facturers are producing them. Men are needed to make the best use of them, to test and maintain them, to improve them and to devise new ones. These men are of many kinds, from high-school graduates to doctors of philosophy, but one thing they must have in common—knowledge of the fundamental laws of physics on which the operation of these tools depends.

Training in physics for all these operations and at all these levels is urgently needed.

(3) EMPHASIS UPON THE STUDY OF PHYSICS

Even before the war the place of physicists in industry was becoming increasingly recognized. This is made evident by available statistics concerning the growing number of physicists employed in industrial laboratories, and the expanding membership lists of national societies in the field of physics. In the last two years, as a result of war requirements, the need for physicists, as compared with other professions, has grown very rapidly. Recent estimates indicate that the need is now growing at the rate of 1,500 to 2,000 per year, and that the current annual supply from schools is no more than 500. The need referred to applies to individuals having five or more years experience in physics in the sense of Section 1 (b) above (*i.e.*, at least one year of study or experience after the bachelor's degree). It does not include the much larger need for individuals well enough prepared in mathematics and physics for training in technical war operations. This need has been officially estimated at more than 100,000. The War Policy Committee considers this a very conservative estimate.

Accordingly, it is urged upon officers and faculty members of high schools, colleges and universities to recommend immediately that students enroll in courses in fundamental physics and their prerequisites in mathematics, whatever the stage in the student's educational career. The recommendation should be made only to students who possess natural aptitude for these studies. Such guidance for the student will to a marked degree increase his value to his country in this critical time.

Advisers of students may wish to point out to the latter that the study of physics (irrespective of any post-war career) is immeasurably helpful in any walk of life, because such study improves the ability to understand the new physical environment which man is creating for himself, and which, far more even than now, is bound to exert a major influence upon social, political and economic trends.

Moreover, great new developments now appearing behind the veil of war secrecy are, beyond all possibility of doubt, establishing the basis for unprecedented peace-time applications of physics in industry. Some of the greatest of these are along lines not yet developed as branches of engineering. They give promise of opening large and fruitful fields for the useful and profitable employment of those well equipped with a broad, fundamental training in physics.

The committee recommends to high schools that they emphasize mathematics through trigonometry and that in teaching physics the aim should be to give a well-planned, thorough course in the fundamentals of the subject. Unless the high school is properly equipped to offer specialized training in the applications of physics, it should leave this to the higher institutions.

To colleges and universities the committee recommends making provision for the most advanced courses for which students are qualified and, where facilities are suitable, the establishment of intensive courses, with laboratory practice, in electronic devices and high frequency circuits.

(4) SPECIAL TRAINING OF PHYSICISTS

Since the demand for physicists exceeds the supply which can be expected from the normal operations of schools and colleges, this committee endorses the program of special agencies operating to supplement this supply.

(5) USE OF PHYSICISTS

The need for physicists in the total war effort is so vital, and the demand so greatly exceeds the supply, that it is essential that every available individual trained in physics be placed in a position in which full use is made of that training. The committee therefore would strongly endorse the adoption of any policies and regulations by the Selective Service System, personnel divisions of the Armed Services and other government agencies concerned to achieve this end more effectively.

SPECIAL ARTICLES

THE BIOCHEMICAL SPECIFICITY OF SULFANILAMIDE AND OF OTHER ANTIBACTERIAL AGENTS

EVIDENCE was given from this department[1] which led to the hypothesis that the antibacterial action of sulfanilamide was due to its competitive inhibition of enzymes which normally interacted with *p*-aminobenzoic acid or a closely related substance. The antag-

[1] D. D. Woods, *Brit. Jour. Exp. Path.*, 21: 74, 1940.

onism between these two compounds has now been frequently confirmed, but Johnson,[2] on the basis of a reversal with urethane of the effect of sulfanilamide on luminous bacteria, questioned the hypothesis. We have found that urethane specimens, under certain conditions, may antagonize growth inhibition of *Streptococcus haemolyticus* and *Escherichia coli* caused by sulfanilamide, but that these conditions are limited and illustrate well the reasons for the original hypothesis. The findings are as follows:

(1) Much more urethane than *p*-aminobenzoic acid is necessary to antagonize the antibacterial action of a given quantity of sulfanilamide (Table I). Thus 1

TABLE I

THE DIFFERENT EFFECTS OF URETHANE AND *p*-AMINOBENZOIC ACID

Conditions of testing: *Strep. haem.* (Group A) was grown as previously described[7] with 10^{-7} *M* pantothenate.

Addenda		Growth after (days)		
Sulfanilamide, $M \times 10^{-5}$	Reversing agent, *M*	1	2	3
0	0	+	+	+
5	0	0	0	+
5	*p*-aminobenzoate, 2×10^{-8}	+	+	+
5	*p*-aminobenzoate, 4×10^{-9}	0	+	+
5	urethane, 10^{-2}	0	+	+
5	" 5×10^{-3}	0	+	+
5	" 5×10^{-4} and less	0	0	+
10	0	0	0	0
10	*p*-aminobenzoate, 4×10^{-8}	+	+	+
10	*p*-aminobenzoate, 4×10^{-9}	0	0	+
10	urethane, 5×10^{-2} to 5×10^{-6}	0	0	0
50	0	0	0	0
50	*p*-aminobenzoate, 4×10^{-7}	+	+	+
50	*p*-aminobenzoate, 8×10^{-8}	0	0	0
50	urethane, 5×10^{-2} to 5×10^{-6}	0	0	0

molecule of sulfanilamide is antagonized by about 1/5,000th of a molecule of *p*-aminobenzoic acid, but between 1 and 100 molecules of urethane were found necessary, and this effect was not reproducible with certainty. It is difficult to picture the mode of action of so small a proportion of *p*-aminobenzoic acid except by a specific enzyme mechanism,[3] but this does not necessarily apply to urethane.

(2) The urethane antagonism was shown only towards low concentrations of sulfanilamide, which were just anti-streptococcal. With slightly different concentrations the urethane had no reversing activity or was inhibitory. Five times this limiting concentration of sulfanilamide was not antagonized by many times the concentration of urethane. The urethane effect thus can not be said to parallel that of *p*-aminobenzoic acid, which can be effective against 50 times such a concentration of sulfanilamide. More *p*-aminobenzoic acid is needed to antagonize such higher concentrations of sulfanilamide, the quantities being roughly proportionate. The constancy of the ratio Cs/Cp, where Cs is the minimal concentration of sulfanilamide necessary for bacteriostasis in the presence of a concentration Cp of *p*-aminobenzoic acid, is consistent with sulfanilamide acting by inhibition of an enzyme normally reacting with *p*-aminobenzoic acid. Their similarity in structure makes this feasible. The non-competitive type of antagonism shown by urethane specimens is already known to be given by methionine,[4] which is structurally entirely unrelated to sulfanilamide. It has, however, been indicated by Harris and Kohn[4] that this action is consistent with *p*-aminobenzoic acid being the compound primarily affected by sulfanilamide. Methionine is regarded as biochemically related to *p*-aminobenzoic acid in that the acid is necessary for the normal production or metabolism of methionine.

No mechanism is suggested for the action of urethane. Antagonistic effects of inhibitory compounds are, however, well known under the term "chemotherapeutic interference." Cases of such interaction which have been investigated are, like the effects with narcotics quoted by Johnson,[2] not necessarily between structurally related compounds. Specific biochemical mechanisms can, however, be given,[5] such as the inactivation of hydrogen transporting systems by acriflavine and their replacement by methylene blue. This is in distinction to the suggestion[2] of promiscuous interaction between inhibitors and illustrates the general tendency to biochemical definition of pharmacological action rather than *vice versa*. An approximation to biochemical localization of narcotic action has been made by Michaelis and Quastel.[6]

(3) Other antibacterial agents are now known which in the manner of sulfanilamide are related to

[2] F. H. Johnson, SCIENCE, 95: 104, 1942.

[3] This large difference between the interacting quantities of *p*-aminobenzoic acid and sulfanilamide has been given as an argument against a competitive mechanism for the action of sulfanilamide (S. D. Rubbo and J. M. Gillespie, *Nature*, 146: 838, 1940) and has been repeatedly quoted as such (*e.g.*, by Johnson). The argument is now abandoned or no longer emphasized by its authors (*cf.* S. D. Rubbo and J. M. Gillespie, *Lancet*, I: 36, 1942) and is in fact no objection to, but is best interpreted in terms of competitive enzyme inhibition.

[4] H. I. Kohn and J. S. Harris, *Am. Jour. Physiol., Proc.*, 133: 354, 1941; E. Strauss, J. H. Dingle and M. Finland, *Jour. Immunol.*, 42: 313, 1941; J. S. Harris and H. I. Kohn, *Jour. Pharmacol.*, 73: 383, 1941.

[5] N. von Jancso and H. von Jancso, *Z. Immunforsch.*, 88: 275, 1936; H. McIlwain, *Biochem. Jour.*, in press; summarized in *Lancet*, 2: 762, 1941.

[6] M. Michaelis and J. H. Quastel, *Biochem. Jour.*, 35: 518, 1941.

growth essentials. The "narcotic" hypothesis gives no expectation of mutual specificity between their effects. Such does, however, exist (Table II) and is readily

TABLE II

SPECIFICITY OF ANTIBACTERIAL AGENTS

Organism and reference to conditions of testing	Addenda		Growth
	Inhibitor, *M*	Metabolite, *M*	
Strep. haem.[1]	0	0	+
Bact. coli[8]	sulfanilamide, 3×10^{-4}	0	0
	"	*p*-aminobenzoate, 10^{-7}	+
	"	pantothenate[11], 10^{-7} to 10^{-4}	0
	"	nicotinamide[11], 10^{-7} to 10^{-4}	0
Staph. aureus[9]	0	0	+
	pyridine-3-sulphonamide, 10^{-2}	0	0
	"	*p*-aminobenzoate, 10^{-7} to 10^{-4}	0
	"	pantothenate, 10^{-7} to 10^{-4}	0
	"	nicotinamide[11], 10^{-5}	+
Strep. haem.[7]	0	0	+
Diplococcus pneumoniae[10]	pantoyltaurine, 10^{-4}	0	0
C. diphtheriae[10]	"	*p*-aminobenzoate, 10^{-7} to 10^{-4}	0
	"	pantothenate[11], 10^{-6}	+
	"	nicotinamide[11], 10^{-7} to 10^{-4}	0

explained in terms of competitive enzyme inhibition. Thus the inhibition by pyridine-3-sulfonamide is unaffected by the presence of *p*-aminobenzoic acid or pantothenic acid, but is antagonized by a definite fraction of its concentration of nicotinic acid. Pantothenic acid, but not nicotinic or *p*-aminobenzoic acids, reverses the inhibition due to pantoyltaurine.

HENRY MCILWAIN,
Leverhulme Research Fellow
DEPARTMENT OF BACTERIAL CHEMISTRY
(MEDICAL RESEARCH COUNCIL),
THE UNIVERSITY, SHEFFIELD, ENGLAND

THE EFFECT OF INSULIN SHOCK ON LEARNING IN THE WHITE RAT

SINCE its introduction by Sakel, insulin shock has been successfully used in the treatment of certain cases of dementia praecox and allied psychiatric and psychoneurotic conditions to bring about a remission of the symptoms which in certain cases has lasted indefinitely. There has been, as yet, no agreement as to the theory of its action, although there is no doubt that a cerebral anoxia is produced, with which the therapeutic effect is associated and upon which it is probably dependent. It occurred to one of us that the psychopathological symptoms might be regarded as recently formed habits of response, with younger and metabolically more unstable synaptic patterns of neuronal associations involved. If this were true, the more recently formed habit pattern should be more easily broken up, because of the effects of the cerebral anoxia. It was decided to test this hypothesis by observing the effect of insulin shock on habit formations in the experimental animal.

This is a preliminary report of a study involving the effect of insulin shock on habits of varying degrees of stability and age in the white rat. Exploratory observation established a tentative optimum dosage as one unit of insulin per 12 grams of body weight. In the exploratory group of animals, this medication caused a state of lethargy and/or coma lasting about two hours with a latent period of approximately 40 minutes. In almost half of the cases, there occurred severe convulsive seizures in which movements of the head region were particularly pronounced. All animals seemed to be normal within eight hours after injection.

Two mazes differing in complexity and type constituted the bases for the learning situations. The first group of animals began on a multiple-unit, elevated T maze. When this had been mastered to a criterion of 9 perfect runs in a sequence of 10 trials, 100 additional runs were made. Upon completion of this overlearning, training was begun on a linear arrangement of the Warner-Warden multiple-unit alley maze. The same criterion of learning was used, but the additional overlearning was omitted. During the learning of the alley maze no practise was given on the elevated maze. As soon as an animal had learned both mazes it was given 20 trials on each maze separately. Any animal making more than two errors in this stage was discarded. Following the test period, each rat was injected with the appropriate dose of insulin. Twenty-four hours after injection, the animal was again given 20 trials on each maze. A similar procedure was followed for the second group except that training was begun on the alley maze and the elevated maze habit was made the younger and less well-established habit. All rats were males.

The results are given in the appended table. It will be noted that, because of the rotation of groups, the first six animals who began their training on the elevated maze are found in the lower right side of the table, when the newer or alley habit is considered. That is, rat No. 1 began on the elevated maze and continued on the alley maze, whereas rat No. 7 reversed this procedure.

The present report will deal only with comparisons in terms of total errors during the pre-post-shock test

[7] H. McIlwain, *Brit. Jour. Exp. Path.*, 20: 330, 1939.
[8] P. Fildes, *ibid.*, 19: 239, 1938.
[9] H. McIlwain, *ibid.*, 21: 136, 1940.
[10] H. McIlwain, *ibid.*, in press; summarized in *Chem. Ind.*, 61: 96, 1942.
[11] Low concentrations of these compounds are in some cases necessary for growth, and were then present in the inhibited cultures; further quantities (those quoted) were necessary for reversal.