

lowed to salt her food to taste. If the physician feels compelled to treat asymptomatic edema, bed rest with the patient positioned in lateral recumbency usually results in effective diuresis, and if pre-eclampsia is suspected, hospital observation is preferable to diuretic therapy.

Finally, we note that debate surrounding this topic is often more emotional than factual. Questions concerning salt and diuretics in pregnancy are not likely to be solved by political organizations or pharmaceutical advertisements but by trained scientists conscientiously doing their work.

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ALLERGY TO HUMAN SEMINAL PLASMA

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THE infrequency of the syndrome of allergy to human ejaculate¹ prompts us to report another such case. In addition, we present immunologic data including histamine release, and the finding that the antigen is a relatively low-molecular-weight constituent of seminal plasma, present in seminal plasmas of all 15 men tested.

CASE REPORT

A 29-year-old married woman, seen in May, 1972, had been essentially healthy except for ragweed hay fever of 15 years' duration. In May, 1971, within 1 hour after intercourse, her eyes became itchy and severely swollen, and nasal congestion and sneezing developed. The symptoms and signs gradually subsided over 3 days. Ten days later, she engaged in sexual intercourse again, and within 5 minutes after her husband's ejaculation, itchy, swollen eyes, nasal obstruction and sneezing developed. This time she also noticed swelling and itching of the perivaginal area, diffuse urticaria and a sensation of swelling in her throat. These symptoms gradually subsided over a period of 4 days. After this episode, she suspected that the reactions were related to coitus. For the next 18 months, either a condom or coitus interruptus was employed during sexual intercourse. However, there were 4 more episodes occurring each time these preventive measures were not used successfully. All episodes began within 5 minutes after coitus. The symptoms were severe and consisted of nasal obstruction, sneezing, periorbital swelling, diffuse urticaria, perivaginal swelling and the sensation of throat swelling. Periorbital edema persisted longest, subsiding over a period of 3 to 6 days. There was never faintness, palpitation, wheezing or abdominal cramps.

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The patient's allergic history included ragweed hay fever of 15 years' duration treated by "hyposensitization" therapy, and allergy to penicillin and sulfonamide (type unknown) as a child. There was no history of asthma. The past gynecologic history included 2 abortions by dilatation and curettage between the ages of 18 and 22 years, and 1 abortion by dilatation and curettage at the age of 27. She had 1 full-term induced delivery at the age of 25. During the last 6 years, she had been having infrequent sexual intercourse (approximately once in 10 to 12 weeks). Her mother had ragweed hay fever, her father had allergic rhinitis to danders and dust, and her half-sister (paternal) had immediate allergic reactions to shellfish.

IMMUNOLOGIC STUDIES

Skin Tests

Ejaculates were obtained from three normal medical personnel and from healthy men with functioning vasectomies. The ejaculate supernatants were diluted in Tris-buffered saline, pH 7.4, containing 0.2 mg per milliliter of human serum albumin. The patient was tested with serial 10-fold dilutions of the seminal plasmas by scratch tests and by intradermal tests, with readings at 15 minutes. All 15 seminal plasmas gave intensely positive (4+) reactions (15-mm wheal plus pseudopods plus surrounding erythema) at 1:10,000 dilutions, and gave weakly positive (1+) reactions (wheal of 4 to 6 mm plus surrounding erythema) to 1:10,000,000 dilutions. All 15 seminal plasmas were about equally reactive by this test. Seminal plasma dilutions of 1:1000 gave negative reactions (bleb of 1 to 3 mm without erythema) in five control patients (two male and three female). Seminal plasmas were negative for Australia antigen. Skin tests with the husband's serum at 1:1000 were negative. Skin tests with a battery of the common allergens gave strongly positive wheal-and-flare reactions to ragweed extract (1 PNU per milliliter) and to mixed feathers (100 PNU per milliliter), and moderately intense reactions to plantain (10 PNU per milliliter), house dust from Center Laboratories (200 PNU per milliliter) and kapok (100 PNU per milliliter).

Histamine Release from Whole Blood

Aliquots (0.05 ml) of heparinized whole blood were mixed with 0.5-ml dilutions of seminal plasma or its fractions.² There was 37 per cent histamine release with seminal plasma at a dilution of 1:20,000. All of seven seminal plasmas gave histamine release. No unequivocal release was observed without the addition of seminal plasma or using blood from five normal controls.

Serum Tests for Sperm Agglutination

The patient's serum at 1:5 dilution agglutinated the husband's sperm in whole ejaculate, but undiluted serum did not agglutinate thrice-washed sperm in phosphate-buffered saline.

Fractionation of Seminal Plasma

Six milliliters of pooled (four vasectomized men) seminal plasma was centrifuged, and the supernatant was subjected to molecular sieving (Fig. 1). All the allergenic activity as assayed by skin test and histamine

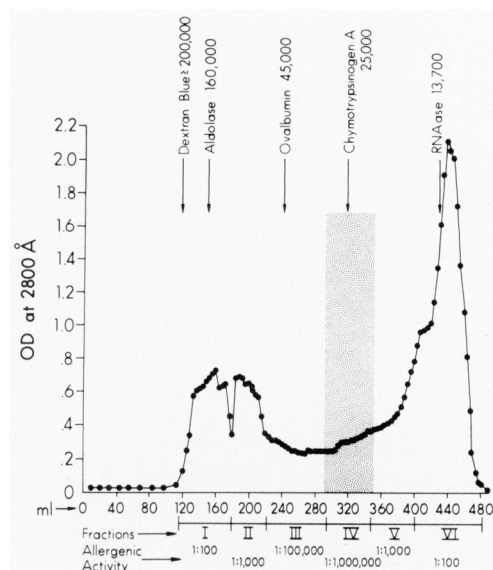


Figure 1. Molecular Sieving of Pooled Seminal Plasma.

Six milliliters of pooled seminal plasma was put through a Sephadex G-200 column, 98 by 2.5 cm (25°C, 0.01 M Tris buffer, pH 8.0, flow rate 16 ml per hour); 2-ml aliquots were collected, and optical density (OD) read at 2800 Å. The aliquots were pooled into six fractions, and serial dilutions used for both skin tests and histamine release. The allergenic activity of the fraction is expressed as the highest dilution giving a weakly positive (1+) wheal-and-flare reaction in the patient. The Sephadex G-200 column was calibrated for molecular size.

release was recovered from the column. Roughly 90 per cent of the activity was in fraction IV, corresponding to a molecular weight of 20,000 to 30,000 daltons. The other 10 per cent appeared to tail, mainly in fraction III. There was no other activity peak. Fraction IV showed an ultraviolet spectrum typical of protein (maximum of 2800 Å, and minimum of 2550 Å), except that the optical-density 2800:2600 ratio was relatively low (1.15). Fraction IV contained approximately 250 µg per milliliter of protein and elicited a positive skin test in the patient at dilutions of 1:1,000,000 — i.e., at concentrations of protein as low as 2.5×10^{-1} µg per milliliter.

DISCUSSION

The present case and one previously published¹ establish in women a syndrome of immediate allergic reactions of a frightening nature to human seminal plasma. Immediate occurrence after coitus, cutaneous edematous eruptions and congestion of mucous membranes were common to both cases. Asthma and loss of consciousness were features of Halpern's case¹ but not of ours. This discrepancy may depend in large part upon nonimmunologic factors (e.g., whether the patient is of "asthmatic constitution" etc.). This immediate syndrome is very rare. Since most women having this syndrome would probably recognize the immediate temporal association of explosive symptoms with coitus, the syndrome is apparently not being missed. However, it is possible that there is also a syndrome of accelerated allergic reaction to seminal plasma in

which the onset of symptoms might occur several hours to one or more days after coitus and persist for several days. In this situation, the relation of symptoms to sexual intercourse would not be so clearly evident. Such an "accelerated reaction" with urticarial symptoms starting three to 72 hours after initiation of penicillin therapy has been observed.³

It is probable that these immediate reactions to seminal plasma are mediated by the homocytotropic antibody (or antibodies) detected by skin test and by the histamine-release test. Our recent (unpublished) studies with passive transfer and absorption with an anti-IgE serum indicate the mediating antibody to be IgE.

Human seminal plasma contains at least 11 distinct antigenic materials,⁴ most derived from prostatic and seminal-vesicle secretions.⁴ The present data show that seminal plasmas from subjects with functioning vasectomies were as active allergenically as seminal plasmas from normal men. This finding indicated that the antigen is derived from the prostate or seminal vesicles (or both) rather than from the epididymis or testis. Neither we nor Halpern et al.¹ found any antibodies against sperm; rather, the antibodies were directed against a seminal-plasma constituent. The exact nature of the seminal-plasma allergen is not yet known. The present data show it to fractionate with proteins of molecular weights in the range of 20,000 to 30,000 daltons. Our data indicate the seminal-plasma antigen to be present in seminal plasmas of all (or most) men.

Finally, a provocative question — why this syndrome seems to be so rare — cannot be clearly answered, but deserves some speculation. A group of factors, both genetic and environmental, must occur together in a given patient to permit the generation of this kind of a hypersensitivity reaction to any allergen. These factors may include the ability to recognize the allergen as foreign, which is under genetic control by Ir-genes,⁵ and the ability to respond immunologically to allergens presented at mucous membranes with the production of high-avidity reagins, which may be under both genetic and environmental control. In this unique situation, local gynecologic circumstances that permit the absorption and handling of the allergen may also be important. The probability that all the necessary factors will be present in the same person is likely to be very small, and this fact may define the rarity of this clinical event.

We are indebted to Dr. Samuel Bukantz, of Tampa, Florida, for referring the patient to us and to Dr. Jeanne Epstein, of the Margaret Sanger Clinic, for performing the sperm agglutination assays.

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BY THE LONDON POST

The Health of Pilots, and Others — G.M.C. Inquiry — Strange Times

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THE prolonged inquiry into the cause of the crash of the BEA Trident aircraft as it took off from London Airport last June received daily cover in all the news media.¹ There was much discussion about the value of the whole exercise, especially since there seemed to have been a preoccupation among many of those participating in the inquiry to apportion blame rather than to help determine the precise cause of the accident. The final report has not yet been published, but in the summing up of the evidence for BEA, it was suggested that the captain of the aircraft was probably incapacitated by a heart attack, which deprived him of his higher powers of judgment and led him to take irrational action and move the droop lever that brought about a fatal stall. It was further suggested that the onset of his symptoms was gradual and not obvious to himself or his crew so that neither of his assistants on the flight deck took over the controls. He had had no previous cardiac symptoms, and his routine medical examination and electrocardiograms had been satisfactory, but much emphasis was placed on disturbing reports of the effect that an argument in the briefing room before takeoff, apparently over matters of discipline and training standards, may have had upon the captain, who was a senior and most experienced pilot.

The British Air Line Pilots Association claimed that holding the inquiry in public had undermined confidence in aviation to a greater degree than could have been envisaged. This view was not shared by the Daily Telegraph, which pointed out that the function of the inquiry was not to allay public fears but to get at the truth; if the truth should be disturbing, the public should know about it.

Certainly, the inquiry has led to closer scrutiny of the factors likely to affect the efficiency of pilots — already, some medical requirements have been made stricter. More frequent electrocardiograms will be required, and discussions are in progress between the airlines and aircrew associations about the use of modern preventive medical techniques to promote better flight safety and the long-term health of aircrews. Pilot fatigue is being studied by a group under the Chairmanship of Group Captain Douglas Bader to see whether changing conditions such as faster aircraft and more crowded airspace may require changes in the flight-time limitations in operation at present. The Guild of Air Pilots and Air Navigators has submitted a memo-