in several assays in the manner described in the B.P. 1958. Fig. 1 is a record of an assay.

This method of estimation has three advantages. Firstly, it is sensitive enough to permit the assay of concentrations of ergometrine as low as 100 ng./ml. Secondly, the use of height of contraction as the response rather than latency as in earlier methods (Vos, 1943; Foster and Stewart, 1948) increases the accuracy of measurement. Finally, the absence of tachyphylaxis permits the use of a standard assay design and consequently simplifies calculation of results.

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Modification of Histamine Sensitivity after 48/80 Treatment

SIR,—Feldberg and Talesnik (1953) and Parratt and West (1957) have shown that in the rat treatment with the histamine liberator, compound 48/80 causes a prolonged fall in the levels of histamine in tissues.

Female rats were treated with a single intraperitoneal dose of 48/80 (2 mg./kg. found to be the LD33). They were killed after the times shown in Table I. Histamine sensitivity was determined on the isolated oestrous uterus which was stimulated electrically by a method similar to that described by Csapo and Corner (1952) for the rabbit uterus. Stimulation and recording characteristics were constant throughout the course of these experiments.

TABLE I

DOSES OF HISTAMINE (μG./10 ML.) PRODUCING 20 PER CENT INHIBITION OF UTERINE CONTRACTIONS IN 48/80 TREATED RATS

Time after 48/80 (days)	Dose of histamine	Mean dose
0·25	100, 100, 120	107
1	20, 20, 40	27
2	2, 5	4
4	4	4
6	2, 5, 10	6
8	4, 5, 8, 8	6
12	4, 6, 8, 8	7
20	2, 2	2
28	5, 7	6
40	20, 20	20
50	20, 20	20

As on the spontaneously contracting rat uterus, the action of histamine against electrically-induced contractions was inhibitory. The doses of histamine which when added to the organ bath (10 ml. capacity) produced 20 per cent inhibition of the height of contraction was taken as the index of sensitivity.

Determinations of the histamine sensitivities of 11 untreated rats gave a value of 27 μg. $\pm$ 3 (mean $\pm$ S.D.). Table I shows the histamine sensitivies of rats after 48/80 treatment.

It can be seen that the sensitivity to histamine decreased 6 hr. after treatment. However, 2 days later there was observed an increase in sensitivity which persisted for 28 days. 40 to 50 days after treatment sensitivity decreased towards the control figure for untreated rats. The sensitivity of the uteri to the inhibitory action of adrenaline was unaltered throughout the course of these experiments.

These results show that 48/80 treatment selectively modifies the sensitivity of the uterus to applied histamine. There is a similarity in the period during which increased sensitivity persisted in these experiments and the period during which tissue levels of histamine remain low after 48/80 treatment. Feldberg and Talesnik (1953) have shown that after 48/80 treatment the tissue content of histamine is lowered, remaining low up to and sometimes beyond 50 days after treatment. It may be that there is an inverse relationship between histamine sensitivity and histamine tissue content. Paton (1957) has observed that those species like the rat with high tissue histamine levels are relatively insensitive to the effects of injected histamine, whereas those species like the guinea-pig with low histamine levels are more susceptible.

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A Reaction between Prednisolone Phosphate and Sodium Metabisulphite

SIR,—The reactivity of bisulphites with certain substances of pharmaceutical interest has been previously noted (Higuchi and Schroeter, 1959).

We observed the pH values of certain aqueous experimental preparations containing prednisolone phosphate and sodium metabisulphite to rise for several days after preparation. A close examination of the ultra-violet absorption spectra of their aqueous dilutions showed slight bathochromic shifts (1–2 mμ); increased amounts of sodium metabisuphite produced greater shifts. The maximum shift attainable was 8 mμ, when λ_{max} occurred at 255 instead of at the normal wavelength of 247 mμ. A recently developed enzyme method for prednisolone phosphate (Boon, 1960), which is specific for phosphoric esters of solvent extractable alcohols, when applied to fresh mixtures of prednisolone phosphate and sodium metabisulphite gave the expected values. After the spectral change had occurred, the prednisolone phosphate contents, as determined by the enzyme method, were unexpectedly low. In a series of solutions of constant prednisolone phosphate and various metabisulphite contents there was after equilibration a rank correlation between the shift in λ_{max} and the deficit of