SULPHUR METABOLISM IN SENILE CATARACT

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THE supposition that human senile cataract might be associated with some disorder of sulphur metabolism was based upon two facts. First, sulphur containing compounds such as cystine and glutathione, which are believed to play an important rôle in normal lens metabolism, are known to disappear from the lens during the development of cataract. Second, there is some evidence that the experimental cataract akin to the human senile type which can be readily produced in rabbits by the administration of naphthalene, may be due to the withdrawal of cystine from the body as a whole and consequently from the lens. For it has been shown that naphthalene is detoxicated in the body of the rabbit by conjugation with cystine and that it is excreted as α -naphthyl mercapturic acid (Bourne and Young, 1934); while Nakashima (1934) has made the converse observation that if extra cystine were given the toxicity of naphthalene was reduced and the lens lesions were prevented. These findings suggest a relationship between cystine deficiency and cataract formation; and it seemed reasonable to suppose that in senile patients some defect of sulphur metabolism might create a deficiency of sulphhydryl compounds in the lens, thus initiating the cycle of degenerative changes culminating in mature cataract; or, alternatively, that some toxic substance, resulting from metabolic failure or tissue breakdown peculiar to old age, might by requiring cystine for its detoxication divert this substance from the lens.

As a means of testing this hypothesis it was decided to investigate the distribution of urinary sulphur in cataractous patients. Normally, sulphur is ingested by human beings chiefly in the form of sulphur-containing proteins, very little inorganic sulphate being present in the common foodstuffs. The metabolism of sulphur is almost wholly the metabolism of cystine, methione, and related compounds derived from protein digestion. The bulk of such sulphur is oxidized in the body and excreted in the urine as *inorganic sulphate*; a small fraction is used for the detoxication of substances such as indole and skatole which are

excreted in the urine as *ethereal sulphates*. Organic sulphur compounds present in the urine are grouped together in what is called the "*neutral sulphur*" fraction; they are believed to arise from the breakdown of body tissues and to represent endogenous sulphur metabolism. Normally, therefore, the amount of neutral sulphur remains relatively constant while the inorganic sulphate varies with the protein intake. Ethereal sulphate excretion depends upon the amount of toxic substance absorbed.

The distribution of the total sulphur of the urine among the three fractions, *inorganic sulphate*, *ethereal sulphate*, and *neutral sulphur*, may be taken as an index to the sulphur metabolism of the body. In the case of patients with senile cataract it was expected that any failure of the normal mechanism for the oxidation of ingested protein sulphur would be revealed by a diminution in the inorganic sulphate and a corresponding rise in the neutral sulphur (organic) fraction; while, if the cataract were due to a toxic process, a rise in the ethereal sulphate or neutral sulphur fractions would be observed.

Experimental

The plan of experiment was to estimate the three urinary sulphur fractions in a group of patients with senile cataract and in a control group over a period of several days. The numerous practical difficulties involved in this type of experiment as applied to hospital patients are obvious. In order to minimise them it was decided to investigate cataractous and control cases simultaneously and under identical conditions, and to base all conclusions on a comparison of the results obtained from these two groups. Five patients with senile cataract and six control cases were studied. All were patients in the wards of the Birmingham and Midland Eye Hospital, the controls being selected from among those patients with ocular conditions such as retinal detachment, squint, etc., in which the lens was not affected. In no case was there any evidence of albuminuria. The diet of each subject was controlled as rigidly as possible, chiefly with a view to standardizing the protein and sulphur intake, and also in the hope that, if any abnormality of sulphur metabolism were present, it would be more sharply defined by contrasting the effect of high and low protein diets. Just over 2,000 calories per day were allowed, the patients being in a resting condition, *i.e.*, either in bed or sitting quietly throughout. Each diet was continued for three or four successive days, and the urine was collected in 24-hour periods. Details of the diets are given in Table I.

TABLE I
SCHEDULE OF DIETS (Daily Allowance).

Food	Normal 2261 calories			High Protein 2325 calories			Low Protein 2328 calories		
	oz.	Protein gm.	Sulphur gm.	oz.	Protein gm.	Sulphur gm.	oz.	Protein gm.	Sulphur gm.
Bread -	8	20.61	0.227	7½	19.40	0.206	8	20.61	0.227
Butter -	2½	0.63	0.006	2	0.21	0.002	3½	0.84	0.008
Egg -	2	7.50	0.109	2	7.50	0.109	—	—	—
Cheese -	1	7.73	0.071	2½	19.39	0.184	—	—	—
Beef -	4	21.17	1.283	4	21.17	1.283	—	—	—
Potato -	4	2.24	0.033	—	—	—	4	2.24	0.033
Cabbage -	4	1.78	0.066	—	—	—	—	—	—
Apples -	8	0.89	0.013	—	—	—	8	0.89	0.013
Sugar -	1½	—	—	1½	—	—	2½	—	—
Cream -	1	0.70	0.008	—	—	—	1	0.70	0.008
Marmalade -	1	0.16	—	—	—	—	2	0.32	—
Milk -	5	4.62	0.047	15	13.80	1.39	4	3.69	0.37
Oatmeal -	—	—	—	2	9.02	0.123	—	—	—
Ham -	—	—	—	2	11.08	0.642	—	—	—
Beans -	—	—	—	3	5.85	0.048	—	—	—
Cauliflower -	—	—	—	—	—	—	6	3.03	0.110
Banana -	—	—	—	—	—	—	2½	0.91	0.097
Total -	—	68.03	1.863	—	107.42	3.987	—	33.23	0.866

(Figures taken from Sherman, 1933.)

Inorganic sulphate, ethereal sulphate, and total sulphur were estimated gravimetrically on the 24-hour urine specimen by the method of Folin (1905). The gravimetric method, although tedious, was found to be the most accurate method available for the determination of urinary sulphates. Denis's (1910) reagent was used for oxidation in the total sulphur estimations. The amount of sulphur present in the neutral sulphur fraction was obtained by subtracting the combined inorganic and ethereal sulphur from the total sulphur.

Results

In Table II are collected the results from two groups of patients on normal protein diet. Each patient received the diet for three or four successive days, the analytical results for the first 24-hour specimen are omitted from the table. As the figures show, there is no striking difference to be observed between the cataractous and control groups.

TABLE II

Distribution of Urinary Sulphur in Patients with Senile Cataract and in Control Cases.
(Normal Diet: Protein, 68 gm.; Sulphur, 1.8 gm.; Calories, 2340.)

Subject	Age	Sex	Day of Diet	gms. Sulphur excreted in 24 hours as				Per cent. of Total Sulphur excreted as		
				Total Sulphur	Inorganic Sulphate	Ethereal Sulphate	Neutral Sulphur	Inorganic Sulphate	Ethereal Sulphate	Neutral Sulphur
CONTROL CASES										
L. H. -	33	♂	2nd	0.363	0.270	0.020	0.073	74	6	20
			3rd	0.520	0.401	0.032	0.087	77	6	17
Y. W. -	40	♀	2nd	0.552	0.425	0.40	0.087	77	8	15
			3rd	0.382	0.274	0.037	0.071	72	10	18
			4th	0.652	0.451	0.040	0.161	69	6	25
I. N. -	50	♂	2nd	0.616	0.489	0.039	0.088	80	6	14
			3rd	0.224	0.154	0.015	0.055	69	7	24
			4th	0.457	0.335	0.029	0.093	74	6	20
J. J. -	59	♀	2nd	0.448	0.333	0.037	0.078	75	8	17
			3rd	0.441	0.347	0.034	0.060	79	8	13
			4th	0.344	0.258	0.021	0.065	75	6	19
SENILE CATARACT										
G. H. -	63	♀	2nd	0.585	0.466	0.042	0.077	80	7	13
			3rd	0.578	0.412	0.026	0.140	71	5	24
			4th	0.671	0.474	0.037	0.160	70	6	24
J. B. -	65	♂	2nd	0.996	0.821	0.041	0.134	82	4	14
			3rd	0.421	0.332	0.024	0.065	79	6	15
E. J. -	68	♀	2nd	1.028	0.870	0.079	0.079	84	8	8
			3rd	0.770	0.632	0.073	0.065	82	10	8
			4th	0.820	0.645	0.033	0.142	79	4	17

In Table III the effect of varying the protein and hence the sulphur content of the diet is shown. Each diet was given for three successive days; the analytical figures for the last two day's specimen only are given in the table. Again the results obtained from the cataractous patients are similar to those of the control group.

Discussion

The results of this investigation do not reveal any difference in the urinary sulphur distribution in the cataractous patients as compared with the control cases. Although the individual variations are great, the results are in all cases similar, and in general follow the classical distribution of urinary sulphur first described by Folin (1905). That is, the largest fraction of the total sulphur is excreted as inorganic sulphate which varies with the amount

TABLE III

Distribution of Urinary Sulphur in Patients with Senile Cataract and in Control Cases on Diets of Varying Protein Content.

Subject	Age	Sex	Diet	gms. Sulphur excreted in 24 hours as				Per cent. of Total Sulphur excreted *		
				Total Sulphur	Inorganic Sulphate	Ethereal Sulphate	Neutral Sulphur	Inorganic Sulphate	Ethereal Sulphate	Neutral Sulphur
CONTROL CASES										
J. M.	38	♂	low	0'494	0'316	0'046	0'132	64	9	27
			protein	0'480	0'276	0'043	0'161	58	9	33
			normal	1'122	0'880	0'085	0'157	79	7	14
			protein	0'455	0'376	0'016	0'063	83	3	14
			high	1'390	1'165	0'076	0'149	84	5	11
			protein	0'980	0'718	0'073	0'127	78	8	14
			low	0'372	0'227	0'062	0'083	61	17	22
			protein	0'495	0'336	0'046	0'113	68	9	23
E. N.	28	♀	normal	0'626	0'447	0'051	0'128	72	8	20
			protein	0'699	0'510	0'043	0'146	73	6	21
			high	0'646	0'456	0'041	0'149	71	6	23
			protein	0'746	0'563	0'045	0'138	75	6	19
SENILE CATARACT										
D. DT.	73	♂	low	0'341	0'243	0'034	0'064	71	10	19
			protein	0'289	0'172	0'049	0'068	60	17	23
			high	0'621	0'468	0'038	0'125	75	5	20
G. S.	68	♂	protein	0'910	0'695	0'031	0'184	76	4	20
			low	0'641	0'450	0'028	0'163	70	4	26
			protein	0'233	0'138	0'009	0'086	59	4	37
			normal	0'424	0'290	0'028	0'106	68	7	25
			protein	0'454	0'324	0'019	0'093	75	4	21
			high	0'734	0'532	0'048	0'154	73	6	21
			protein							

of protein ingested; while the ethereal sulphate and neutral sulphur fractions remain more or less constant and independent of the total sulphur excretion. In none of the patients with senile cataract is any deviation from the normal to be observed in the behaviour of any fraction. Therefore the results lend no support to the hypothesis that a disorder of sulphur metabolism might be the basis of the pathological changes in the lens in senile cataract; but the experiments are not sufficiently extensive or conclusive to rule out the suggestion completely. A detailed study of the neutral sulphur fraction, the composition of which even in normal individuals is not completely understood, might show the presence of some specific compound associated with senile cataract. The fact that no increased excretion of ethereal

sulphates was found in any of the cataractous patients in our series makes it unlikely that senile cataract is due to a toxic process. Blood glutathione estimations were done on a number of these patients; the results, which have already been published (Campbell, 1936), showed a normal blood glutathione in every case.

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ABSTRACTS

MISCELLANEOUS

- (1) **McKee, S. Handford (Montreal).**—A syphilitic ulcer of the eyelid. *Canadian Med. Assoc., Jl.*, September, 1936.

(1) McKee's patient was a man aged 40 years who had been treated for syphilis in 1925. Symptoms had been present for three weeks beginning as a pimple in the lower lid. On examination an ulcerative process involving the outer $\frac{2}{3}$ of the lid on its margin was found. A good deal of destruction had taken place. The condition was diagnosed as a gumma and appropriate treatment brought about rapid improvement.

Photographs of the lid on admission and after a fortnight's treatment are appended.

R. R. J.

- (2) **Kalt, M. M. (Faris).**—Bilateral orbital tumour with double exophthalmos cured by mercurial treatment. (Tumeur orbitaire bilatérale avec double exophtalmie guérie par un traitement mercuriel). *Arch. d'Ophthal.*, Vol. LII, p. 656, 1935.

(2) Kalt reports an interesting case of a male aged 35 years, a brick labourer who had suffered from bilateral exophthalmos for