of the modification of the active transport of glucose through the intestine in different functional states, such as diabetes[4], fasting[5] and hyperthyroidism[6], and these results suggest that in studying the maintenance of homoeostasis of certain body constituents it is necessary to take into account this activity of the intestinal mucosa, in addition to increased ingestion and other variations in the activity of the digestive system.

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PHARMACOLOGY

Antagonism of Colistin-sulphonamide Synergism by *para*-Aminobenzoic Acid

Russell[1] reported an *in vitro* synergism between colistin methane sulphonate and sulphonamide drugs using a number of *Proteus* isolates. He found that the combinations were bactericidal at therapeutic levels, that the ratios of the drugs were not critical, and that the effect was present over a wide range of hydrogen ion concentration. The observations were extended to polymyxin *B* sulphate and sulphonamides with similar results.

Since colistin alters the permeability of certain bacteria[2], the possibility was considered that the synergism may be mediated by an alteration of the cytoplasmic membrane to a degree insufficient to cause bacteriostasis in itself, but sufficient to permit the passage of sulphonamides into the cell. If such were the case, the actual inhibition of growth would be a result of a block in folic acid formation and would be overcome by *p*-aminobenzoic acid[3].

To test this, *Proteus vulgaris* and *P. mirabilis* were inoculated into culture tubes containing 'Bactotryptic' soy broth (Difco), with and without *p*-aminobenzoic acid (PABA), and with colistimethate sodium and certain sulphonamide drugs, singly and in combination. Growth was assessed by means of the optical density of each culture after incubation for eleven hours at 37° C. Results were expressed as the percentage of inhibition as compared with appropriate control cultures without drugs.

Table 1 shows the results of one experiment in which sulphanilamide was used; Table 2 shows a similar pattern when the sulphonamides used were extracted with water from sensitivity disks (Baltimore Biological Laboratories) each of which contained 1·0 mg total of a mixture of sulphadiazine, sulphamethazine, and sulphamerazine (triple sulpha). The *Proteus* isolates had a low order of sensitivity to sulphonamides alone and to colistimethate sodium alone. The combination of the two drugs resulted in much greater inhibition, and this enhanced activity was largely overcome by PABA. Attempts to antagonize the synergism with folic acid were not successful; the extent to which this may be related to the inability of the organisms to incorporate or utilize pre-formed folic acid has not been determined.

Table 1. Synergism between Colistimethate Sodium and Sulphanilamide and its Reversal by PABA

	P. vulgaris Inhibition (per cent)		*P. mirabilis* Inhibition (per cent)	
	No PABA	With PABA	No PABA	With PABA
Sulphanilamide	7	0	25	2
Colistimethate sodium	10	2	8	15
Combined	71	7	86	15

Sulphanilamide, 400 μg/ml.; colistimethate sodium, 50 μg/ml.; PABA, 0·01 per cent.

Table 2. Synergism between Colistimethate Sodium and Triple Sulpha and its Reversal by PABA

	P. vulgaris Inhibition (per cent)		*P. mirabilis* Inhibition (per cent)	
	No PABA	With PABA	No PABA	With PABA
Triple sulpha	13	0	5	0
Colistimethate sodium	14	7	10	3
Combined	61	10	72	4

Concentrations same as in Table 1.

The present results tentatively suggest that the sulphonamide-colistin synergism is mediated through an initial alteration by colistin of the permeability of the cytoplasmic membrane of *Proteus* species in such a way as to permit entry of the sulphonamide into the cell. The sulphonamide then retards cell replication by interference with folic acid synthesis.

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HISTOLOGY

Branched Cells in the Epidermis of the Sheep

Branched cells positive for alkaline phosphatase, and which are darkened by osmium iodide, have been found in the epidermis of certain African primates[1–3]. Other dendritic cells have been revealed by gold impregnation and methylene blue in the non-pigmented epidermis of guinea-pigs, rabbits and man[4], and by gold impregnation and electron microscopy in the epidermis of man[5].

Histochemical preparations for acetylcholinesterase have revealed numerous large branched cells in the epidermis and upper external sheaths of the follicles of several breeds of sheep (Merino, Southdown, Suffolk, English Leicester and Border Leicester). By contrast, such acetylcholinesterase-positive branched cells were not revealed in other species investigated at the same time (bandicoot *Perameles nasuta*, possum *Trichosurus vulpecula*, laboratory rabbit, laboratory rat, and ox). Neither the techniques for butyrylcholinesterase nor for alkaline phosphatase revealed these branched cells in sheep skin. Moreover, they did not stain with osmium iodide or gold chloride and did not produce a positive 3,4-dihydroxyphenylalanine (DOPA) reaction.

The regions of the sheep examined included several producing hair and several producing wool. Samples were also taken from four regions (lower lip, between nares, nipple and vulva) devoid of follicles. In addition, samples were taken from the placenta of a full-term sheep foetus with plaques of wool follicles on the amnion[6]. Acetylcholinesterase-positive branched cells were found on all of the regions where there were follicles, but they were not found in the non-follicular regions. Even on the amnion the branched cells were confined to the plaques having follicles.

The processes of the branched cells (Fig. 1) extend throughout the epidermis, some even to the cornified layer, but the perikarya are evenly spaced (about 50μ