divided into three groups, each of which was fed one of the diets shown in Table 1 (a, b, and d).

As shown in Table 2, the high protein diet showed a protective effect and the high lard diet an unfavorable effect in comparison with that which was high in carbohydrate.

TABLE 2

Time after operation (mos.)	High protein diet		High carbohydrate diet		High fat diet	
	Diabetes		Diabetes		Diabetes	
	Total	%	Total	%	Total	%
1	4/16	25	2/18	11.1	7/17	41.1
2	9/16	56.2	14/18	77.7	17/17	100
4	10/16	62.5	15/17	88.2	15/15	100
5	10/16	62.5	12/13	92.3	15/15	100
6	11/15	73.3	11/12	91.6	14/14	100
7	11/15	73.3	11/11	100	10/10	100
8	9/12	75.0	10/10	100	5/5	100

In overfed rats (fed three times daily with a high carbohydrate diet) the evolution of diabetes was much faster than in those fed once a day and eating less food. Furthermore, the same diet but restricted in quantity (about 80 per cent of the amount of food eaten by a normal rat) produced a marked delay in the time of initiation of diabetes (see Table 3).

TABLE 3

Time after operation (mos.)	Underfed		Overfed		Ad libitum	
	Diabetes		Diabetes		Diabetes	
	Total	%	Total	%	Total	%
1	1/13	8	4/17	23.5	2/18	11.1
2	5/12	41.6	15/15	100	14/18	77.7
4	3/7	42.8	10/10	100	15/17	88.2
5	1/7	14.3	7/7	100	12/13	92.3
6	4/7	57.1	5/5	100	11/12	91.6
7	3/7	42.8	3/3	100	11/11	100
8	3/7	42.8	3/3	100	10/10	100

Diabetes appeared first in those rats which received their food once a day (in a quantity proportional to their body weight) rather than in those receiving the same amount of food divided into three feedings at 7-hour intervals. It may be supposed that the higher postprandial hyperglycemia of the former diet exerts an unfavorable effect, whereas the postprandial hyperglycemia resulting from the latter is less intense.

SUMMARY

In the experiments described the following observations have been made:

(1) The toxic and diabetogenic action of alloxan increases in rats fed a low protein diet and even more so in the case of a high lard or ox fat diet.

(2) The action of these fat diets was corrected by the addition of methionine, thiouracil, or coconut oil, but there was no modification either by addition of choline or sulfonamide or by increase in the protein proportion.

(3) In rats fed other high fat diets (olive oil, butter) the actions of alloxan were not modified, but there was a slight diminution when high oleomargarine or corn oil diets were fed. However, complete protection was observed when a high coconut oil diet was administered.

(4) The unfavorable effect of the high lard diet was observed also on the initiation and evolution of diabetes due to subtotal pancreatectomy. Contrarily, feeding a high protein diet and especially treatment with thiouracil had a favorable effect.

(5) Diabetes appeared first in subtotal pancreatectomized rats which were overfed, then in those which ate ad libitum, and finally in those which were underfed. Diabetes appeared in rats fed a single meal before it did in those eating the same amount of food divided into three meals.

Mechanism of the Antibiotic Action of Certain Quinones

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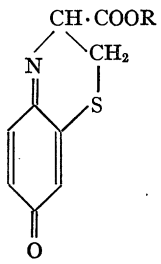
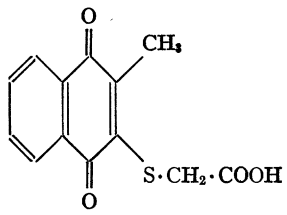
A widely accepted theory suggests that many antibiotics function chiefly because of their ability to interfere with the sulfhydryl groups of enzymes concerned in bacterial metabolism (*2*).

In a recently published report by Colwell and McCall (*3*) it is claimed that the inhibition of bacterial and fungus growth by 2-methyl-1,4-naphthoquinone and related quinones also is due to a reaction of the quinones with sulfhydryl compounds. This theory is supported by the fact that excess amounts of sulfhydryl compounds are able to suppress the antibiotic properties of 2-methyl-1,4-naphthoquinone. Kuhn and Beinert (*8*) have shown that p-benzoquinone and cysteine-ethylester-hydrochloride react by addition of the —SH compound to a free position in the quinone molecule; in two further steps a condensation product (I) is formed. Fieser and Fieser (*4*) describe the reaction between 2-methyl-1,4-naphthoquinone and thioglycolic acid, where an addition product of the formula (II) is formed.



(I)



(II)

As far as quinones are concerned, the theory described is, however, not a satisfactory one. As Colwell and McCall (*3*)

state, it does not explain the antibacterial and antifungal potencies of 2-methyl-3-methoxy-1,4-naphthoquinone, because this quinone has no free position on the quinone side of the molecule. Oxford (*9*) has shown that among p-benzoquinone derivatives the spinulosin-trimethylether (trimethoxytoluquinone) is one of the strongest bacteriostatics of this group; certainly, no possibility of addition exists in this compound. The effect of excess amounts of sulfhydryl compounds on the bacteriostatic potency of some quinones does not prove conclusively the existence of a specific antagonism between quinones and —SH groups. The inactivation of the quinones can be achieved by excess amounts of other strongly reducing substances (e.g. sodium bisulfite) as well.

Quinones are very reactive substances. In experimental work done in this laboratory (*6*), the inhibitory potency of many quinone derivatives on some enzyme systems (urease, papain, catalase, etc.) was tested. It was found that some of the very strongest antibiotics had no, or nearly no, effect on the activity of these enzymes. In the case of urease and papain, certainly —SH groups, which function as activating groups for the enzymatic process, are involved. A certain parallelism between antibiotic properties and inhibitory potency on urease and papain should be expected, if really the reaction with sulfhydryl compounds would be the dominant mechanism of the antibiotic action. By the same experiments it was shown that some enzymes, in which certainly no sulfhydryl groups play any role, also are inhibited by quinones. Of course, the inhibition of enzymes without —SH groups also could be one of the means by which the quinones exert their antibiotic effects. It is also known that quinones can react with amino groups of proteins and amino acids; the tanning properties of p-benzoquinone are used in industry to a certain extent (*5*). It could be imagined that, by tanning the protein compounds of the bacterial cellular membranes, normal cell division could be inhibited. Another possible mechanism can be derived from the relatively elevated oxidation-reduction potential of most of the quinones. Wieland (*10*) has demonstrated that p-benzoquinone is a strong inhibitor of some dehydrogenases. Thus, quinones could act as antibiotics by interfering with bacterial respiratory enzymes and thereby inhibit the synthesis of essential cell components.

The theory that the mode of antibiotic action of the quinones is a complex one can be supported by the fact that some of the quinones with strongest bacteriostatic potency on *Staphylococcus* have very little effect on *Escherichia coli* or on some species of yeast as *Saccharomyces cerivisiae* or *Torula utilis* (*7*), while other quinone derivatives, whose toxicity on *Staphylococcus* is quite negligible, exert rather strong effects on the other organisms mentioned. In experiments with *Planaria gonocephala* we were able to show that, using one compound, it was possible to distinguish two different dominant factors, progressing from higher to lower concentrations of the toxic agent. The data obtained lead us to believe that the effect of higher concentrations of the quinones is dominantly due to the tanning property of these compounds, while in lower concentration the quinones exert their antibiotic effects by the inhibition of some enzyme of the organism, most probably some of the oxidative-reductive enzymes.

The experiments mentioned suggest clearly that the antibiotic action of the quinones is not due to a single reaction, but to a very complex mechanism. The mode of action proposed by Colwell and McCall is certainly only one of the means by which the quinones exert their effects and, in most cases, seems not to be the dominant one.

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Virus Hemagglutination[1]

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The phenomenon of virus specificity is a familiar biological problem, but, with the possible exception of the bacteriophage group of viruses, the nature of the factors responsible for this specificity has not been clearly defined. With respect to the bacteriophage there is evidence that the virus unites with a specific component on the cell—in the case of *coli* and coliphage, for instance, with an antigenic surface polysaccharide (*5*). In the animal virus group, Curnen and Horsfall have shown that the P.V.M. virus can unite with some cellular component of lung tissue (*2*). The combining material was described as tissue particles.

It is evident that accurate characterization of the specific combining tissue components, especially with respect to their structural chemistry, might lead to an understanding of virus specificity in terms of chemical or metabolic relations between the virus and cell. In this connection it was thought that one possible approach to the problem would be the elucidation of the factors responsible for the hemagglutination phenomenon first described by Hirst (*3*) and studied further by Burnet, McCrea, and Stone (*1*) with respect to the alteration of cell receptors by virus action. The results of some preliminary studies along these lines are the subject of this communication.

From red blood cells[3] which are specifically agglutinated by certain viruses it has been found possible to prepare lipid

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[2] Fellow of National Health and Medical Research Council of Australia.

[3] Human red cell residues from plasma fractionation were kindly supplied by the Antitoxin and Vaccine Laboratory, Massachusetts Department of Public Health.