(4E 00676). The washers withstand repeated autoclaving, but are usually replaced after approximately six cycles. The caps tend to become rough and difficult to unscrew after two or three cycles, but this difficulty can be overcome by application of a film of Silicone MS 550 (Savory and Moore).

Sterilisation is carried out in the late afternoon when the rest of the day's autoclaving has been completed. The pressure is increased gradually up to 10 lb. per sq. in. over a period of 10–15 minutes. At the end of the sterilising period all cocks are closed except an " atmospheric balancing valve " and the door is left sealed overnight. This ensures that the bottles are not removed while their internal pressure remains high and obviates the risks of injury to the autoclave attendant from explosion of bottles. Using this technique it is exceptional for a bottle to break and sterility tests with Browne's tubes and bacteriological cultures have invariably been satisfactory.

Suitable storage and warming cupboards were made in the hospital workshop from standard steel office equipment two-door cabinets measuring approximately 60 in. high by 36 in. wide by 18 in. deep. The upper one-third is fitted with a steel liner. Three 250-watt heating elements are spaced beneath the lower plate of the liner. In the heating compartment two wire racks constructed in the manner of wine racks, each holding 12 bottles, are placed horizontally. The heating elements are controlled by a thermostat which can be adjusted to suit individual circumstances and temperature requirements. If the racks are used in rotation there is adequate time for the fresh bottles to reach an adequate temperature and there are always 12–24 bottles of heated water available. The lower unheated shelves accommodate a further 70 bottles. Antiseptic lotions are prepared by adding one measure of a suitable concentration of antiseptic solution from an automatic measuring dispenser to one bottle of water.

The bottled water supply, which has now been in use for nearly two years, is popular with nursing and medical staff. Success depends particularly on proper attention to details, such as temperature regulation, siting of cabinets and containers, and closures which are convenient to handle. The system involves minimal capital outlay, is cheap to maintain, and results in economy of antiseptic solutions.

B. M. HIBBARD
G. HESKETH.

Liverpool, 6.

SPIRONOLACTONE AND GYNÆCOMASTIA

SIR,—Dr. W. G. Smith's letter of Oct. 27 prompts me to report a similar experience.

A 56-year-old white male was troubled by painful thighs sixteen months ago. Pitting œdema of both upper and lower extremities was prominent a month later (September, 1961). The white-blood-cell count was 10,500 per c.mm. (18% eosinophils). Skin and stool tests excluded trichinosis. Paper electrophoresis disclosed a moderate reduction of the serum-albumin to 3·4 g. per 100 ml. (normal $4·2 \pm 0·2$ g. per 100 ml.), and slight elevation of the gamma-globulin. The creatine excretion was 211 mg. in 24 hours. Muscle biopsy was not performed. Skin lesions suggestive of dermatomyositis were never seen. Relatively small doses of prednisone were soon followed by a fall in the number of eosinophils, diminution in muscle tenderness, and partial subsidence of œdema. Discrete elevations appeared on the ridged forearm skin: they were usually about the size of a matchhead and unaccompanied by inflammatory reaction. There was no proteinuria. X-ray study of the gastrointestinal tract, lungs, and paranasal sinuses disclosed no abnormalities. Chemical investigations of the blood were within normal limits. No evidence pointed to disseminated lupus erythematosus. Kidney, liver, and heart functions were normal.

On Nov. 13, 1962, benzydroflumethiazide (' Naturetin ') was added to prednisone, in 5 mg. doses twice daily. Pitting œdema continued to trouble the patient, and spironolactone (' Aldactone ') was introduced as 100 mg. tablets, three times daily, and was continued for two months. Pain and paræsthesiæ of both breasts prompted the systematic withdrawal of first, the benzydroflumethiazide on Feb. 1, 1962, and then spironolactone on Feb. 16. The sensory disturbance did not abate until the patient had stopped taking the spironolactone for a fortnight. During this time he continued to take 10 mg. of prednisone daily.

After a lapse of two months a further trial of spironolactone was arranged. In the interim the 24-hour creatine excretion had fallen to 87 mg.; the blood-count was within normal limits, and the serum-protein partition was within the expected range. Between April 19 and May 15, 1962, the patient received 7·5 g. of spironolactone in 300 mg. daily divided doses; from May 16 to Aug. 26, 7·27 g. of ' Aldactone A ' was given (25 mg. three times a day). On Aug. 26 painful breasts disturbed the patient again, but this time they were much larger and firmer, receding in size quite slowly after spironolactone was withdrawn. While the breasts are still larger than they were originally, they are no longer tender or paræsthetic. Prednisone was stopped in September, 1962. From April 11 to Aug. 26 the patient received 50 mg. of hydrochlorothiazide daily as replacement for benzydroflumethiazide.

I am inclined to view the gynæcomastia as related to the chemical structure of spironolactone, which so resembles progesterone. Indeed, it has been shown that progesterone can inhibit the sodium-retaining action of aldosterone and desoxycorticosterone, although the introduction of a hydroxyl group annuls this action.[1] It is possible that spironolactone gives rise to related compounds which have the capacity to produce this unpleasant side-effect. It is of interest that 18·6 g. of the compound produced the symptoms initially, whereas 14·77 g. gave rise to much the same result on second trial.

New York. RALPH M. SUSSMAN.

MUSHROOMS AND TOADSTOOLS

SIR,—The so-called sacred mushroom of the Mexican Indians *Teonanácatl*, erroneously designated *Teonanacatyl*, is only briefly mentioned in your leader (Nov. 3). Scientific interest in the higher mushrooms, particularly the Mexican magic mushrooms, is shown by the large number of publications which deal with the historical, ethnographic, botanical, chemical, pharmacological, and medical aspects of this subject.

The sacred mushroom of the Aztecs, *Teonanácatl*, is not *Panaeolus campanulatus*, as you state, but includes several closely related types of mushroom, especially the genus Psilocybe and some species of the genera Stropharia, Panaeolus, and Conocybe.[2] These mushrooms, together with the other magic drugs such as *peyotl* and *ololiuqui*, played an important part in the religious ceremonies and medicinal practices which were part of the ancient Indian cultures of Mexico. They are still used today for the same purposes in remote mountainous districts of South Mexico. We are indebted particularly to the American research-workers Wasson and Wasson for the exhaustive investigation of the mushroom cult in its present-day form. They have recorded the results of their 30 years' of ethnomycological studies in their book *Mushrooms Russia and History*.[3] Prof. R. Heim, director of the Muséum National d'Histoire Naturelle, Paris, has classified most of the magic mushrooms still in use today and has managed to cultivate some species in his laboratory.[2]

The isolation, chemical characterisation, and final synthesis of the hallucinatory substance in the Mexican magic mushrooms were carried out in the research laboratories of Sandoz Ltd., Basle.[4–6] Two new active principles were isolated from

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Psilocybe mexicana Heim for the first time—psilocybin and psilocin. Psilocybin is 4-phosphoryloxy-N,N-dimethyltryptamine, and psilocin is 4-hydroxydimethyltryptamine. They are indole compounds which, like serotonin (5-hydroxytryptamine), an important widely distributed neurohumoral factor in warm-blooded organisms, belong to the group of hydroxylated tryptamine derivatives.

Psilocybin and psilocin are, therefore, in no way specifically toxic. The psychotomimetic and hallucinatory effect of psilocybin and psilocin is added to an excitation syndrome which is manifested in animals by pupillary dilation, pilo-erection, slight hyperglycæmia, electroencephalographic activation, &c., attributable to a stimulation of sympathetic centres. The stimulation of monosynaptic reflexes and serotonin antagonism is a further pharmacological characteristic of these substances.[7–9]

The psychic effects of psilocybin and psilocin in man are identical with those which have been described many times as the consequence of taking magic mushrooms. The first clinical investigations with the pure substance were carried out in the university psychiatric clinic in Basle by Gnirrs and Rümmele [10] and by Delay and coworkers in Paris.[11] Many trials have since been carried out on healthy human beings and on psychiatric patients.[12] Small doses of about 4 mg. have a greater effect on mood, usually producing a sense of wellbeing. Higher doses—i.e., 6–12 mg. or more—produce profounder psychic changes associated with an altered spatial and temporal perception, and with a change in the awareness of the self and the body image. Combined with these changes, is visual stimulation that can lead to illusions and hallucinations. In this dream-like state, long-forgotten events, even some from earliest childhood, are often vividly recalled.

These effects of the substances contained in the Mexican magic mushrooms are now being tested for their usefulness in aiding psychiatric exploration. The applications of psilocybin to drug treatment in psychotherapy is also being investigated.

Pharmacological and
Pharmaceutical-chemical Laboratories,
Sandoz Ltd.,
Basle.

A. CERLETTI
A. HOFMANN.

INTRA-ARTICULAR STEROIDS AND DESTRUCTIVE ARTHROPATHY

SIR,—Your annotation of Dec. 1 recalls a dermatological instance. Two " punched-out " circular ulcers each about the area of a penny had developed rapidly on the middle third of one leg of a patient with chronic rheumatoid arthritis.

Prednisolone (1 mg. b.d.) and prednisone cream (0·25%) were prescribed. Signs of exudation and the slight surrounding induration disappeared, but the ulcers remained completely stagnant for four weeks without a trace of granulation or epithelial ingrowth; they had all the appearance of dead flesh.

Systemic prednisone was continued while an antiseptic cream containing 0·065% digitoxin was used topically instead of prednisolone. Signs of active circulation reappeared almost at once, granulation and epithelial encroachment followed quickly, and healing was complete in less than four weeks.

In view of the detailed researches of the late Valy Menkin [13] on inflammation, and the recent work of Zweifach [14] and others on the microcirculation, it is surely time to abandon the vague umbrella expression " anti-inflammatory " and try to establish the exact pharmacology of drugs influencing the inflammatory process. A flight-engineer would not be content to explain the action of the blades of a helicopter by saying that they were anti-gravitational!

London, S.E.13 ALLAN CHATELIER.

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SEMINAL VITAMIN B_{12} AND STERILITY

SIR,—In December, 1961, a 73-year-old grazier consulted me because of angina pectoris and breathlessness. His hæmoglobin level was 4·4 g. per 100 ml., and he had a histamine-fast achlorhydria and a megaloblastic bone-marrow. The administration of intramuscular vitamin B_{12} was quickly followed by restoration of full vigour: the patient has been able to play an active part in sheep-shearing, and his 37-year-old wife is now 4 months pregnant. It is tempting to suppose that the vitamin B_{12} was effective not only in correcting this farmer's anæmia but also in improving the maturation and motility of the spermatozoa in a manner similar to its action in the 35-year-old patient reported by Dr. Sharp and Professor Witts (Oct. 13).

In a recent review on spermatozoa, Lord Rothschild [1] stated that the free energy for sperm movement is provided by the dephosphorylation of adenosine triphosphate (A.T.P.) the enzyme adenosine triphosphatase being distributed all along the tail. For experimental convenience the scheme for resynthesis of A.T.P. in spermatozoa has been studied under anaerobic conditions, fructose (secreted into seminal plasma by the male accessory organs) being converted into lactic acid to supply energy for this process. Rothschild has measured the anaerobic heat production of bull spermatozoa by microcalorimetry, and has found that the actual heat production is about 20% less than the theoretical heat production based on the conversion of 1 mole of fructose to 2 moles of lactic acid. In asking the question " where did the lost heat go?", he offers two possible explanations. Firstly, spermatozoa may not convert fructose stoichiometrically to lactic acid. Secondly, during lactic-acid production the seminal plasma may become too acid to support movement and hence heat production tails off. A third explanation which offers itself is that under natural (i.e., non-experimental) conditions fructolysis does not occur since an adequate blood-supply to testicular tissue allows the aerobic metabolism of fructose to proceed to completion. It is in the field of oxidative phosphorylation that vitamin B_{12} may have an important part to play.

In his communication on seminal B_{12} and sterility (Sept. 29, p. 644), Dr. Watson quoted the work of Busch,[2] who showed that the addition of vitamin B_{12} to stored bull serum improved its eventual motility and enhanced its degree of fertility. A relationship between the presence of vitamin B_{12} and facilitation of energy release in spermatozoa might be found by consideration of a piece of work in an entirely different field by Dr. George and Dr. Haan (Sept. 22). Prompted by the death of a patient with thyroid storm and macrocytic anæmia, these workers have made a study of the relationship between thyrotoxicosis and vitamin B_{12}. They demonstrated a fall in temperature and gain of weight in thyrotoxic patients treated with vitamin B_{12}, suggesting that this effect may be due to protection against the uncoupling of oxidative phosphorylation produced by thyroxine. Since cytochrome oxidase is the terminal member in the chain of respiratory enzymes—serving to pass electrons to oxygen, Dr. George and Dr. Haan were moved to speculate on whether one can be certain that cytochrome oxidase is not vitamin B_{12} or one of its derivatives. They point out that cytochrome-oxidase preparations have never been freed completely of copper,[3] and since the absorption spectra of copper and cobalt are quite similar this could lead to confusion of these two metals by spectrophotometric analysis.

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