

**Table 1. Chemoselective Reduction of Esters with  $\text{KEt}_3\text{BH}$  in Tetrahydrofuran at 0°C<sup>a</sup>**

entry	compounds	product	yield, <sup>a</sup> (%)
1	ethyl caproate	hexanol	99
	cyclohexene oxide	cyclohexene oxide	100
2	ethyl cyclohexanecarboxylate <sup>b</sup>	cyclohexylmethanol	94
	cyclohexene oxide	cyclohexene oxide	99
3	ethyl benzoate	benzyl alcohol	95
	cyclohexene oxide	cyclohexene oxide	94.9
4	ethyl benzoate	benzyl alcohol	96
	N,N-dimethylhexaneamide	N,N-dimethylhexaneamide	98.6
5	ethyl benzoate	benzyl alcohol	95
	capronitrile	capronitrile	94.9
6	isopropyl benzoate <sup>c</sup>	benzyl alcohol	93
	capronitrile	isopropyl benzoate capronitrile	7 95
7	ethyl benzoate	benzyl alcohol	94
	quinoline	quinoline	98.6
8	ethyl benzoate	benzyl alcohol	100
	2-bromooctane	2-bromooctane	93
9	ethyl benzoate	benzyl alcohol	99.4
	bromocyclohexane	bromocyclohexane	98.6
10	ethyl benzoate	benzyl alcohol	100
	1-dodecene	1-dodecene	97
11	ethyl caproate <sup>d</sup>	hexanol	85
	isopropyl benzoate	ethyl caproate	14
		benzyl alcohol	12
		isopropyl benzoate	83
12	ethyl caproate <sup>d</sup>	hexanol	95
	<i>t</i> -butyl benzoate	<i>t</i> -butyl benzoate	95
13	ethyl benzoate <sup>d</sup>	benzyl alcohol	94
	<i>t</i> -butyl caproate	<i>t</i> -butyl caproate	100

<sup>a</sup>A mixture of one mmol each of an ethyl ester and other substrate was reacted with 2.2 mmol  $\text{KEt}_3\text{BH}$  at 0°C for 15 min. Yields were estimated by GLC, using naphthalene as an internal standard.

<sup>b</sup>Reaction for 3 h. <sup>c</sup>Reaction for 6 h. <sup>d</sup>At -15°C.

$\text{KEt}_3\text{BH}$  (1.37 ml) solution in THF at 0°C. After 15 min, the reaction mixture was quenched with 1 ml of water and oxidized with  $\text{H}_2\text{O}_2\text{-NaOH}$  for 2 h at 30°C. After drying with

anhydrous  $\text{K}_2\text{CO}_3$ , the GLC analysis of THF layer showed a 99% yield of hexanol and cyclohexene oxide (100%) intact. The results are summarized in Table 1. As shown in the Table, ethyl caproate, ethyl cyclohexanecarboxylate and ethyl benzoate can be reduced in the presence of cyclohexene oxide, N,N-dimethylcaproamide or capronitrile (entry 1-5) with excellent chemoselectivity. The reduction of ethyl cyclohexanecarboxylate is a little slower and completed in 3 h at 0°C (87% in 1 h). The reduction of isopropyl benzoate is also slow, however good selectivity is realized in 6 h (entry 6).  $\text{KEt}_3\text{BH}$  is also able to reduce ester selectively leaving quinoline, 2-bromooctane, bromocyclohexane or 1-dodecene intact (entry 7-10). We do not expect these kinds of selectivity with  $\text{AlH}_3$ , BMS (at 65°C), or  $\text{LiBH}_4$  with a MeO-9-BBN catalyst. And  $\text{KEt}_3\text{BH}$  is also susceptible to steric effect. Thus ethyl esters could be selectively reduced in the presence of *t*-butyl esters at -15°C (entry 12 and 13). When the competitive reduction of ethyl benzoate and *t*-butyl caproate was carried out at 0°C, the selectivity was not satisfactory. Thus benzyl alcohol was obtained in 83% yield at 0°C, but only 75% of *t*-butyl caproate remained unattacked. Even at -15°C, the chemoselectivity between ethyl caproate and isopropylbenzoate was less satisfactory giving the mixture of 85% hexanol and 12% benzyl alcohol together with unreacted esters (entry 11).

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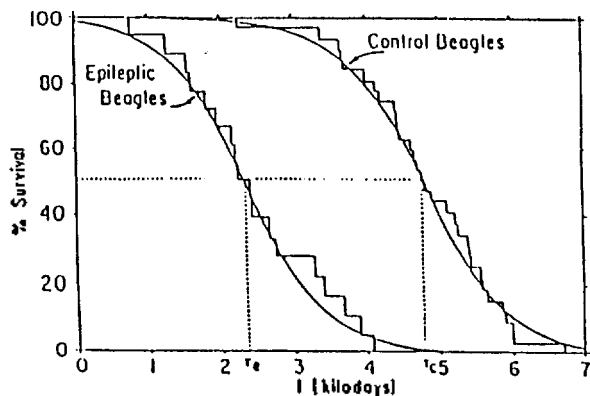
## Role of Water as Our Life Expectancy due to the Agings and Various Cancers

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In a series of my recent papers and lectures, we discussed the roles of water in modern diseases such as cancers, dia-

betes and AIDS (Acquired Immune Deficiency Syndrome)<sup>1-3</sup>. According to our water environment theory, the local di-



**Figure 1.** Percent survival as a function of age for protected control beagles and for protected, but epileptic, beagles.

ordered water environment changes in our body such as cells or tissues *etc.* brings the diseases. The occurrences of diseases can be explained by some changes of ordered water environment in cells or tissues to the new disordered water environment observed locally. Some of them can be observed experimentally.

In this paper, we will discuss the problem of agings as well as the diseases from our water environment model.

Of course, the definition of aging is not so simple since it is a process that all observe and understand on an intuitive basis. The progressive processes that lead to aging are characterized by loss of organization at the organ, tissue, cellular, subcellular, and molecular levels.

The basis of these aging processes, we believe, is that the loss of ordered water inside the body which bring the increase of disordered water outside the body make the major roles.

As early as 1839, Verhulst suggested that the fraction, *S* of a human population surviving can be represented by an equation which can be written as

$$S = \frac{1}{1 + \exp[-(a - bt)]} \quad (1)$$

Now, let us explain some of survival data versus age which exhibit a reverse sigmoid shape by our water environment theory as follows. Case I; Nonsurvival from the diseases due to the single cause or the agings due to the homogeneous populations.

Assume that the fraction of disordered water which have been altered is *q* and that of ordered water which are unchanged is *p*. Here *p* + *q* = 1. We also assume that the increase of disordered water versus time is proportional to the product of the values of *p* as well as *q*.

This assumption is based on the recognition of autocatalysis equation.

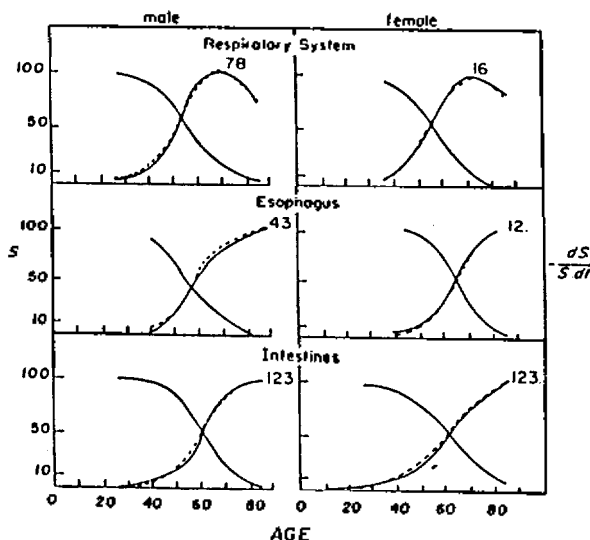
Then

$$\frac{dq}{dt} = kqp = kq(1 - q) \quad (2)$$

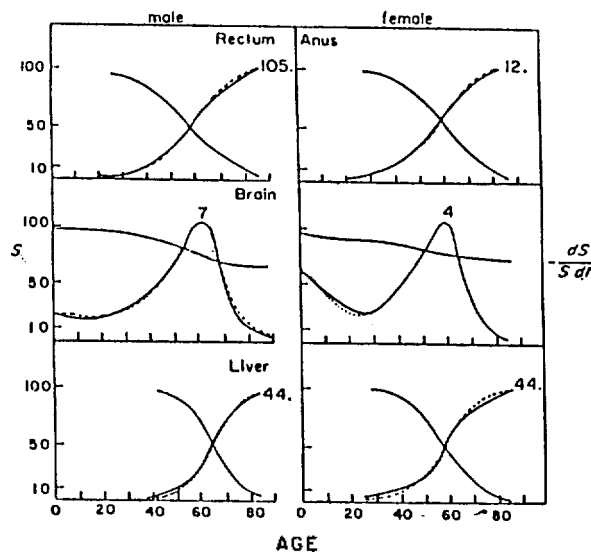
then,

$$k dt = \int \frac{dq}{q(1 - q)} = \int \frac{dq}{q} + \int \frac{dq}{1 - q} \quad (3)$$

$$k(t - \tau) = \ln \frac{q}{1 - q} \quad (4)$$



**Figure 2.** The solid curve starting at 100 is the postulated survival curve *S*. The derivative of *S* divided by the corresponding ordinate gives the broken curve, which is superimposed on Dorn's curve for the number of cases of cancer occurring per 100,000 population at the age indicated by the abscissa. The agreement is good. The scale for each Dorn curve is determined by the maximum incidence of that cancer and is given on each curve at the age of maximum incidence.



**Figure 3.** The solid curve starting at 100 is the postulated survival curve *S*. The derivative of *S* divided by the corresponding ordinate gives the broken curve, which is superimposed on Dorn's curve for the number of cases of cancer occurring per 100,000 population at the age indicated by the abscissa. The agreement is good. The scale for each Dorn curve is determined by the maximum incidence of that cancer and is given on each curve at the age of maximum incidence.

or

$$q = [1 + \exp k(\tau - t)]^{-1} \quad (5)$$

here  $\tau$  is the time at which *p* or *q* equals one-half.

or

$$p = 1 - q = [1 + \exp -k(\tau - t)]^{-1} = S \quad (6)$$

which is equivalent to equation (1).

Table 1. Parameters for Dorn curve fits

Type	$\tau_1(\text{yr})$	$k_1(\text{yr})^{-1}$	$C_1$	$\tau_2(\text{yr})$	$k_2(\text{yr})^{-1}$	$C_2$	$\tau_3(\text{yr})$	$k_3(\text{yr})^{-1}$	$C_3$
Respiratory System (M)	55	0.146	0.95	85	0.082	0.05			
Respiratory System (F)	55	0.146	0.985	92	0.11	0.015			
Esophagus (M)	58	0.172	1						
Esophagus (F)	64	0.172	1						
Intestines (M)	61	0.164	1						
Intestines (F)	62	0.113	1						
Rectum (M)	60	0.133	1						
Rectum (F)	61	0.115	1						
Brain (M)	0.5	0.15	0.07	57	0.11	0.15	129	0.20	0.78
Brain (F)	0.5	0.155	0.12	55	0.12	0.08	135	0.11	0.80
Liver (M)	62	0.177	1						
Liver (F)	57	0.158	1						

To test the equation (1), for example, the age at death of each these 32 protected control beagles or protected but epileptic beagles are illustrated by the step function for fractional survival<sup>4</sup> in Figure 1.

The smooth curves are calculated from our water environment theory. The survival parameter = 4778 (controls) or 2335 (epileptics) days and  $k = 1.77 \times 10^{-3}$  (controls) or  $1.86 \times 10^{-3}$  (epileptics) day<sup>-1</sup> are used to get the smooth curve in Figure 1.

Case II; Nonsurvival from the diseases due to the multiple causes or the agings due to the heterogeneous populations.

For the case II, survival  $S$  is the product that results from several independent causes or homogeneous populations and is given by

$$S = \Sigma C_i S_i \quad (7)$$

Here

$$S_i = C_i [1 + \exp - k_i (\tau - t)]^{-1} \text{ and } \Sigma C_i = 1 \quad (8)$$

$C_i$  is the probability of  $i$ th causes or homogeneous population.

Dorn<sup>5</sup> has reported death rates per 100,000 at age  $t$  from 21 different kinds of cancer for both men and women.

Some of the statistics are for the years 1937-1939 for the white population of the United States.

Representative curves are shown in Figures 2 and 3.

The following survival parameters in Table 1 are used to fit the Dorn curve. The agreements are quite satisfactory.

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## Reduction of *o*-Cyanobenzenesulfonyl Chloride with Zinc in an Acidic Medium

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In our research on new heterocyclic compounds containing sulfur and nitrogen, it became important to prepare some 2-substituted benzenethiols and the corresponding disulfides such as 2-mercaptobenzamide(3), dithiosalicylamide(4) and bis(*o*-cyanophenyl) disulfide(6). These compounds are not available commercially, and few synthetic procedures for these compounds have been reported.<sup>1-11</sup> Because the reported methods are inconvenient, we designed new synthetic methods and report the results herein.

We selected *o*-cyanobenzenesulfonyl chloride(2) as the starting material for our study, because it useful functional groups such as -CN and -SO<sub>2</sub>Cl on 1,2-position of benzene

ring. In a previous report,<sup>12</sup> we described a synthesis of *o*-cyanobenzenesulfonyl chloride(2) from saccharin(1) in 85% yield.

Treatment of *o*-cyanobenzenesulfonyl chloride(2) with zinc and concentrated HCl in refluxing EtOH gave 2-mercaptobenzamide(3) in 85% yield. Reduction of *o*-cyanobenzenesulfonyl chloride(2) with zinc-dust and 6N-HCl in methanol at 5°C afforded dithiosalicylamide(4) in 76% yield, whereas in refluxing MeOH the product was 2-mercaptobenzoic acid(5, 71% yield). Treatment of dithiosalicylamide(4) with zinc-dust and concentrated HCl in refluxing water gave 2-mercaptobenzoic acid(5) in 50% yield. On the other hand, the reac-