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Antigenic Relatedness of Human Enteric Coronavirus Strains to Human Coronavirus OC43:
A Preliminary Report

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Legend. Findings in patients with Kawasaki disease.

Characteristic	Patient		
	1	2	3
Age (years)	4	1 10/12	2
Sex	F	M	M
Ethnic group*	H	B	H
Clinical manifestations			
Fever (39.4–40.6 C)	+	+	+
Conjunctival injection	+	+	+
Dry, fissured lips	+	+	+
Strawberry tongue	+	+	+
Generalized rash	+	+	+
Peripheral erythema	+	+	+
Cervical lymphadenopathy	+	+	+
Laboratory findings			
†ESR [†] (>65 mm/hr)	+	+	+
Thrombocytosis	+	+	+
Nail color abnormalities	+	+	+
Fingers (no.)	10	10	10
Toes (no.)	5	6	5

* H = hispanic, B = black.

† ESR = erythrocyte sedimentation rate.

fore the present illness and were transient. This type of leukonychia has been associated with tuberculosis, arteriosclerosis, nephritis, Hodgkin's disease, chilblains, metastatic carcinoma, anemia, and hepatic cirrhosis [1, 2]. Most researchers agree that it is caused by abnormal keratinization [2–4]. Some [2] postu-

late that altered vascular patterns of the nailbed or intravascular changes (anemia and hypoproteinemia) may also lead to increased whiteness of the nail. Since our patients were not anemic or hypoproteinemic, we suggest that vasculitis was the cause of leukonychia partialis. Although the heart and coronary arteries are mainly involved in Kawasaki disease, other small and medium-sized arteries may exhibit intimal thickening, round cell infiltration, and, rarely, fibrinoid necrosis [5]. According to Kawasaki et al. [6] an arteritis similar to that seen in infantile periarteritis nodosa and accompanied by coronary thrombosis and aneurysm was found in 13 autopsy cases.

We would welcome correspondence from others who have seen nail color abnormalities in Kawasaki disease.

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A Preliminary Report

COLLEAGUES—We examined paired sera from 62 infants with acute nonbacterial gastroenteritis and from 50 age-matched controls (admitted to the hospital for nondiarrheal diseases) for antibody to human coronavirus (HCV) OC43 and neonatal-calf diarrhea coronavirus (NCDCV). Antibody response was observed with greater frequency in patients (27.4%) than in controls (2.0%). It was characterized by the presence of neutralizing and often HAI antibody to HCV OC43, but not to the antigenically related NCDCV [1]. These serological data suggested indirectly the existence of a human enteric coronavirus (HECV) antigenically related to HCV OC43, and prompted us to examine both infants and young children with acute gas-

troenteritis and age-matched controls for detection of antibody to coronavirus in sera and coronavirus-like particles in stools. Coronavirus-like particles were detected by electron microscopy in 34 (16.3%) of 208 patients and in 3 (1.6%) of 182 controls tested ($P < .01$).

Subsequently, we purified HECVs from stools of two patients (VA 24 and VA 35) by sucrose density gradient centrifugation. Antisera from mice and guinea pigs immunized with purified virus were examined by conventional immune electron microscopy (IEM) [2] for reactivity to HCV OC43, NCDCV, and the two HECV strains. Results showed a two-way cross-reactivity between HCV OC43 and the two HECV strains. The antigenic relatedness to HCV OC43, as well as the typical morphology (figure), suggest that the coronavirus-like particles detected were actually HECVs. Furthermore, the buoyant density of HECV-24 and HECV-35 in sucrose was approximately 1.20 g/ml, a value in agreement with those reported for human and animal coronavirus. Convalescent-phase sera from all the patients positive for excretion of coronavirus-like particles in stools, and seronegative for previous HCV OC43 infections, reacted by IEM with HECV-24 and HECV-35 and, to a lesser extent, with HCV OC43. Acute-phase sera from the same patients were poorly reactive or nonreactive by IEM. Conversely,

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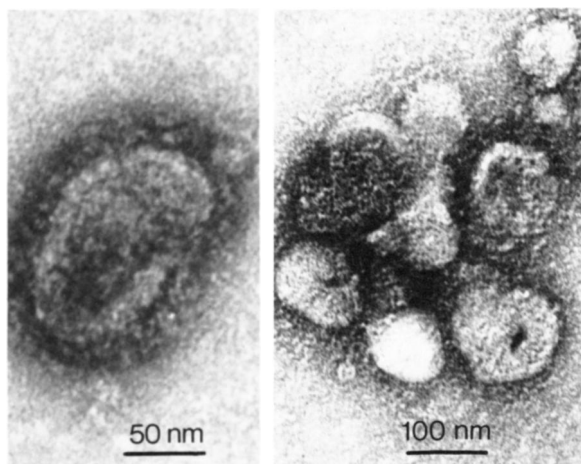


Figure 1. EM appearance of human enteric coronavirus (strain HECV-35). (*left*), Single virus particle in a fecal specimen; (*right*), immune aggregate by homologous antiserum.

the antisera to the two HECV strains and, to a lesser extent, antiserum to HCV OC43, reacted with the coronavirus-like particles in stools from all the positive patients by conventional IEM and also by solid-phase IEM [3].

In summary: (1) In infants and young children with acute

gastroenteritis, fecal excretion of HECVs is more frequently detected than in age-matched controls; (2) HECV strains are antigenically related to HCV OC43, and their detection in feces is consistently associated with antibody response to HECV as well as to HCV OC43; (3) our results support the existence of HECV strains [4] and suggest that they could play an enteropathogenic role in infants and young children with acute gastroenteritis.

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Pneumocystis carinii in Germ-Free Rats

TO THE EDITOR—I read with interest the letters of W. Beautyman and W. T. Hughes concerning *Pneumocystis carinii* [1, 2] and would like to add a cautionary note from our own experience with “germ-free” Sprague-Dawley rats.

In May 1981, we purchased 70 germ-free, Cesarean-delivered, barrier-sustained Sprague-Dawley rats from the Charles River Company (Wilmington, Mass). These rats were shipped in sterile containers. Five rats that were randomly selected and killed immediately upon arrival in our laboratory were subsequently found to have *Pneumocystis carinii* organisms in their lung tissue. An order placed to the Harlan Sprague-Dawley Company (Indianapolis, Ind) for gnotobiotic rats yielded the same result—all six of the animals shipped were infected with *P. carinii*. The methods and the results of this serendipitous investigation have been published in detail and should serve as a warning to those who employ “germ-free” research animals [3]. The Charles River Company refunded us for their “germ-free” rats after I visited their facility and demonstrated appropriate histological techniques for screening for *P. carinii*. Since then, Dr. Hughes has ascertained that the animals purchased by him for use in his transmission studies [4, 5] were from a different isola-

tor maintained by the Charles River Company (personal communication) than the ones in which our rats were born.

We still do not know how gnotobiotic rats from two highly reputable breeders became infected with *P. carinii*, especially since oral swabs and fecal cultures from the same animals were negative for growth. Possible routes include (1) undetected lapses in technique employed by the companies, (2) unusual resistance of *P. carinii* to physical and/or chemical agents, or (3) in utero transmission. Whatever the route, this experience underscores the need for great caution when attempting to reach conclusions based upon experiments conducted in gnotobiotic animals, especially when the companies breeding the animals do not screen for the infective organisms in question.

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