

Family Functioning and Stress as Predictors of Influenza B Infection

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A prospective cohort study was designed to study the effects of family functioning and stress on the incidence of influenza infection. Families from the clinic roster, containing two adults and at least one child between the ages of 1 and 18 years, were asked to participate. Baseline (pre-influenza) data included a serum determination for influenza A and B antibodies, family functioning as measured by the Family Adaptability and Cohesion Evaluation Scales (FACES) II and the Family APGAR, and parental stress as measured by the social readjustment rating scale (SRRS). During the study all family members of patients with upper respiratory tract infection symptoms or fever were seen, and throat swabs were obtained for viral culture. Approximately 2 weeks after the influenza epidemic ended (March 1984), sera for antibodies were again collected on all family members. Chi-square analysis showed that infection (defined as a fourfold titer rise or a positive viral throat culture) was significantly associated with both cohesion and adaptability as measured by FACES II. Neither the Family APGAR nor the SRRS was associated with influenza B infection. It was concluded that family functioning affects the frequency of influenza B infection within families. This finding raises the possibility that family dysfunction may lead to altered immune responses, which increases susceptibility to infection.

Scientific understanding of human susceptibility to infection and immune responses has greatly expanded over the last several decades. The naive concept that exposure to a single organism leads invariably to a defined illness no longer is suitable for most infectious diseases. Instead, the spectrum of infection ranges from colonization to asymptomatic infection to full clinical illness. Factors involved in individual susceptibility to infection and the specific manifestations of illness include the virulence of the organism, the number of organisms exposed to, the mechanism of exposure, one's age, and the immune competency of an individual, which in turn is affected by multiple factors including medications, underlying disease processes, and nutritional status. With respect to immune competency, numerous investigators¹⁻¹⁴ have recently ad-

ressed how psychosocial factors may be affecting an individual's immune response to an invading organism.

Several recent reviews have outlined the complex relationships between psychosocial factors, immune function, and infections. Specific stressors may produce changes in immune measurements such as lymphocyte counts,⁶ lymphocyte response to mitogen stimulation,⁷⁻¹⁰ natural killer cell activity,¹¹ salivary IgA,^{12,13} or the delayed hypersensitivity reaction.¹⁴ Other studies have shown the relationship between stressful life events and symptomatic infections, including upper respiratory tract infections,¹⁵⁻¹⁷ streptococcal disease,¹⁸ infectious mononucleosis,^{19,20} and tuberculosis.²¹ Few studies, however, have addressed family functioning and susceptibility to infectious disease.

Three studies^{17,18,22} addressing family lifestyles deserve special mention. First, Meyer and Haggerty¹⁸ followed 16 lower middle-class families, each with two or more children, for 12 months, and recorded life events that were distressing to the family. Among the children 2 years of age or older, a greater degree of family-related stress occurred during the 2-week interval before a clinical acute respiratory tract illness or a documented streptococcal infection than occurred during the 2-week interval after such

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infection or illness. Second, Boyce et al¹⁷ noted an association between stressful family situations and the duration of illness in young children. Children from families with high life-stress scores had more severe and longer lasting respiratory tract illnesses. Furthermore, strong family routines were associated with more severe respiratory tract illness, especially in the presence of high stress. This finding may indicate that family routine scores actually reflect family rigidity or the harshness of family rules. Finally, Foulke et al²² reported that lower maternal scores of family function (as measured by Family Adaptability and Cohesion Evaluation Scales [FACES] II-cohesion, Family APGAR, and Index of Family Relationship) were associated with more frequent visits for otitis media or upper respiratory tract infections. Whether this finding reflects family reporting behavior to physicians or an increase in incidence of respiratory tract illness is unclear.

An epidemic of influenza B in 1984 provided an opportunity to test the hypothesis that family dysfunctioning and stressful life events increased one's risk of developing an influenza infection.

METHODS

Families consisting of two adults and at least one child between the ages 1 and 18 years who attended a day care, preschool, or school were eligible to participate. Families were recruited from one university-based and two community-based family medicine clinics. Families were excluded if any member was known to have cardiac, pulmonary, or neurologic diseases; if a female member was pregnant or actively trying to become pregnant; if any member had received the influenza vaccine during the past year; or if any member was taking medications that might interfere with the study. Written informed consent was obtained from a parent or legal guardian prior to participation. Many of these families were participants in other influenza studies as reported elsewhere.²³

At the time of enrollment, parents completed FACES II,²⁴⁻²⁶ Schedule of Recent Events,²⁷ Family APGAR,²⁸ and family demographic information. Adolescent children also completed FACES II. A serum sample was obtained from each family member in advance of the influenza season. All participants were instructed to return to the clinic within 24 hours of onset of any respiratory tract illness, regardless of its severity, for a history and physical examination by a physician and a throat swab specimen for viral culture. Each symptomatic patient was given a daily illness form to complete and return after recovery from the illness. Families were called weekly to monitor respiratory tract symptoms. Two weeks after the influenza season, a second serum sample was obtained from all participants.

Virology and Serology

For virus isolation, the throat swabs were obtained and placed in veal-infusion broth, supplemented with 0.5% bo-

TABLE 1. SUMMARY OF DEMOGRAPHIC DATA

| Characteristics | Adults | Children |
|---|------------------|------------------|
| Male/female | 58/58 | 54/76 |
| Race (white/other) | 109/7 | 120/10 |
| | Mean ± SD | Mean ± SD |
| Age (years) | 33.8 ± 7.54 | 7.9 ± 6.5 |
| Family members | 2.0 ± 0.0 | 2.2 ± 0.9 |
| Education (years of schooling) | 13.4 ± 2.1 | NA |
| Initial serologic results (1:2 ^x) | | |
| Influenza B/Texas/84 | 2.96 ± 1.12 | 2.31 ± 1.12 |
| Influenza B/Singapore/79 | 2.67 ± 1.24 | 2.21 ± 1.04 |

vine serum albumin. Specimens were stored at 4 °C for no longer than 4 days and tested in Madin-Darby canine kidney cultures for influenza using procedures previously described.²⁹ Serum specimens were tested for hemagglutination-inhibition antibodies to influenza B/Texas/84 and influenza B/Singapore/79 by described methods, except the concentrations of reagents were altered and sera were absorbed with chicken red blood cells to permit tests with a starting dilution of 1:4.³⁰

Definitions and Data Analysis

Visits for respiratory tract illness represented a clinic visit by an individual with any respiratory tract complaint. Influenza-like illness was defined by (1) the presence or history of fever (oral temperature >37.7 °C), (2) two respiratory symptoms (cough, nasal obstruction, sore throat, hoarseness, or chest pain), and (3) at least one of the following: myalgias, headaches, chills, or anorexia. Influenza infection was defined by the isolation of an influenza virus from a throat swab or a fourfold or greater titer rise of hemagglutination inhibition antibodies. Illness associated with infection was defined by influenza-like illness and a laboratory-documented infection defined above.

The Circumplex Model of Family and Marital Functioning proposed by Olson and colleagues²⁴ has been operationalized into FACES, a self-report questionnaire.²⁵ In this study the second version of this questionnaire was used—FACES II.²⁶ The Circumplex Model proposes that cohesion and adaptability are two of the most important dimensions of family systems. Cohesion is defined as “the emotional bonding that family members have towards one another,” while adaptability is defined as “the ability of a marital or family system to change its power structure, role relationships, and relationship rules in response to situational and developmental stress.”²⁶ These two dimensions are hypothesized to be related curvilinearly to family health. The extremes of cohesion—enmeshment and disengagement—are theorized to be unhealthy, whereas the midrange or moderate cohesion is thought to be healthy. This curvilinearity is theorized for the adaptability dimension as well, with the extremes—rigidity and chaos—being unhealthy and the midrange or moderate adaptability thought of as being healthy.

TABLE 2. FACES II (ADAPTABILITY SCALE) AS PREDICTORS OF INFLUENZA B INFECTION

| | Adaptability | | |
|---|------------------|---------------------|--------------------|
| | Rigid No. (%) | Balanced No. (%) | Chaotic No. (%) |
| Infected* (Among the sample as a whole) | 15/55 (27.3) | 41/174 (23.5) | 10/17 (58.8) |
| Infected** (Among those moderately cohesive) | 12/32 (37.5) | 28/131 (21.4) | 9/15 (60) |

* $P = .007$
** $P = .002$

TABLE 3. FACES II (COHESION SCALE) AS PREDICTORS OF INFLUENZA B INFECTION

| | Cohesion | | |
|---|-----------------------|---------------------|---------------------|
| | Disengaged No. (%) | Balanced No. (%) | Enmeshed No. (%) |
| Infected* (Among the sample as a whole) | 3/32 (9.4) | 49/178 (27.5) | 14/36 (38.9) |
| Infected** (Among those moderately adaptive) | 0/8 (0) | 28/131 (21.4) | 13/35 (37) |

* $P = .02$
** $P = .04$

The Family APGAR is a five-item questionnaire that potentially taps the respondent's satisfaction with family adaptability, partnership, growth, affection, and resolve. It was included in the study to determine whether a short family satisfaction scale could provide associational information not manifested by FACES. The Schedule of Recent Events (SRE) of Holmes and Rahe²⁷ is a self-report questionnaire that measures the number of recent events—such as a death in the family, divorce, financial changes, change in employment status—that have happened over a set period. It is theorized that individuals experiencing more of these changes are also experiencing more psychosocial stress.

The primary hypothesis of this study is that individuals who perceive their families as being more dysfunctional—enmeshed, disengaged, chaotic, or rigid—are more likely to develop influenza B infection than those persons who perceive their families as more moderately cohesive and adaptive. A secondary hypothesis is that persons who have experienced more life event changes are more likely to manifest influenza B infection than persons experiencing fewer such changes. It was also a goal to determine whether family dysfunction as measured by the Family APGAR questionnaire is associated with the incidence of influenza B and correlated with FACES II.

Differences in proportion of infection and illnesses were compared using contingency table analysis with chi-square as the test for statistical significance (α was set at 0.05). Data for adults and adolescents were analyzed using each individual's own FACES score; the younger children were assigned the mother's FACES score.

RESULTS

Two hundred eighty-one patients in 66 families were recruited during the fall of 1983. Two hundred forty-six patients in 58 families were followed during the entire period. Families that did not complete the study either refused to have final blood drawn or moved away from the

study area. Family demographic data and initial serology findings are summarized in Table 1.

Of the 246 participants who completed the study, 66 (26.8%) developed laboratory-documented influenza B infection; 46 of 130 (35.4%) children and 20 of 116 (17.2%) adults developed influenza B infection. While 70.8% of the children and 32.8% of the adults in this sample had a visit for respiratory tract illness, only 9.2% of the children and 5.2% of the adults had influenza-like illness associated with laboratory-documented influenza B infection.

The proportions of laboratory-documented influenza B infection were associated with scores on both the adaptability and cohesion scales of the FACES instrument. Influenza B infections were more common among individuals who described their families as "rigid" or "chaotic" rather than "balanced" or midrange (Table 2). To control for the cohesion dimension, families who scored moderately cohesive ($n = 178$) were compared along the adaptability dimension; the elevated levels of infection among the rigid and chaotic groups rose even higher (Table 2).

Increased family cohesion was associated with an increased incidence of infection (Table 3) in the sample as a whole and in the subset of individuals who perceived their families as "balanced" as measured by the FACES adaptability scale. Thus, the adaptability and cohesion dimensions, independent of each other, are associated with the incidence of influenza B infection. Utilizing the Circumplex Model as described by Olson,²⁴ 33% of individuals who perceived their families as dysfunctional as compared with 21% of members of balanced families had documented laboratory evidence of influenza B infection ($P = .04$, Table 4). (Given the Circumplex Model, a family is considered dysfunctional if it is not balanced on both the adaptability and cohesion dimensions.) There was no difference in the mean initial serology values for influenza B among the various dysfunctional groups and the balanced groups.

Neither the Family APGAR nor the Holmes and Rahe Schedule of Recent Events showed any significant correlation with the development of influenza B infection. There

TABLE 4. FACES II (CIRCUMPLEX MODEL) AS PREDICTORS OF INFLUENZA B INFECTION

| | Balanced No. (%) | Dysfunctional (No. (%)) |
|---|---------------------|----------------------------|
| Infected* (Among the sample as a whole) | 28/131 (21.4) | 38/115 (33.0) |
| * $P = .04$ | | |

was also no association demonstrated between the three measures—the Schedule of Recent Events, FACES II, and the Family APGAR. Furthermore, neither the Schedule of Recent Events nor the Family APGAR were determinants of clinical illness.

DISCUSSION

An influenza B epidemic in Oklahoma in 1983–84 provided an opportunity to study the effects of family functioning and stress on influenza B infection. The finding that family dysfunction as measured by FACES II was associated with influenza B infection was consistent with the primary hypothesis. An unexpected, interesting finding was that disengaged families had a significantly lower incidence of influenza infection as compared with balanced families or enmeshed families. This finding challenges the original interpretation of the meaning of the relationship between family functioning as operationalized by FACES II and influenza: the initial interpretation revealed in the hypotheses was that any increased incidence of influenza would be due to increased susceptibility secondary to changes in the immune system. Results with the adaptability dimension are consistent with such an interpretation: both chaotic and rigid families manifested higher incidences of influenza B. The extremely low proportion of infection among disengaged families may be due to physical proximity: disengaged families—who theoretically are purported to spend less time together—may also touch less, kiss less, and share eating and drinking utensils less. Thus, family functioning may be a measure of both exposure (physical proximity) and disease susceptibility.

Even with the lower incidences of influenza B among disengaged families included within the dysfunctional categorization, dysfunctional families still manifested significantly higher proportions of infection. Should the disengaged families be considered separately from the other dysfunctional groups (such a comparison was not presented, as it was not part of the original hypotheses), the difference between dysfunctional and functional families is even larger.

The lack of association between stressful life events and influenza B infection does not strongly refute the data in the literature that suggest that stress does lead to an in-

creased incidence of infection and suppression of the immune system. In this population, none of the families had major life events changes, ie, death of a spouse or a divorce. Furthermore, some studies^{17,31} indicate that a variety of daily hassles not measured by the Holmes and Rahe instrument may have an impact on disease outcome.

It is possible that the differences in the proportions of persons manifesting influenza B infection between functional and dysfunctional families could be due to confounding. Several potential confounders were anticipated, such as socioeconomic status, family size, and initial serology levels; none of these measured factors significantly alter the reported differences in proportions of influenza infection. Thus, confounding is not a major threat to the validity of these results.

The effect of family functioning on the duration and severity of clinical illness cannot be adequately assessed by this study. The frequency of severe clinical illness was low. In addition, many of the families did not return their illness records to the clinic or keep their daily illness record at home, so that the duration of illness could not be adequately assessed.

CONCLUSIONS

Family dysfunctioning, as measured by FACES II, increases the risk of acquiring influenza B infection. Families that are enmeshed, chaotic, or rigid have increased frequencies of influenza B infection during the epidemic compared with balanced families. Disengaged families manifest lower levels of infection than balanced families. Further studies are needed to address the interaction of stress on family functioning and disease outcome. In addition, further studies are needed to demonstrate whether family functioning affects the immune system and, consequently, increases the risk of developing influenza B infection or whether family functioning simply increases one's risk of exposure to influenza.

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References

- Jemmott JB III, Locke SE: Psychosocial factors, immunologic mediation, and human susceptibility to infectious diseases: How much do we know? *Psychol Bull* 1984; 95:78–108
- Rogers MP, Dubey D, Reich P: The influence of the psyche and the brain on immunity and disease susceptibility: A critical review. *Psychosom Med* 1979; 41:147–164
- Udelman DL: Stress and immunity. *Psychother Psychosom* 1982; 37:176–184

4. Borysenko M, Borysenko J: Stress, behavior, and immunity: Animal models and mediatory mechanisms. *Gen Hosp Psychiatry* 1982; 4:59-67
5. Locke SE, Hornig-Rohan M: *Mind and Immunity: Behavioral Immunology*. New York, Institute for the Advancement of Health, 1983
6. Fischer CL, Daniels JC, Levin SL, et al: Effects of the spaceflight environment on man's immune system: II. Lymphocyte counts and reactivity. *Aerospace Med* 1972; 43:1122-1125
7. Kimzey SL, Johnson PC, Ritzman SE, et al: Hematology and immunology studies. The second manned Skylab mission. *Aviat Space Environ Med* 1976; 47:383-390
8. Palmbald J, Bjorn P, Wasserman J, et al: Lymphocyte and granulocyte reactions during sleep deprivation. *Psychosom Med* 1979; 41:273-278
9. Bartrop RW, Lockhurst E, Lazarus L, et al: Depressed lymphocyte function after bereavement. *Lancet* 1977; 1:834-836
10. Schliefer SJ, Keller SE, Camarino M, et al: Suppression of lymphocyte stimulation following bereavement. *JAMA* 1983; 250:374-377
11. Locke SE, Kraus L, Leserman J, et al: Life change stress, psychiatric symptoms, and natural killer cell activity. *Psychosom Med* 1984; 46:441-453
12. Jemmott JB III, Borysenko JZ, Borysenko M, et al: Academic stress, power motivation, and decrease in salivary secretory immunoglobulin A secretion rate. *Lancet* 1983; 1:1400-1402
13. McClelland DC, Floor E, Davidson RJ, et al: Stressed power motivation, sympathetic activation, immune function, and stress. *J Hum Stress* 1980; 6(2):11-19
14. Smith GR, McDaniel SM: Psychologically mediated effect on the delayed hypersensitivity reaction to tuberculin in humans. *Psychosom Med* 1983; 45:65-70
15. Hinkle LE, Plummer N: Life stress and industrial absenteeism. *Industrial Med Surg* 1952; 21:363-375
16. Jackson GG, Dowling HF, Anderson TO, et al: Susceptibility and immunity to common upper respiratory viral infections—The common cold. *Ann Intern Med* 1960; 53:719-738
17. Boyce WT, Jensen EW, Cassel JC, et al: Influence of life events and family routines on childhood respiratory tract illness. *Pediatrics* 1977; 60:609-615
18. Meyer RJ, Haggerty RJ: Streptococcal infections in families. *Pediatrics* 1962; 29:539-549
19. Kasl SV, Evans AS, Neiderman JC: Psychosocial risk factors in the development of infectious mononucleosis. *Psychosom Med* 1979; 41:445-466
20. Roark GE: Psychosomatic factors in the epidemiology of infectious mononucleosis. *Psychosomatics* 1971; 12:402-411
21. Holmes TH, Hawkins NG, Bowerman CE, et al: Psychosocial and physiological studies of tuberculosis. *Psychosom Med* 1957; 19:134-143
22. Foulke FG, Reeb KG, Graham AV, et al: Family function, respiratory illness, and otitis media in urban black infants. *Fam Med* 1988; 20:128-132
23. Clover RD, Crawford SA, Abell TD, et al: Effectiveness of rimantadine prophylaxis of children within families. *Am J Dis Child* 1986; 140:706-709
24. Olson DH, Bell R, Portner J: *FACES: Family Adaptability and Cohesion Evaluation Scales*. St Paul, Minn, University of Minnesota Press, 1978
25. Olson DH, Sprenkle DH, Russell CS: Circumplex Model of Marital and Family Systems: I. Cohesion and adaptability dimensions, family types, and clinical applications. *Fam Process* 1979; 18:3-28
26. Olson DH, et al: Family inventories: Inventories used in a national survey of families across the family life cycle. In *Family Social Science*. St. Paul, Minn, University of Minnesota, 1982
27. Holmes TH, Rahe RH: The social readjustment rating scale. *J Psychosom Res* 1967; 11:213-218
28. Smilkstein G: The family APGAR: A proposal for family function test and its use by physicians. *J Fam Pract* 1978; 6:1231-1239
29. Baxter BC, Couch RB, Greenberg SB, et al: Maintenance of viability and comparison of identification methods for influenza and respiratory viruses of humans. *J Clin Microbiol* 1977; 6:19-22
30. Tauraso WM, Gleckman R, Pedreira FA, et al: Effect of dosage and route of inoculation upon antigenicity of inactivated influenza virus vaccine (Hong Kong strain) in man. *Bull WHO* 1969; 41:507-516
31. Schmidt DD, Schmidt PM: Family systems, stress, and infectious diseases. In Ramsey CN Jr (ed). *Family Systems in Medicine*. New York, Guilford. In press