol propellants. *JAMA* 219:8, 1970.
3. Randolph TE: Specific adaptation syndrome. *J Lab Clin Med* 48:934, 1956.
4. Randolph TE: *Human Ecology and Susceptibility to the Chemical Environment*. Springfield, IL: Charles C Thomas, 1962.
5. Ibid.
6. Rea WJ: Environmentally triggered phlebitis. *Ann Allerg* 37:101, 1976.
7. Rea WJ: Environmentally triggered small vessel vasculitis. *Ann Allergy* 38:245, 1977.
8. Hare F: *The Food Factor in Disease*. London: Longmans, 1905, page 274.
9. Harkavy J: *Vascular Allergy and Its Systemic Manifestations*. Washington: Butterworths, 1963, page 93.
10. Ibid, page 92.
11. Ibid, page 92.
12. Ibid, page 93.
13. Davidson, HM Thoronghan JC and Bewcock H: *South Med J* 436:560, 1945.
14. Kern RA: Critical discussion of functional cardiac disorders caused by sensitiveness to heat or cold (by W.W. Duke). *J Allerg* 4:67, 1932.
15. Werly G: Is allergy a factor in angina pectoris and cardiac infarct? (abstract) *J Allerg* 4:65, 1932.
16. Harkavy J: *Vascular Allergy and Its Systemic Manifestations*. Washington: Butterworths, 1963, page 93.
17. Schookhoff C and Lieberman DL: Hypersensitivity to acetyl salicylic acid, expressed by an angina pectoris syndrome, with and without urticaria. *J Allerg* 4:506, 1933.
18. Boxer RW: Cardiac Arrhythmias due to Foods in *Clinical Ecology* X Dickey. Springfield, IL: Charles C. Thomas, 1976.
19. Klotz SD: Allergy and the Cardiovascular System in *Clinical Ecology* X Dickey. Springfield, IL: Charles C. Thomas, 1976.
20. Harkavy J: *Vascular Allergy and Its Systemic Manifestations*. Washington: Butterworths, 1963, page 92.
21. Randolph TE: Personal communication.
22. Taylor GS and Hern WS: Cardiac arrhythmias to aerosol propellants. *JAMA* 219:8, 1970.
23. Spizer FE, Wegman DH and Ramiers A: Palpitation rate associated with fluorocarbon exposure in a hospital setting. *New Eng J Med* 292:624, 1975.
24. Nour-Elden R: Uptake of phenol by vascular and brain tissue. *Micovasc Res* 2:224, 1970.
25. Yevick P: Oil pollutants in marine. Eighth Advance Seminar Society of Clinical Ecology Instatepe, Tape 11, 1975.
26. Morgan J: Personal communication.

27. Randolph TE: Personal communication.
28. Sandberg D: Personal communication.
29. Glaze R: Personal communication.
30. Stewart RD and Hake CL: Pain remover hazard. *JAMA* 235:288, 1976.
 31. Bell IR: A unified theory of mechanism for disease caused by maladaptation to exogenous substances such as foods and chemicals, failure of inhibition in the kinin, intrinsic coagulation-fibrinolysis complement system. Society of Clinical Ecology, Instatape, Tape IV, 1974.
32. Ibid.
 33. Papish WE: Studies on vasculitis, immunoglobulins. BIC. C-reactive proteins and bacterial antigens in cutaneous vasculitis lesions. *Clin Allerg* 1:92, 1971.