

The False Drug Side-Effect: Which Patients Complain

By WILLIAM S. APPLETON

INTRODUCTION

At the Massachusetts Mental Health Center (M.M.H.C.), a well-staffed university psychiatric hospital, an outbreak of alleged chlorpromazine-induced skin rashes recently occurred involving five dramatic young female patients. Investigation of the complaints led us to doubt whether medication was the cause. Why then did these women blame chlorpromazine? Thus, the central concern of this investigation: which patients are likely to complain of drug-induced side-effects and under what conditions? A second issue arising from our study and described in the literature is the need for care when differentiating the true from the alleged medication side-effect.

SETTING AND PROCEDURE

The M.M.H.C. is a public mental hospital affiliated with the Harvard Medical School, which specializes in the care of acutely psychotic patients, training and research. There are 220 in-patients, 70 residents and 70 staff psychiatrists. Sixty per cent. of the patients receive drugs and 70 per cent. psychotherapy.

A Somatic Therapy Unit (16, 1, 2, 6), established in 1956, consults on the wards, educates residents and carries out research projects. The unit is led by the author, and includes several staff psychiatrists, advanced and first-year residents and a full-time attendant.

Within a two-week period, five patients complained of skin rashes, possibly induced by chlorpromazine. The author was consulted and he interviewed and submitted a questionnaire to each patient's doctor, reviewed drug records and recorded nurses' observations. A dermatologist was not consulted, because these rashes were transitory and were easily managed by the patients' physicians.

THE PATIENTS

A brief summary of each of the five patients follows:

1. A 22-year-old woman wanted several small isolated spots on her chest, face and neck looked at daily. Her psychiatrist reluctantly agreed to a consultation so that she might be reassured by another physician. This insignificant-appearing dermatitis was in the usual sites for menstrual acne, from which the patient had frequently suffered. In addition, her extensive use of facial cosmetics was halted. The rash disappeared less than three days after termination of her menstrual period and her cosmetic use, in spite of the continuance of chlorpromazine.

At the time of complaint, this dramatic and exhibitionistic young woman rushed about seeking social contact. Her history revealed frequent psychosomatic symptoms, plus many improbable and bizarre drug side-effects. One of the latter was uncontrollable tearfulness when changed from chlorpromazine to trifluoperazine, which immediately ceased when chlorpromazine was reinstated.

The patient's doctor and the author each concluded that this rash was not a medication allergy, but served as a demand for attention. The young woman continued to insist that her dermatitis was drug-induced.

2. A 22-year-old woman developed a warm, moist erythema on her face, legs and thighs. Her psychiatrist considered that this atypical eruption was not phenothiazine-induced, but the patient insisted it was. The history revealed that the dermatitis had been produced by excessive swimming in the chlorinated pool, at least six daily showers and repeated skin scrubbing. The skin trauma was stopped, chlorpromazine continued, and the erythema immediately disappeared.

At the time the patient blamed chlorpromazine for her dermatitis her psychotherapy was terminating. Phenothiazine treatment had been initiated to control her hypomanic, demanding and annoying behaviour. Her psychiatrist noted that she was friendly with patient 3 below.

3. A 19-year-old girl developed a mild rash over her lower jaw and neck. The patient thought it might be drug-induced, and her psychiatrist agreed to consultation with the Somatic Therapy Unit. The diagnosis reached was menstrual acne, from which she had previously suffered. The rash promptly subsided with no treatment, while pharmacotherapy was continued.

This schizophrenic girl gave a history of food and dust allergies, hay fever and a previously questionable dystonic reaction to chlorpromazine. The drug had been started to ease her fright and confusion. Her current attitude was that chlorpromazine was "terrible". She was described as a conflict-causing patient around whom staff disagreement frequently centred. She followed patient 2 round the ward and each complained of a "chlorpromazine skin reaction" within a few days of the other.

4. A 21-year-old girl developed a dermatitis limited to the left side of her forehead and face. The psychiatric resident requested consultation because the alleged drug rash was causing the patient distress. A diagnosis of neurodermatitis was made because (1) there was a history of a similar skin rash occurring before phenothiazine treatment; (2) a similar dermatitis developed on chlorpromazine and later on thioridazine; and (3) a drug rash is usually not confined solely to the left side of the forehead and face.

This schizophrenic girl showed phobic and hysterical characteristics in addition. In the past she had often broken out in a rash when angry, and now she was furious with her psychiatrist and with her family. Chlorpromazine had been initiated to control her hostility.

5. A 21-year-old schizo-affective girl on medication for management and control developed fissuring near the corners of her mouth which was considered chlorpromazine-induced. The drug was continued, benadryl was added, and the skin reaction subsided. One month later, facial oedema and pruritus occurred. Benadryl treatment was again instituted and chlorpromazine continued, while hair spray and "pancake" cosmetics were discontinued. Since the oedema rapidly disappeared, all concluded that this was not a drug reaction.

FINDINGS

1. *Patient Characteristics*

All five patients reporting rashes were young (age 19–22) females. Three had long histories of psychosomatic illness. All were manic, angry or dramatic and had a rash located on the face.

2. *Attitude and Interaction Factors*

In every instance the doctor initiated medication to control behaviour or psychotic thinking, rather than for a reason the patient considered helpful. Those receiving drugs became more negative toward them as time passed. In four cases the staff were angry and psychotherapy was in an unsatisfactory state. All five patients complaining of a drug rash within the two-week period interacted closely with one another.

3. *Rashes not Drug-Induced*

None of the five patients had a true medication dermatitis. The appearance and distribution were not typical; the skin rapidly cleared despite continuation of the drug; and the dermatitis quickly subsided when some other aetiological factor was altered. Evidently the patients had complex intrapsychic and interpersonal reasons, for believing medication responsible for their rashes.

DISCUSSION

The Psychology of the Side-Effect Complaint

Hospitalized psychiatric patients are greatly concerned about the medicines they take for a variety of reasons ranging from normal caution to paranoid delusions. They discuss drug effects and side-effects not only with ward staff, but with one another. One may be reluctant to begin a drug because it has previously failed to help another. Similarly, side-effects are of great concern to them. Patients look them up in books, ask doctors about them, and discuss them among themselves. One patient invaded the nurse's station to read a list of lithium side-effects which her doctor had obtained for the ward personnel.

Striking similarities in personality and patterns of interaction were found to exist among those blaming chlorpromazine for their skin rashes. Typically, such a patient was a young unmarried female on medication for control of behaviour, who thought the drug unhelpful. She had many psychosomatic complaints, wished attention, feared abandonment, and related closely with another "rash" patient. Such patients were angry at the staff, who responded with equal negative feeling, resulting in unsatisfactory milieu and psychotherapy. The individual who complains of a false side-effect will be discussed under three headings: (1) Imitation, (2) Body Language, and (3) Anger.

1. *Imitation*

All five patients interacted closely. Their relationships were described as: friendly, jealous, symbiotic and increasing one another's pathology. Each of the young women reported the same symptom within a brief time span. This exemplifies Caudill's (5) "ground swell" phenomenon originally described in relation to a majority of hospitalized patients he observed, who, as a group, did "well or poorly at a particular time". The cluster of drug rash complaints represents a similar phenomenon. Our patients influenced one another consciously and/or unconsciously to use the vehicle of an alleged drug dermatitis in order to seek attention and care at a time when they had the staff angry, and to voice a complaint against the

spirit in which the drug was started, namely the staff's desire to control their behaviour.

2. *Body Language*

These young women were histrionic, exhibitionistic and hyperactive. They made extensive use of symbolic bodily representation of affect in psychosomatic illnesses, hypochondriasis, allergies, promiscuity, exhibitionistic tendencies and conversion defences. The five used a drug rash to relate to their doctors and reveal their bodies. In the author's experience, those who use bodily symptoms to win care and attention prior to drug treatment are more likely to complain of medication side-effects than those who do not.

Another patient I followed repeatedly described the feeling that her eyes were being drawn up into her head. While this never actually occurred, the complaint represented both imitation and body language. As an inpatient she had heard about and witnessed oculogyric crises due to trifluoperazine. Having wearied the staff with her endless psychosomatic, hypochondriacal and conversion symptoms, she was glad to find an audience for her alleged dystonic reaction.

Hankoff (11) mentions dizziness, nausea and blindness occurring in a patient on placebo, and relieved when the original meprobamate medication was reinstated. This recalls our first patient who used uncontrollable crying to force her doctor to start chlorpromazine again.

3. *Anger*

The side-effect complaint was associated in every instance with a disturbance in verbal communication between staff and patient, because of anger. Since in four of five cases drug was initiated to control behaviour, medication was regarded by the patient as being for the doctor's and staff's benefit rather than her own. Angrily started on drug to control her behaviour, the patient repaid in kind by denouncing medication as responsible for her skin rash. The message of the side-effect could be translated: "Look how the drug my doctor gave me has harmed me!"

At the time of reporting a skin rash, the psychotherapy of four of the group was unsatisfactory: two angry, one about to terminate, and

one the subject of staff disagreement. The patient, feeling the staff's hostility, was glad to turn to both the author and the drug attendant, who are interested in side-effects. This represented an attempt to find a new caring person, at a time when she felt (perhaps accurately) that her own doctor had withdrawn from her. The dermatitis provided a convenient means to regain her own physician's attention and to express revenge for abandonment.

Separating the False from the True Side-Effect

The rashes attributed by our patients to chlorpromazine all proved due to other causes. Nevertheless, one wonders how frequently in the literature medication is erroneously blamed. Had we been studying the efficacy of chlorpromazine in 5,000 patients rather than five, while secondarily recording side-effects, would we have carelessly listed at least some of these patients as having drug-induced skin rashes? I think we might have done.

Many authors have been concerned with the need to differentiate the false from the true side-effect. Busfield *et al.* (4) have emphasized that many so-called side-effects occurring on anti-depressant medication actually represent somatic symptoms of depression, and have been present before drug treatment began. A "true side-effect" is defined as a "somatic complaint or clinical sign not present prior to treatment but present during the treatment period", and the authors caution that when evaluating side-effects, it is necessary to obtain a careful pre-treatment baseline. They say nothing, however, about the differentiation of false from true side-effects during the treatment period.

Over the past dozen years many descriptions of side-effects occurring during placebo administration have appeared. These observations again serve to emphasize the need to distinguish the false from the true side-effect. Honigfeld (13, 14) has covered the side-effects of placebos in his excellent review; Beecher (3), the Medical Research Council (18), Honigfeld (12), Sheard (20), Meanock and Lewis-Faning (17), Glaser and Whittow (8), Gartner (7), and Green (9), have all listed side-effects occurring on placebo; Greenblatt *et al.* (10) noted that a placebo group of hospitalized depressed patients revealed "the

same side-effects that are found among patients on active medication". They attributed these "so-called side-effects" partly to "somatization of the illness" and partly to the "product of suggestion". Wolf (21) described a "typical dermatitis medicamentosa" occurring on placebo. Kasich *et al.* (15) have reported a higher incidence of side-effects in a placebo group than in either of two drug groups. Green (9) has suggested that females report more side-effects while taking placebo than do males.

Pogge (19) reviewed 67 publications, and recorded 38 different types of side-effects during placebo administration; nervous system depression or stimulation were the most common effects, headache and tremor next. He noted four cases of skin rash out of 1,066 on placebo tranquilizer therapy. He urged that physicians should keep in mind, when attempting to evaluate the significance of side-effects occurring during the administration of medicine, that similar effects can be associated with placebo. He offered no explanation for his findings.

It has therefore been established in the literature that an apparent side-effect may represent somatization of the illness, or a placebo response. The five cases I have described suggest that the inclination to complain about drug ill-effects is influenced by personality, by imitation of other patients, and by feelings toward the doctor and staff. It remains for further study to prove whether such individuals are significantly more prone to placebo side-effects.

SUMMARY

Five dramatic young female patients complained within a brief time span of alleged chlorpromazine skin rashes, which proved not to be drug-induced.

These women shared several intrapsychic and interpersonal states: (1) they imitated one another's complaint; (2) they made habitual use of symbolic bodily representation of affect in psychosomatic illnesses, allergies, promiscuity, exhibitionistic tendencies and conversion defenses; and (3) there was a disturbance in verbal communication between staff and patient because of anger.

From the cases recorded here, plus a brief literature review, the author emphasizes the

need to distinguish the false from the true drug side-effect.

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