

NEUROGENIC BLADDER ASSOCIATED WITH BRAIN TUMORS

With Presentation of a Case Study

W. JAMES GARDNER, M.D.

Until fairly recently, the top level for the control of the autonomic functions of the body has been assumed to be the basal ganglia of the brain. The work of experimental physiologists, particularly Sherrington, Denney-Brown, and Robertson in England, Fulton, Bucy, Langworthy, and Kolb in America has proved conclusively the existence of autonomic representation in the cerebral cortex. These highest autonomic centers are located in the cortex of the frontal lobes and they exert a governing effect on the centers in the hypothalamus and medulla which regulate visceral activity. Blood vessel tone, glandular secretions, sweating, and gastro-intestinal motility are a few of the visceral functions which have been proved to be definitely under the control of the frontal lobes of the brain.

In a study on the physiology of micturition in man, Denney-Brown and Graeme Robertson observed the variations in intravesical pressure which occur with increasing distention of the bladder. They concluded that apart from a faint background of maintained tonic activity, spontaneous vesical activity takes the form of waves of contraction appearing in rhythmical progression. An effort to void evokes powerful contractions of the bladder, whereas a voluntary effort of restraint completely inhibits the nervous discharges responsible for spontaneous vesical activity.

In pursuing the center for micturition cephalad, Longworthy and Kolb studied intravesical pressures in normal animals and in animals with sections through the brain stem at various levels. They first established the volume of contents necessary to induce reflex micturition in the intact animal. They found this to be 155 cc. in the cat. After removal of the motor cortex on one side, this volume was reduced to 30 cc. After removal of the other motor cortex, the volume was further reduced to 20 cc. After a section at the upper border of the pons, it was 11 cc. When the section was at the middle of the pons or below, reflex micturition was very weak and incomplete. That is, there was retention with overflow. The conclusions to be drawn from these findings are that tone in the musculature of the bladder is similar to tone in striated muscles, that it is under the control of the motor cortex which exerts an inhibiting action on the reflex centers in the cephalic portion of the hind brain.

The bladder symptoms of patients with cerebral lesions have not received very serious consideration in medical literature. The reason for this is probably that the incontinence has been dismissed under the assumption that it was a mental symptom. Although this is true perhaps in the majority of cases, it certainly is not true in all instances.

NEUROGENIC BLADDER ASSOCIATED WITH BRAIN TUMORS

Every neurological surgeon has observed retention of urine in certain patients with cerebellar tumors. This is the result of pressure on the medulla with interruption of the reflex arc to the centers in the upper portion of the pons. With this arc interrupted, the tone of the bladder musculature is lost. This was demonstrated experimentally by Langworthy and Kolb by their sections through the middle of the pons.

It is well recognized now that true vesicle incontinence can occur as a result of lesions of the frontal lobes. Our experience seems to indicate that the lesion must affect both frontal lobes, although exactly what portion must be damaged is not entirely clear. We have seen it in unilateral frontal lobe tumors which were of sufficient size to markedly compress the opposite frontal lobe. It has always cleared up with removal of the tumor even though this involved amputation of one frontal lobe or even removal of an entire cerebral hemisphere.

The patient who has elicited our greatest interest in this problem is one in whom it was necessary to amputate both frontal lobes for an infiltrating tumor.

This patient was a woman of 52 years who presented a typical picture of brain tumor and who in addition was incontinent of urine. The significance of this symptom was not realized at the time of her original study and it was ascribed to intellectual deficit. Ventriculography indicated the presence of a bilateral frontal lobe tumor. At operation on August 28, 1933, an infiltrating tumor of the right frontal lobe was found and an amputation of this lobe was performed at a point anterior to the motor area. The patient immediately became continent but lapsed again into incontinence seven days later. As the first operation showed the tumor extending into the left frontal lobe, this lobe was amputated at a second operation 12 days later. The patient made a satisfactory recovery from these operations but has remained absolutely incontinent to date. The patient is rational. She shows some memory defect and complicated mental processes are impossible. She, however, is tidy about her appearance and in her habits. She is never conscious of a feeling of fullness in the bladder and even when it is full, voluntary urination is impossible. The urine does not dribble. It discharges involuntarily after several hours of filling. She has never been catheterized to determine whether or not there is retention.

Cystoscopic study was performed by Dr. Higgins. His notes are as follows: Cystoscope passed with ease. There is no loss of sensation in the urethra. Hot water was allowed to run into the bladder which the patient could differentiate from cold solution. The bladder is quite atonic but there is no fine trabeculation present. Upon irritating the wall of the bladder with a catheter there was but very little response. The internal sphincter shows a marked degree of loss of tone.

Here, then, we have the picture of a patient who cannot tell when her bladder is full and cannot voluntarily empty it. This, in spite of the fact that there is no paralysis and no loss of cutaneous sensibility. These findings are in agreement with the experimental evidence that the centers for voluntary control of micturition are located bilaterally in the frontal lobes.

FACTORS RESPONSIBLE FOR THE LOWER MORTALITY IN PROSTATIC SURGERY

W. J. ENGEL, M.D.

That the mortality in prostatic surgery has been reduced sharply in recent years has been repeatedly demonstrated by the published statistics of various clinics, and we have shared in this experience. The advent of transurethral resection marked the turning point. In reviewing our statistics, the average mortality over a period of years prior to resection was 8.9 per cent whereas, in a like period since resection, the average mortality has been 1.8 per cent. Although resection is unquestionably the largest single factor responsible for this favorable trend, I feel there are other factors which should be given due credit in the consideration of this subject, which may be discussed under the following headings:

1. Earlier diagnosis and acceptance of treatment.
2. Preoperative preparation.
3. The operation itself.
4. Postoperative care.

EARLIER DIAGNOSIS AND ACCEPTANCE OF TREATMENT

In recent years, I have been impressed with the fact that we are seeing patients with bladder neck obstruction earlier in the course of the disease. More patients are coming in immediately following their first attack of urinary retention, and many are presenting themselves for relief of symptoms of urinary obstruction before they have progressed to the stage of complete urinary retention. I believe this is attributable in the main to two factors. First, the general physician is to be congratulated for recognizing symptoms of bladder neck obstruction earlier and advising corrective surgery. As a result, the layman has gradually learned that obstructive urinary symptoms are not just a necessary torment of old age, but the manifestation of a disease that may be remedied. Second, there can be little doubt that in the patient's mind, fear of operation, in years past, has been the greatest deterrent to accepting early operation. Today, however, the layman himself has become aware of the greater safety in prostatic surgery, and this confidence prompts him to seek operative relief at an earlier date. Gone is the treacherous hat-band catheter and rare indeed is the patient who practices self-catheterization in preference to operation.

As a direct result of this earlier acceptance of operation for bladder neck obstruction, we are naturally operating upon better risk patients and fewer with advanced renal damage from prolonged back pressure. An important corollary to early treatment is the fact that the glands are smaller and are, therefore, more suitable to relief by transurethral resection, so that in the past several years I have found that approxi-

THE LOWER MORTALITY IN PROSTATIC SURGERY

mately 90 per cent of the cases can be relieved by resection while only 10 per cent are of such large size that prostatectomy is necessary. Of especial interest to me is the fact that the patient's confidence in all prostatic surgery has been increased and they accept advice for prostatectomy as readily as for resection.

PREOPERATIVE PREPARATION

Certain essentials in the preoperative study of the prostatic patient, such as adequate blood chemistry studies and renal function tests, have long been known and so firmly established that they merely need to be mentioned here. If renal function is impaired, corrective measures must be instituted before operation can be carried out safely. More recently, however, we have learned to depend upon intravenous urography for guidance, not only as to the functional capacity of the kidneys, but also as an aid in prognosing the surgical convalescence. In general, it may be said that prompt function and a normal delineation of the upper urinary tract encourages one to predict an uneventful outcome, while delayed function with bilateral dilatation of ureters and kidney pelvis is a warning that the patient requires deliberate and careful preoperative preparation if he is to be carried safely through the operation.

In 1939¹ I called attention to the preoperative prostatic mortality and showed at that time that a significant number of patients died during the course of preoperative preparation and that by revising the preoperative management, we were able to sharply reduce the number of preoperative deaths and indirectly to influence favorably the mortality following surgical operation. At that time attention was drawn to the dangers associated with urethral instrumentation in prostatics, particularly undue urethral trauma at the moment of first urinary retention, the inlying urethral catheter, and also diagnostic cystoscopy. The danger lies in the increased susceptibility of the obstructed urinary tract to infection which may be initiated in one of these ways.

Certainly, one cannot overemphasize the importance of the first contact with the patient who has acute urinary retention, for it may be the first chapter of a story with a happy ending or the beginning of a tragedy. The one great watchword should be gentleness which must be combined with an adequate instrumentarium and a scrupulous aseptic technic. Attention to these details, which must be observed especially by the general physician, can be one of the greatest factors in reducing the prostatic mortality still further. In this connection it seems well to discourage the use of the rigid metal catheter as it is an instrument of extreme danger. If a soft rubber catheter will not pass, it is much wiser to employ a semirigid silk woven instrument and to remember that no instrument should be forced—merely passed.

The value of adequate preoperative drainage in increasing the safety of prostatic surgery has, of course, long been recognized, and the use of the inlying catheter for this purpose is rather firmly entrenched in the mind of the physician. We, however, have convinced ourselves that this method of preoperative drainage possesses a hazard which can be avoided. It not infrequently is responsible for setting up urinary infection which, even if the patient recovers, is very debilitating; but worse, may even prove fatal. Our experience justifies the conclusion that the avoidance of the inlying catheter has been a large factor in increasing the safety of prostatic surgery. As a substitute, we prefer intermittent catheterization, or if more prolonged and continuous drainage seems necessary, suprapubic puncture is done, the technic of which was described in the article previously referred to.¹

In summarizing our present method of preoperative preparation, which we believe has been of importance in reducing the prostatic mortality, the patients may be divided into four groups.

The first group includes patients in whom no inlying catheter and no other type of catheterization is employed. This includes those who present themselves with definite symptoms of obstruction but who never have had complete urinary retention. In such cases where the residual urine is not large and the renal function is satisfactory, as measured by urea clearance, other kidney function tests, or intravenous urogram, preliminary catheter drainage is not required and operation may be carried out safely the day after entrance into the hospital.

In group two are those patients who are prepared by intermittent catheterization. This group includes the patients with recent, acute retention in whom we prefer to carry out intermittent catheterization, this being done every six or eight hours or more often if the case demands.

The third group is comprised of those who present themselves with chronically overdilated bladders and with rather severely impaired renal function, in which we feel that a prolonged period of drainage is necessary. Suprapubic puncture has been more preferable in this group of cases.

In the fourth group is a very small number in which the inlying catheter is still employed, and ordinarily constitutes only those patients who are sent to us wearing inlying catheters, together with the rare patient with a severely infected and contracted bladder in whom suprapubic puncture cannot be done.

We have been impressed with the fact that preoperative management of patients according to this plan has markedly reduced the preoperative mortality and has certainly resulted in a smoother postoperative convalescence and a lower operative mortality. The risk of infection from wearing the inlying catheter condemns its use and undoubtedly its elimination has distinctly reduced the mortality in prostatic surgery.

THE LOWER MORTALITY IN PROSTATIC SURGERY

In order to evaluate the success of this method of preoperative management, I recently reviewed one hundred consecutive cases managed by this plan. The ages of this group of patients are shown in Table 1, from

TABLE 1
SUMMARY OF 100 CONSECUTIVE OPERATIONS ON THE PROSTATE
Age of Patients

50-59	12
60-69	39
70-79	41
80-89	8

which it will be seen that the usual age group of prostatics is included, the highest number occurring in the eighth decade.

Of this group of one hundred patients, ninety-two had transurethral resections and eight had suprapubic prostatectomies. No catheterization was done in twenty-six cases. The preoperative period was only one day in nineteen cases and two days in the remaining seven. The longest postoperative period was ten days while nineteen of the twenty-six cases were in the hospital seven days or less following operation, all cases having had prostatic resection. No operative deaths occurred in this group and no noteworthy complications were noted. The range of blood ureas is shown in Table 2, from which it is seen that only patients without significant urea retention are selected for this type of management.

TABLE 2

	<i>No Catheter</i>	<i>Intermittent catheter- ization</i>	<i>Supra- pubic puncture</i>	<i>Inlying catheter</i>
Cases	26	53	16	5
UREA (mg. %)				
30-40	10	17	..	1
40-50	12	14	3	2
50-60	4	10	4	..
60-80	..	8	1	1
80-100	..	4	3	1
100-150	3	..
150-200	2	..

There were fifty-three patients who had intermittent catheterization. We believe this is less likely to be followed by urinary infection, particularly if done at regular intervals without allowing the bladder to become overdistended. Of this group, five had prostatectomies and the remaining forty-eight had resections. Twenty-seven cases or 51 per cent spent only one or two days in the hospital before operation and in the remaining twenty-six the preoperative period ranged from three to seven days, the higher ureas requiring the longer periods of preoperative preparation.

Suprapubic puncture was carried out in sixteen of the hundred cases. When first seen the majority of these patients had large, palpably distended bladders reaching almost to the umbilicus. It is particularly this type in which we advocate suprapubic puncture as a means of avoiding infection which plays such havoc, once introduced. As will be seen in the table, the higher blood ureas occurred in this group and therefore a longer period of preoperative drainage was required. In fact, six of the sixteen patients were sent home wearing a suprapubic catheter for a period of from three weeks to two months, and we encourage all patients to do so in whom we believe a long period of drainage is essential. The remaining ten patients in this group were operated upon after seven to fourteen days of drainage. Fourteen patients had resections and two had prostatectomies.

There were only five patients in whom an inlying catheter was used and in every instance it had been inserted elsewhere. Resection was performed in four of these and prostatectomy in one, and all recovered satisfactorily.

We feel that this plan of preoperative preparation has been one of the most important factors, not only in reducing the preoperative prostatic mortality, but also in reducing the operative mortality.

THE OPERATION ITSELF

As has already been stated, there can be little question that transurethral resection has been the greatest single factor in reducing the operative mortality in prostatic hypertrophy. It is true, of course, that the mortality statistics of this operation will depend to a large extent upon the experience of the surgeon and it is equally true that as experience has increased, the safety of the operation has also increased, as has also the completeness of the resection. Contributing to the greater safety of prostatic resection is the fact that the confinement to bed is shortened tremendously. Most patients having this operation spend only two to three days in bed, as it has always been our practice to allow patients up just as soon as the urethral catheter is removed. Another factor undoubtedly contributing to the safety is the improvement in methods of anesthesia, and it is my own personal belief that spinal anesthesia has

THE LOWER MORTALITY IN PROSTATIC SURGERY

contributed greatly to the safety of operation. We have found that otherwise bad risk patients with cardiovascular disease and other associated complicating conditions tolerate spinal anesthesia exceptionally well, and I am convinced that there is less hazard in this than in inhalation anesthesia, or anesthetics of other types.

One of the early hazards of transurethral resection, namely hemorrhage, has been almost entirely eliminated and in the present day of resection it is rare indeed to see a patient in whom hemorrhage constitutes any threat to recovery. This, of course, is due in large part to improved cutting and coagulating currents, but its incidence diminishes as the experience of the surgeon increases.

I have previously indicated that there is approximately 10 per cent of patients in whom we feel that prostatectomy is still the operation of choice. It has been interesting to observe, however, that the mortality from prostatectomy has also diminished and this, I feel, is indirectly due to resection. This apparently contradictory statement is explainable because of the fact that since the advent of transurethral resection, we may be much more selective in patients for whom we advise prostatectomy, choosing only the better risk patients with a large gland. In such cases, we have been able in every instance to perform a one-stage suprapubic prostatectomy, and since 1933 there have been under my care thirty-four prostatectomies without a death. Although suprapubic prostatectomy has been our preference, those who advocate perineal prostatectomy likewise have reported a diminishing mortality rate.

It is thus seen that, irrespective of the type of operation selected for the patient, the lower mortality obtains.

POSTOPERATIVE CARE

In consideration of postoperative care, the question arises as to what is the common cause of postoperative deaths which have occurred following prostatic surgery. I should like to consider first the postoperative deaths following prostatic resection. In reviewing the operative deaths from resection, the one fact that stood out was that 56.2 per cent were due to postoperative urinary sepsis with resultant uremia. This fatal complication has been largely controlled by two measures, (1) the institution of a closed system of postoperative irrigation and (2) by the use of the newer chemotherapeutic agents. In crediting closed irrigation one needs only to observe the striking reduction in this complication following its institution some years ago. Whereas urinary sepsis was a relatively common postoperative complication before the adoption of closed irrigation, this complication now is exceedingly rare and when it does occur, it is ordinarily mild and easily controlled with one of the newer chemotherapeutic agents, particularly sulfanilamide and sulfa-pyridine.

Another important measure in postoperative care to which we attach significance is the early removal of the inlying catheter. The catheter should be removed just as soon as all risk of hemorrhage is passed, which, in many cases, is at the end of twenty-four hours and never later than forty-eight hours. The same objection to the preoperative use of the inlying catheter holds for its postoperative employment, and to leave it in beyond forty-eight hours is to invite trouble. Its early removal not only tends to reduce the risk of postoperative urinary sepsis, but also sharply reduces the incidence of epididymitis and other complications, and enhances the comfort of the patient. If the resection has been adequate, we feel there is no need to leave the catheter in beyond the time the danger of bleeding is passed, and its early removal avoids many difficulties. As previously stated, we insist upon the patient getting out of bed as soon as the catheter is removed and this early increase of normal activity lessens the chance of pulmonary complications.

In considering the postoperative care of the patient who has had a prostatectomy, there have been no significant changes in the routine which has been employed for a long period of time. Because continuous through and through irrigation may be carried out, the danger of urinary sepsis is not so great as following prostatic resection. The usual causes of death following prostatectomy have been, in the past, shock, circulatory failure, renal failure and pneumonia. These have been largely removed because we are now able to select better risks for this operation.

In summary, we believe that today there is a changed outlook for the prostatic patient who faces operation, and he can contemplate it with much less fear. Whether or not the ultimate in safety of this operation has been reached is difficult to say, although it must be admitted that there must be some end-point. Where one is carrying out a surgical procedure on patients in this age group, it would seem that a certain mortality is inevitable, but it should be our constant aim to seek improvement until this mortality has reached its lowest possible level.

REFERENCE

Engel, W. J.: Preoperative prostatic mortality, *J. Urol.* 41:505-514, (April) 1939.

CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

Case Reports and Observations

C. R. K. JOHNSTON, M.D.

Urticaria is a lesion familiar to almost everyone and has been described in the medical literature since the time of Hippocrates. Yet the cause of chronic hives is frequently baffling and the treatment often unsatisfactory. No therapy may be necessary for acute hives, although abstaining from food for twenty-four hours, purgation and adrenalin hypodermically will probably result in more prompt relief. Chronic urticaria presents an entirely different problem, as is illustrated in the following case reports. No attempt is made to distinguish between urticaria and angioneurotic edema except in diagnosis, because the lesion is essentially the same in either case. In fact, both frequently occur in the same individual and the causes and treatment are similar.

Case 1: The patient was a housewife twenty-six years of age, who complained of recurring attacks of localized edema for the past three years, involving the feet, hands, fingers, arms, lips, and eyelids. The attacks occurred ten to fourteen days prior to the menstrual period and lasted about five days. The areas were painful and at times blood was vomited during the attacks. She felt sure that taking aspirin would precipitate an attack. The personal history otherwise was negative for allergic disease. Her father had similar attacks of edema, which he attributed to the use of aspirin.

Physical examination was relatively negative. Routine blood counts and urinalysis were normal. Roentgen examination of the gastro-intestinal tract showed a normal stomach, gallbladder and colon.

Allergy studies revealed sensitivity to feathers, house dust, orris root, brewer's yeast, cow's milk, corn, cherry, plum, and to several other less frequently used fruits and vegetables.

On a program of avoidance of the inhalants and foods to which she reacted, as well as the drug she suspected, she became free from symptoms. A letter two years later stated that she had slight attacks of swelling only when she failed to follow the allergy diet. She was using goat's milk as a substitute for cow's milk. The angioneurotic edema in this case was apparently due chiefly to foods, though a drug (aspirin) would precipitate an attack also.

Case 2: The patient, a woman twenty-five years of age, was seen in April, 1938, complaining of headaches and hives. The headaches had been present for some time, but for the preceding six months they had been very severe, lasting three days and recurring about twice a month. She usually had a headache during or after the menstrual period, and a second headache in the intermenstrual period. They were the hemicrania type, and accompanied by no gastro-intestinal upset except for a tendency to constipation during the attacks. The hives, which were usually on the face, neck, and arms, had been present almost daily for several years. As a rule, the lesions were few and lasted only a few hours, although they were quite itchy and annoying. She also exhibited a tendency at all seasons for easy sneezing, nasal obstruction and postnasal mucoid discharge. Her mother and sister had similar headaches, while her father and a maternal aunt suffered from asthma.

C. R. K. JOHNSTON

Physical examination was entirely negative. The routine urinalysis and blood counts were negative except for a mild anemia (hemoglobin 69 per cent). The eosinophil count was 2 per cent.

Allergy investigation revealed sensitivity to numerous inhalants, including feathers, dust, orris root, tobacco, silk, and several animal danders. The food reactions were quite marked to wheat, white potato, pineapple, brewer's yeast, cherry, strawberry, and Brussels sprouts, and less marked reactions to egg, milk, and many others.

On a regime of avoidance of the significant inhalants and foods, she made marked progress. Three months after beginning the regime, she reported that she had had no hives, and the headaches were much improved. Those headaches she had had could be attributed to a break in her diet.

Twenty-two months after the institution of the allergy program, she was still free of hives. She had had only one attack of giant hives, this following the ingestion of three empirin compound tablets. The headaches also were completely gone except on a few occasions when she broke her diet. She had found that eating white potatoes or wheat would result in headaches, as well as hives. Both the migraine and urticaria in this case could be attributed to foods. A drug (empirin compound) had also precipitated an attack of hives on one occasion.

Case 3: The patient, a woman twenty-six years of age, complained of swelling of the lips, the right side of the forehead and the right forearm. The swelling had been present almost three years and occurred in close relation to the menstrual period, either just before, after, or during the period. Headache and nausea always accompanied the attacks. About one year prior to her visit, following an attack of pain in the right side, she had the appendix and right ovary removed. From the time of the operation to the present attack she had had only one subsequent attack of angioneurotic edema. Various elimination diets in the past had failed to help.

With the exception of the areas of angioneurotic edema, physical examination was entirely negative, as were the routine blood counts and urinalysis.

Because of the obvious relationship of her attacks to the menstrual periods, allergy tests were omitted and glandular therapy given a trial. She was advised to have 1 cc. of antuitrin S (100 units per cc.) daily for five to seven days, beginning about ten days before the period was expected. This was carried out for two consecutive periods, during which time no swelling occurred. The therapy was stopped and she remained free from attacks for the next three months as well. The edema then recurred, involving the same three sites as before. She was advised a similar program, this time using A. P. L., (Ayerst, McKenna, and Harrison) in doses of 1/5 cc. (500 units per cc.). For approximately five months this program was continued. About five doses of the A. P. L. preceding each period were taken, and she remained free of edema. This freedom continued for five months after taking the last dose of A. P. L. when once more the edema recurred in the same areas. She was again advised to resume the same type of therapy and has not returned, although over a year has elapsed since the last visit. This patient's angioneurotic edema was controlled by treating only the endocrine factor.

Case 4: The patient, a man aged forty-two, came to the Clinic because of hives and headaches. The hives had begun some three and one-half years previously, at which time he was in apparently good health. He was an auditor and was working hard and under considerable nervous tension. Attacks had occurred almost every day since the onset, the only free period being for one or two days while on a brief vacation. The hives were generalized at first; later

CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

they recurred more often on the back and upper chest. No angioneurotic edema was present. The hives were worse during the day, while at work, and bromides would give some relief.

He took a proprietary preparation, containing antipyrine, potassium bromide and sodium salicylate, one or more times per week for headache but used no other drugs. An interesting observation was that he had seen thirteen doctors for the above complaint before consulting the Clinic. He had found that eating eggs would cause hives but no other foods were suspected.

Since childhood he had had severe generalized headaches, recurring on the average of once a week, and lasting about twenty-four hours. Until some fifteen years ago they had been accompanied by nausea and vomiting. Since then nausea occurred but rarely. Substituting kapok pillows for feather pillows had resulted in some improvement and wearing glasses also helped, but the headaches continued.

The personal history was otherwise negative for allergy. His mother had "sick headaches," and her mother and brother had asthma. A paternal aunt had hay fever.

Physical examination revealed a well developed and nourished, apparently healthy individual. Several urticarial wheals were present on his back and his skin exhibited a mild dermatographia. The physical examination otherwise was not significant.

Dental examination revealed a retained root, one devitalized tooth, and two molars which showed questionable apical involvement. Routine blood counts and urinalysis were normal. Blood eosinophilia was not present.

Allergy studies by the scratch method were all negative. Intradermal tests showed immediate reactions to many inhalants, including kapok 3+, house dust, feathers, orris root, tobacco, silk, cat and dog dander 2+, and 1+ readings for pyrethrum, mattress dust, yeast and several molds. Delayed reactions were 2+ to oidiomycin and 4+ to trichophytin. No significant reactions were obtained to bacteria. Many positive food reactions (chiefly 1+) were found, including corn, oat, pork, duck, goose, turkey, coffee, tea, chocolate, the berry group, onion, asparagus, mushroom, nuts, canteloupe, cucumber, watermelon, and olives.

A very careful program of treatment was outlined, including avoidance as far as possible of all inhalant and food allergens. He was instructed to avoid rigidly the use of the proprietary he had been taking and all other drugs. Hypo-sensitization therapy was begun for the inhalant allergens, including dust, feathers, orris root, kapok, tobacco smoke and ashes and the significant molds, all in a 1:10,000 concentration. He was strongly advised to obtain extra rest, have the dental foci removed, and was temporarily given a sedative of bromides and belladonna.

One month later the patient stated that his headaches had ceased and that the hives were much improved. Further extract was supplied and the above program continued.

Five months after beginning this treatment, the patient returned and reported that he had only an occasional hive and seven to ten days would pass without any at all. The headaches were almost entirely absent, although an occasional, mild ache still occurred. He reported one severe flare-up in hives after a dose of concentrated extract (1:10) and he had found that inhalation of tobacco smoke or orris root would precipitate an attack of hives in about half an hour.

In this case the urticaria may have been due to one or several factors. Food and inhalant allergy seem definitely incriminated, but a proprietary, fatigue, and focal infection may also play a definite role.

DISCUSSION

In cases of urticaria and angioneurotic edema, skin tests are admittedly of less value than in other allergic diseases. Investigation of patients complaining of either of these lesions must be very thorough, and all possible factors should be treated if one is to achieve satisfactory results. In a small number of cases, the history may strongly incriminate a significant factor, such as the endocrine factor in Case Three, or some drug frequently taken by the patient. Skin tests may be postponed in such a case until a trial of removal of the suspected food or drug or control of the glandular factor has been attempted and if successful, allergy tests may not be necessary. Seldom, however, is the problem solved so simply.

When the history indicates the coexistence of one or more allergic manifestations (Cases 2 and 4), or a family history of allergy (Case 1), the greater is the likelihood that the case under investigation will prove to be on an allergic basis. Such allergy usually is dependent on food, drug, or bacterial sensitivity, but occasionally it may be due to inhalants or physical agents. The foods commonly incriminated include milk, eggs, wheat, chocolate, shellfish, and many others. Drug allergy is frequent and includes many widely used drugs, such as aspirin and other salicylates, phenolphthalein, quinine, ipecac, barbiturates, opium derivatives, iodides, etc. Focal infection is undoubtedly a common cause of chronic hives and it may be explained on a basis of bacterial toxins or bacterial sensitivity. Search should always be made for foci in teeth, tonsils, sinuses, gallbladder, appendix, prostate, etc. In some cases where no focus can be found, we have had considerable success with bacterial vaccines made from stool cultures.

When the personal and family history are entirely negative for allergic disease, many allergists believe that drugs or foci of infection are the most likely causes. The psychogenic factor is also important. It may at times be primary, and frequently is a contributing factor of significance. I feel that thorough testing should be carried out in these cases, however, as food or other allergy also may be present and its removal will lighten the "allergic overload." It is not infrequently noted that certain foods will cause an increase in symptoms, although the removal of these foods from the diet may not result in disappearance of all hives. The endocrine factor is probably not of great significance as a primary cause although it may contribute secondarily in many cases in the form of lowered metabolic rate, for example, or in women nearing the menopause.

CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

In conclusion, I should like to emphasize that chronic urticaria or angioneurotic edema may have many causative factors, either primary or secondary. A few illustrative case reports have been given, although needless to say, the conclusions are by no means based on these alone.

It seems worthy of emphasis that when a personal or family history of other allergy exists, the cause of hives or angioneurotic edema is more likely an allergic one. In the absence of any allergic history, drug allergy or focal infection are very frequent offenders. The psychogenic factor is an important one, although I believe every attempt should be made to rule out other causes before one admits this to be the primary factor.