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assimilated into a general pattern of fibrosis. Ellik claims seven cures by this technique.

Edwards and Beebe[3] locate the diverticulum by a direct urethral approach. After the anterior vaginal wall has been fully opened, as for major cysto-urethrocele repair, they slit up the urethra to the opening of the diverticulum, going no further than the junction of the upper and middle thirds to avoid damaging the bladder neck. Granulating edges are trimmed, and multiple openings unified, and the diverticulum is dissected out. The urethra is approximated over the catheter with interrupted submucosal sutures of 000 chromic catgut, the fascia is approximated, and the vaginal wall closed. The Foley catheter is left in for eight days. Five cases have been successfully treated with this technique.

RESULTS

Krieger and Poutasse after considerable experience at the Cleveland Clinic report the results of surgery as good. Rarely a urethro-vaginal fistula may require a secondary repair, and rarely a difficult case may require a second operation, the recurrence presumably being due to incomplete removal.

SUMMARY

Diverticulum of the female urethra has been often overlooked.

The patient with recurring pyuria, distress in voiding, and what is apparently a urethrocele, may have a diverticulum. A new technique for urethrography is greatly facilitating its detection.

The classical treatment is surgical removal—the earlier the easier. Edwards and Beebe suggest an approach by splitting the urethra.

As an alternative to a difficult dissection, Ellik advises a return to the simpler method of incision and packing, which he has improved.

Indebtedness is acknowledged to Dr. J. Victor Berry, senior surgeon, Genito-urinary Division of the Department of Surgery, and to Dr. Douglas W. Cockburn, Assistant Director of Radiology, Ottawa Civic Hospital, for their co-operation in this study.

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RÉSUMÉ

On a tendance à oublier que l'urètre féminin peut être porteur de diverticules. La malade qui accuse de la pyurie périodique et de la dysurie et dont le tableau clinique évoque la présence d'un urétrocèle peut avoir un diverticule. Une nouvelle méthode d'urétrographie a rendu le dépistage de ces lésions assez facile. Le traitement classique repose sur l'exérèse chirurgicale (le plus tôt sera le mieux). Edwards et Beebe suggèrent un abord qui consiste en une incision longitudinale qui s'étend jusqu'à l'ouverture du faux passage. Comme alternative à une dissection laborieuse Ellik recommande le retour à une technique plus simple et qu'il a améliorée, d'incision et de méchage.

THE STATUS OF PHENYLBUTAZONE (BUTAZOLIDIN) IN THE TREATMENT OF RHEUMATIC DISORDERS

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THIS STUDY was undertaken to determine the therapeutic value of phenylbutazone in a wide range of rheumatic conditions and to establish its position in relation to other anti-rheumatic drugs, keeping in mind the degree of relief obtained and the incidence of complications.

PHYSIOLOGY AND PHARMACOLOGY

The mode of action of phenylbutazone is not clearly understood, but experimental work has shown that the drug has analgesic, antipyretic, antihistaminic, uricosuric and anti-inflammatory properties.[1, 2] Absorption from the gastro-intestinal tract is rapid and complete, peak plasma levels occurring about two hours after oral administration and six to ten hours after intramuscular injection.[1] The drug is slowly metabolized in the body, about 20% of the administered dose disappearing in 24 hours and the drug having a half-life in man of approximately 70 hours.[3] At doses of 800 mg. daily the plateau plasma level is only slightly higher than at doses of 400 mg. daily. There is little to be gained therefore by the administration of larger doses, which greatly increase the hazard of toxicity.

RESPONSE TO THERAPY

Two hundred and seventy patients on phenylbutazone therapy have been seen and followed up by the author during the past year. Many gave a history of other forms of therapy — gold, steroids, etc., but phenylbutazone was not given to any who had an adequate response to salicylates. It will be noted in Tables I and II that the response in different rheumatic disorders varies widely. Patients who experienced major improvement had prompt and

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TABLE I.—RESPONSE TO TREATMENT

Diagnosis	Major improvement	Moderate improvement	Poor or no improvement	No. of patients
Gouty arthritis	75%	20%	5%	24
Ankylosing spondylitis	65%	26%	9%	23
Osteoarthritis	43%	22%	35%	58
Rheumatoid arthritis	36%	16%	48%	86

almost complete relief of pain and stiffness, which could be maintained on a small maintenance dose. Those classified as moderately improved had less relief, but felt that the therapy was well worth while, and wished to continue, sometimes in spite of minor complications. In those with a poor response the drug was discontinued after seven days.

TABLE II.—RESPONSE TO TREATMENT

Diagnosis	No. of patients	Major improvement	Moderate improvement	Poor or no improvement
Disc syndrome	12	4	4	4
Tendonitis	11	5	—	6
Bursitis	25	4	2	19
Episodic rheumatoid arthritis	1	1	—	—
Psoriasis with rheumatoid arthritis	2	2	—	—
Palindromic	2	2	—	—
Hæmophilic arthritis	2	2	—	—
Paget's disease	2	2	—	—
Costen's syndrome	2	2	—	—
Calcaneal spur	1	1	—	—
Post-herpetic neuralgia	5	3	1	1
Osteitis condensans ilei	2	1	1	—
Acute bunions	1	1	—	—
Reflex dystrophy	1	—	—	1

Relief of pain and stiffness usually occurs at from one to three days after administration, and if no improvement is obtained in one week the drug should be discontinued. When the drug is stopped there are no withdrawal effects, but symptoms return in a few days.

GOUTY ARTHRITIS

In this group, as in those reported by others, acute gouty arthritis responded more dramatically and more consistently to phenylbutazone therapy than any other rheumatic disorder. The effective oral dosage in acute gouty arthritis is 200 mg. three times daily until the acute symptoms subside, and then 100 mg. two or three times daily for a week.

Most patients respond dramatically, and within a few hours of oral administration the acute symptoms begin to subside. Toxic effects are rare because of the short period of administration. In those suffering from frequent acute attacks the administration of 100 mg. daily will often prevent recurrence. In those with less frequent episodes the drug may be used repeatedly when attacks occur, with apparently little if any danger of acquired sensitivity.

In this series 95% of patients experienced a satisfactory response, which is superior to our results from oral colchicine. When the diagnosis is in doubt, colchicine with its specific action has the advantage of providing a diagnostic test, but undesirable gastro-intestinal symptoms frequently follow its use. In observations on 520 gouty patients Kuzell *et al.*[4] obtained a good or fair response in 91% of those treated with phenylbutazone and in 80% of those treated with colchicine. Robins *et al.*[5] also consider phenylbutazone superior to colchicine because of the freedom from unpleasant side effects.

Phenylbutazone would appear to be the drug of choice in gouty arthritis, being equal to oral colchicine in effect and with less gastro-intestinal irritation.

ANKYLOSING (MARIE-STRUEMPELL) SPONDYLITIS

A surprisingly good result from phenylbutazone therapy in those suffering from ankylosing spondylitis has been reported in other studies[1, 5-7] and was confirmed in this group. As a rule, after two or three days of treatment, pain, stiffness and muscle spasm diminish with increased spinal mobility. In this study (Table I) the 90% favourable response obtained with phenylbutazone in spondylitis is in striking contrast to the result in rheumatoid arthritis where some 50% received benefit. It is interesting that the two patients with a poor response were women.

These findings and those of others suggest that phenylbutazone should replace x-ray therapy when such treatment is necessary in ankylosing spondylitis. This opinion is supported further by the reported incidence of leukæmia in those treated with more than one course of x-rays where "the observed deaths are probably at least 9 times those expected to occur".[8]

In a long-term comparison study of cortisone, ACTH and phenylbutazone in spondylitis, Holbrook[7] observed a 95% failure rate at the end of four years in those on cortisone and ACTH. In striking contrast, improvement on phenylbutazone was maintained in all but 4%.

The response reported in Table I confirms the opinion of others that, if drug therapy other than salicylate compounds is required in the management of ankylosing spondylitis, phenylbutazone is the drug of choice.

DEGENERATIVE JOINT DISEASE—OSTEOARTHRITIS

Although this treatment in degenerative joint disease is far less effective than in gout and spondylitis, phenylbutazone therapy was found to be worth while in about 60% of patients with peripheral and spinal osteoarthritis.

Most of these patients had distressing osteoarthritis in the hips or knees, and in such cases a trial of phenylbutazone therapy is indicated if less toxic measures of treatment have failed or relief by surgery is contraindicated. However, as Toone[1] has pointed out, the treatment of degenerative joint disease is a long-term project and patients affected usually belong to the older age group who may be more susceptible to toxic side effects.

RHEUMATOID ARTHRITIS

In this group about 50% of the patients felt that phenylbutazone was worth while in helping to control their symptoms. The value of the drug in certain patients was best demonstrated by those who have continued on maintenance doses for periods up to four years, have stopped, and have then started again because of the relief obtained. The percentage of patients with rheumatoid arthritis who maintain prolonged major improvement on a safe daily dosage is small but the possible value of phenylbutazone in an individual patient may be determined in seven days, at which point it may be continued or discarded. It should be clearly understood that phenylbutazone does not suppress the disease nor does it prevent progression of joint destruction. However, in comparison with long-term steroid therapy the side effects are less hazardous, the failure rate over years is less marked, and the problem of withdrawal effect is absent.

The patient suffering from rheumatoid arthritis must first be placed on a basic program which includes rest, proper exercises, local heat and adequate doses of salicylates. If this conservative program fails and the disease continues to progress with increasing severity and deformity, the use of additional therapy should be considered and a choice made from gold, steroids, phenylbutazone or chloroquine. Any beneficial effect from gold or chloroquine will likely not be obvious for six to twelve weeks. In the meantime, if increasing pain and stiffness is a problem, a trial with phenylbutazone is indicated for one week, after which, if no benefit is obtained, the drug should be discarded in favour of other measures.

Favourable results were obtained in episodic rheumatoid arthritis, psoriasis with rheumatoid arthritis, and palindromic rheumatism (Table II), but the number of patients was too small for a strict evaluation. In patients with psoriasis the skin lesions were not aggravated, and the presence of psoriasis is not a contraindication to the use of phenylbutazone.

DISC SYNDROMES

Twelve patients with cervical or lumbar disc lesions were given phenylbutazone for the relief of acute pain. Eight patients had worth-while relief and the drug was discontinued when the acute phase subsided.

TENDONITIS

The effect of phenylbutazone on bi ipital tendonitis, tennis elbow and De Quervain's disease was disappointing, less than 50% responding favourably. Local injection with hydrocortisone and oral steroid therapy is more beneficial in these lesions. In De Quervain's disease surgery is more often the treatment of choice.

BURSITIS

Twenty-five patients with acute or chronic subacromial bursitis were given phenylbutazone for the relief of pain and limitation of shoulder movement. Here also the result was disappointing, only six having major or moderate improvement. The injection of the bursa with hydrocortisone, followed if necessary by oral administration of steroids, is the treatment of choice for this condition.

HÆMOPHILIC ARTHRITIS

Two patients with hæmophilic arthritis, one with severe joint damage, obtained major relief from acute episodes of pain with phenylbutazone. One patient developed bleeding into a joint four days after cessation of therapy, which was probably due to the usual cycle of the disease.

PAGET'S DISEASE

The effect of phenylbutazone on the pain of Paget's disease was striking, major improvement occurring in both patients. If the pain of this disease does not respond to drugs with less toxicity, a trial with phenylbutazone for one week is indicated.

COSTEN'S SYNDROME

This temporomandibular joint syndrome is most often due to malocclusion of the teeth which may cause severe pain and limitation of mandibular movement. Treatment necessitates correction of the bite, a difficult procedure when pain and spasm exist. Two patients had marked relief from pain with phenylbutazone, which also facilitated dental treatment.

POST-HERPETIC NEURALGIA

This painful malady has been resistant to most forms of medication. Out of five patients treated with oral phenylbutazone, three had major improvement and one obtained moderate relief. This result would appear to be superior to other forms of therapy suggested in the past. In a series of eleven patients reported by Partelides[9] no failure occurred after five or six intramuscular injections of phenylbutazone, and it was stated that oral administration is not as effective as the intramuscular route.

OSTEITIS CONDENSANS ILEI

One patient had major and one moderate improvement. Here again, if the pain fails to respond

to drugs with less toxicity, a trial with phenylbutazone is indicated.

DOSAGE AND ADMINISTRATION

The severe toxic reactions reported in early papers were frequently associated with higher doses than are now employed. With a lower dosage schedule, the toxic reactions have shown a significant decline with no apparent impairment in therapeutic effect.[1] As mentioned above, the response to the drug should occur within one week, and if it is not worth while the treatment should be discontinued. Most physicians now use a dosage schedule of 600 mg. daily for two days, 400 mg. for two or three days, and then a maintenance dose of 100 to 300 mg. daily. A daily maintenance dose of 200 mg. is usually sufficient to maintain a constant therapeutic blood level. In this series, particularly in spondylitis, 100 mg. daily has been sufficient in a few patients.

In eight cases of duodenal ulcer, and in one following operation for carcinoma of the stomach, phenylbutazone was given in the form of suppositories, each containing 250 mg. The result from suppositories was equal to that from oral administration, but cessation of therapy was necessary in two patients, because of œdema in one and bloating and constipation in the other.

TOXICITY

Although the incidence of toxic reactions has been reduced by a lower dosage schedule they are still sufficiently common to demand close clinical observation of the patient on phenylbutazone therapy. Reactions are not likely to occur until after seven to ten days, so that short-term therapy as in acute gouty arthritis and bursitis is relatively safe.

TABLE III.
COMPLICATIONS OF PHENYLBUTAZONE THERAPY

Total number of patients	270
Patients with one or more side effects	27%
Major side effects	2.2%
Drug discontinued because of reaction	8%

The majority of complications appear before the twelfth week. This interval between the first and twelfth week is the critical period as far as toxic reactions are concerned.[2] In this series of 270 patients 27% had one or more side effects, most of which were minor and transient in nature (Table III). The major reactions occurring in 2.2% were pulmonary œdema in two, hæmorrhage from a duodenal ulcer in one, severe dermatitis in one, severe vomiting in one patient who later was found to have carcinoma of the liver, and hepatitis in one patient who later was found to have diffuse collagen disease. None of these major reactions was fatal.

Therapy was discontinued because of side effects in 8% (22 patients). Thirteen had gastrointestinal complaints, five had salt retention with œdema, three had dermatitis and one had severe headache. The total number of major and minor complications is shown in Table IV. Nausea was the most common complaint, with occasional vomiting and diarrhœa.

TABLE IV.—COMPLICATIONS OF PHENYLBUTAZONE THERAPY

Gastro-intestinal		Dermatitis	
Gastric irritation	23	Rash	16
Vomiting	3	Stomatitis	3
Diarrhœa	5	Lethargy	7
Irritation of ulcer	3	Headache	4
Hæmorrhage	1	Epistaxis	3
		Dizziness	4
Fluid retention with œdema		Palpitation	2
Peripheral	10	Confusion	2
Pulmonary	2	Swollen salivary glands	2
Face	12	Blood	1

Phenylbutazone may cause a significant retention of sodium chloride producing water retention with œdema, decrease in urine volume and increase in weight. The œdema is most pronounced on higher levels of dosage and often disappears completely when the lower maintenance dose is reached. This initial retention of fluid may cause a temporary drop in red blood cell count and hæmoglobin value by hæmodilution and should not be interpreted as a toxic effect on blood or bone marrow.

The great majority of skin lesions are slight and disappear rapidly when the drug is discontinued. In this series there was only one case of severe dermatitis in which the patient continued therapy after the onset of the rash.

HÆMATOLOGIC STUDIES

Because of previous alarming reports on the possible effect of phenylbutazone on the blood and bone marrow,[10] complete blood studies were carried out at three to four week intervals on the patients who received the drug for more than two weeks. The blood work was done by one technician who was aware of the problem and searched for any abnormality.

Two hundred and sixty-eight blood studies were made, including hæmoglobin determinations, red and white cell counts and smear examinations. In no case was any abnormality found which prompted discontinuing the drug. A few minor fluctuations in Hb. value occurred, but there was no indication of agranulocytosis, thrombocytopenia or aplastic anæmia. In one patient (Table IV) who had been on 400 mg. daily for 18 months, a toxic granulation was found in the cytoplasm which was considered to be due to a chronic genito-urinary infection resistant to antibiotics. One patient had been on maintenance therapy for over four years, seven patients over three years and thirteen patients over two years. Nevertheless, fatalities due to toxic reaction on the bone marrow have been reported. Kersley and Mandel[11] observed agranulocytosis with depression of all marrow elements in a pa-

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tient who received the drug for only 17 days at a dose never exceeding 400 mg. daily. They felt that routine white cell counts were useless and that warning the patient to report malaise, fever, and sore throat was a more important precaution.

SUMMARY

If additional medication other than less toxic salicylate compounds is found to be necessary, phenylbutazone is the drug of choice in the treatment of ankylosing (Marie-Strümpell) spondylitis. In gouty arthritis, phenylbutazone is at least equal to, and in some reports better than, oral colchicine, with less gastro-intestinal irritation. In rheumatoid arthritis, rheumatoid arthritis with psoriasis, osteoarthritis, disc lesions and some other miscellaneous rheumatic disorders reported above, a trial of phenylbutazone should be considered and the drug discarded if no relief is obtained in one week. In post-herpetic neuralgia the results appear to be superior to those with previous forms of therapy, but a larger study is required.

The majority of complications were minor and transient in nature, and the major reactions subsided on cessation of therapy.

The danger of toxicity is reduced by close clinical observation of the patient and prompt withdrawal of the drug at the first sign of reaction. Phenylbutazone should be avoided in patients with a history of peptic ulcer, hypersensitivity, or congestive heart failure. The lowest possible maintenance dose should be used, and the drug discontinued if no improvement is noted in seven days. In this series of patients, blood studies revealed no toxic effect from the drug on blood or bone marrow.

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RÉSUMÉ

Si la conduite du traitement exige un autre médicament que les composés moins toxiques à base de salicylate, la phénylbutazone est le choix par excellence dans la spondylarthrite ankylosante de Pierre Marie. Dans l'arthrite goutteuse, la phénylbutazone s'est montrée égale sinon supérieure à la colchicine *per os* avec cependant moins d'irritation gastro-intestinale. Dans la polyarthrite chronique évolutive avec psoriasis, les rhumatismes chroniques dégénératifs, les lésions discales et d'autres formes d'arthrite décrites dans le texte on peut se permettre l'essai de la phénylbutazone à condition de ne pas insister si aucune amélioration ne s'est manifestée après une semaine de traitement. Les résultats obtenus dans la névralgie post-herpétique semblent meilleurs que tout ce que l'on a vu jusqu'à présent, mais ils demandent à être vérifiés par l'analyse d'un plus grand nombre de cas.

La majorité des complications qui ont surgi au cours du traitement furent passagères et de peu d'importance; les réactions sérieuses disparurent dès que le médicament fut supprimé. Une surveillance étroite du malade avec interruption immédiate du traitement au moindre incident diminue les risques de réaction toxique. Il est préférable de ne pas employer la phénylbutazone chez des malades ayant des antécédents d'ulcus, d'hypersensibilité ou d'insuffisance cardiaque. Dans ces cas comme dans ceux décrits plus haut, il convient d'adopter la plus basse dose d'entretien possible et cesser au bout d'une semaine si l'amélioration espérée ne s'est pas produite. Dans la série de 270 malades sur laquelle porte cet article, on n'observa aucune répercussion toxique sur la moëlle ou sur le sang.

"DURAFOAM"—A NEW MATERIAL FOR REST SPLINTS IN THE PREVENTION OF DEFORMITY IN THE CHRONIC RHEUMATIC DISEASES

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THERE IS NO SPECIFIC CURE at the present for rheumatoid arthritis. It is all important, therefore, to prevent or correct any deformity that may lead to the tragedy of crippledom. The Canadian Arthritis and Rheumatism Society have calculated that the annual loss of wages through disability of the chronic rheumatic diseases is in excess of $75,000,000 (Dominion Bureau of Statistics, figures for 1951). This paper is concerned with a new material that can be used to help prevent some of the disablement in these diseases.

Deformity in rheumatoid arthritis develops in two stages. The most obvious is joint destruction. But even earlier than that can be detected, muscle spasm, the reflex mechanism to minimize pain by limiting movement of a painfully swollen joint, has insidiously started to lead to deformity. This spasm, though perhaps helpful to the joint, is ultimately harmful to the muscle itself by limiting movement and so leading to the wasting of disuse. This is particularly true during the night when the joints are pulled into deformity by powerful flexor muscles that cannot at that time be consciously controlled. Thus deformity becomes inevitable unless corrective measures are applied, especially at night.

This has long been recognized and various types of splints have been devised to offer a "spasm substitute"—one that would rest the joint satisfactorily, but at the same time avoid damaging the muscle and so avoid atrophy.[1] Until recently, plaster of Paris was the chief medium used for this purpose, but unfortunately it has many disadvantages, chief of which is the messiness involved in its use. Both doctor and patient require protective clothing, and

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