confirmed by the clinical normality of blood pressure and pulse in these cases of suprarenal infarction described.

The vascular supply of the suprarenal gland is remarkable. Three arteries converge to produce the most vascular organ per gramme in the body. The vein arises from sinusoids in the medulla. Its walls contain a considerable quantity of muscle, and the blood in it is oxygenated, being "arterial" rather than "venous." Occlusion of this large vein results in a haemorrhagic infarction of the gland, which starts in the loose medullary tissue, destroying it completely. The cortex is also destroyed, but often a thin rind of it escapes, helping to form a capsule round the haemorrhagic area. Later this may rupture, the blood spreading down into the perirenal fat and into the retroperitoneal tissues.

The cause of primary venous thrombosis is unknown, though it occurs as a rarity, the portal vein being the commonest of the visceral veins to be affected.

Pregnancy as a Factor.—One other case occurring in pregnancy has been found—in a girl aged 18 with hyperemesis gravidarum. No other clinical facts are given; but at necropsy it was seen that haemorrhage was into the left suprarenal more than the right. Thrombosis of the suprarenal vein was marked.

Summary

A case of haemorrhagic infarction of the right suprarenal gland is described. The clinical picture is compared with that of cases in the literature, and it is considered that this rare condition may be diagnosed in life. The characteristics of the pain—particularly its site, the repeated vomiting, and the remarkable absence of shock—present a well-defined but hitherto unrecognized syndrome.

Differential diagnosis is discussed, with particular attention to other clinical types of suprarenal haemorrhage: (1) haemorrhage in the newborn; (2) Friderichsen-Waterhouse syndrome; (3) haemorrhagic disease. Examples of these are described.

The failure of laparotomy to diagnose cases is noted and a plea put in for exploration of the suprarenals at operation if no other adequate pathological change is found; ligation of a bleeding-point or excision of the gland are measures which might be adopted.

I would like to put on record my deepest gratitude to Prof. Chassar Moir for his great skill and for his kindness to my wife in her illness and to me afterwards. He made available to me all his case notes, and his help has been invaluable. Dr. A. H. T. Robb-Smith has also been most generous in permitting me to have full details of the pathological findings, and in discussing them with me.—K. D. K.

REFERENCES

- Altschule, M. D. (1939). *Amer. J. med. Sci.*, **198**, 17.
 Arnaud, F. (1900). *Arch. gén. Méd.*, **186**, 5.
 Bailey, H., and Keele, K. D. (1936). *Proc. roy. Soc. Med.*, **29**, 42.
 Barsoum, H. (1936). *British Medical Journal*, **2**, 972.
 Corcoran, W. J., and Strauss, A. A. (1924). *J. Amer. med. Ass.*, **82**, 626.
 Goolden, R. H. (1857). *Lancet*, **2**, 266.
 Hall, E. M., and Hemken, L. (1936). *Arch. intern. Med.*, **58**, 448.
 Hektoen, L. (1909). *Trans. Chicago path. Soc.*, **8**, 87.
 Lavenson, R. S. (1908). *Arch. intern. Med.*, **2**, 62.
 Levinson, S. A. (1935). *Amer. J. Surg.*, **29**, 94.
 Lewis, C. J. (1921). *British Medical Journal*, **2**, 706.
 Michaux, J., and Marsset, H. (1923). *Bull. Mém. Soc. méd. Hôp. Paris*, **47**, 161.
 Munson, J. F. (1907). *J. Amer. med. Ass.*, **49**, 19.
 Pearl, F., and Brunn, H. (1928). *Surg. Gynec. Obstet.*, **47**, 393.
 Ryle, J. A. (1936). *Natural History of Disease*, London.
 Severn, A. G. M. (1923). *Lancet*, **1**, 647.
 Simpson, C. Keith (1937). *Ibid.*, **1**, 851.
 Snelling, C. E., and Erb, I. H. (1935). *J. Pediat.*, **6**, 22.

F. E. Maisel and E. Somkin (*J. Allergy*, 1942, **13**, 397) have published a preliminary report on the treatment of the asthmatic paroxysm with nicotinic acid. They found that (a) severe asthmatic attacks were controlled within 3 to 5 minutes, and improvement lasted 3 to 15 hours, in 16 of 21 patients by the intravenous injection of 0.1 g. of nicotinic acid; (b) 5 of 9 chronic asthmatic patients were benefited by 0.2-g. doses given orally three times a day before meals and on retiring; and (c) 11 of 18 patients receiving intravenous therapy followed by oral therapy showed decided improvement in their asthma. The patients experience a flush and a sensation of heat, then often begin to cough, and expel tenacious mucous plugs. The beneficial effect is thought to be produced by the strong vasodilator properties of nicotinic acid, relieving the bronchospasm or directly affecting the pulmonary vessels, and has no bearing on vitamin deficiency. The patients were mostly beyond middle life, often with a well-marked infective element and not responsive to ordinary allergic methods of therapy. No patient developed any disturbing symptom.

THE HERRING AS A SOURCE OF VITAMINS A AND D

A COLLABORATIVE INVESTIGATION

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Conditions determining Food Value

The importance of a food as a source of any particular nutrient depends primarily on two factors—the amount of the nutrient present and the quantity of the food eaten. Most recent books on dietetics and nutrition include the herring among the "protective foodstuffs," and justify this by referring to its excellence as a source of fat-soluble vitamins (cf. Plimmer and Plimmer, 1938; Bourne, 1941; McDonald, 1938; Mottram, 1938, 1940; McCarrison, 1941). Only Wokes (1941) appears to have had doubts.

Examination of the evidence for this belief is rather disconcerting. In the tables of Fixsen and Roscoe (1937-8, 1938-9) four references are given, and they derive from only three authors, one of whom was reviewing the physiology of the sterols and gave no experimental data of his own. More recent papers have been exceedingly scanty, both in number and in informativeness, though an exception on the latter score may be made for that by Lunde *et al.* (1937), who give values for the body oil of herring as under.

Condition of Herring	Vitamin (I.U. per 100 g. Oil)	
	A	D
Fresh, winter	200 to 2,800	9,000 to 15,000
Kipperd	Unaffected	11,500 to 14,500
Canned and stored	Decreased	} 7,000 to 14,000
Canned, kippered	Trace	

These authors do not clearly differentiate between canned herrings that have been submitted to preliminary kippering and those that have not, but they remark that "since kippered herring contains about 12 to 13% of oil, the canned product is a food with . . . a high vitamin D potency." This seems to us to be a conclusion of little practical bearing unless consumption data are also taken into account, so enabling us to assess the importance of the herring as a source of vitamins A and D in the national diet.

From certain figures published by the Herring Industry Board for the year 1937, and made available to us by the kindness of Dr. Magnus Pyke of the Ministry of Food, an idea is to be had of the *per capita* consumption of herrings in this country. It amounted to approximately 1½ oz. a week, of which just under 0.6 oz. was fresh herring. One of us (J. A. L.) has been able independently to obtain a check on these figures, with very satisfactory agreement. The figures for the vitamin D content of herring-flesh oil have little nutritional significance without an accompanying statement as to the oil content of the flesh, which is known to vary considerably. Our own findings, given below, confirm this and cover a range from 3.6 to 20.2% in fresh herring.

The contribution to their average intake of vitamins A and D obtained by the population from herrings clearly cannot be satisfactorily calculated on the basis of published data. We

therefore decided to reinvestigate the matter, examining both canned and fresh herrings.

Methods of Testing

Vitamin A was determined by the spectrophotometric technique on the unsaponifiable matter separated from the glycerides of the oil; vitamin D was estimated by one or other of the recognized methods of biological assay. The determinations of vitamin A were all carried out in laboratory L. The biological assays for vitamin D were carried out in three different laboratories, though not on any one sample at all of them. In two the line test was used, in the third a radiographic technique; one assay in laboratory R was done by the chemical method of bone analysis. The details of technique and experimental design resembled those recommended in the *British Pharmacopoeia*, 1932, and minor modifications and differences are quite unlikely to have introduced differences in result falling outside the usual range of experimental error encountered in such tests.

Vitamin D Tests

Two main series of samples and certain special oils were examined. The first series consisted of oils expressed from five different brands of canned herrings, some with and others without tomatoes. All were examined in laboratory C, and two in laboratory G (one of them in two independent assays). Exploratory tests had been carried out at levels based on the vitamin D values reported in the literature for herring body oil, and all produced in the test animals healing quite insufficient for assay purposes. Tests were then made at higher dose levels, the oils being separated in laboratory C by pressing the fish in muslin and removing water by centrifuging. (The exploratory samples had been separated by ether extraction of the tissue, after grinding it with sodium sulphate.) The results obtained with these samples are given in Table I. The

TABLE I.—Vitamin D in Canned Herring

Sample	Brand	Tomato	Oil in Flesh (%)	Vitamin D (I.U.)		Laboratory
				Per 100 g. Oil	Per oz.* Flesh	
1	A	+	23.0	750	48	C
2	B	+	10.0	550	15	C
3	C	+	16.5	1,720	80	C
				1,980	92	G
4	C	—	18.8	730	35	C
				2,300 : 1,940	120 : 106	G
5	D	—	18.0	650	33	C

* By calculation from preceding two columns.

discrepancy between the values found by laboratories C and G for oil 4 has not been resolved: of the two assays carried out on that sample in laboratory G, the second (the lower) is the more accurate, the limits of error, for $P=0.05$, being 84% to 119%. The error was calculated from a variance analysis: this assay, which was conducted on 40 animals, exclusive of negative controls, is probably the most accurate of those made on the first series of samples 1 to 5.

It is clear that the values found for the body oil of canned herrings are much below the figures reported in the literature for canned or fresh herrings. This raises the question whether the discrepancy is due to variation in the antirachitic value of the fresh fish, to losses during canning, or to the error of biological assay. In view of the relative consistency of these results, both in themselves and with those reported below, we consider that our values are reasonably correct for the samples examined by us. The results with fresh herrings, given later in this paper, do indeed point to a real difference between the vitamin D contents of canned and fresh herrings, for which we are not able to offer an explanation.

In order to establish that the method of extracting the oil with ether does not give rise to any misleading results, a batch of August herrings containing 15.5% of oil was divided, one fillet from each fish being used for solvent (diethyl ether; S.G. 0.735) extraction of the oil and one for pressure extraction. The resultant oils (samples 6 and 7), which were so prepared in laboratory T, were examined in laboratories R and G. In laboratory R they were compared with the international standard preparation in the usual way, and gave values of 1,800 I.U. per 100 g. (expressed oil, sample 6) and 2,000 I.U. per 100 g. (extracted oil, sample 7). The errors of the logarithms of the potency ratios of oil and standard in the

two tests were ± 0.00726 and ± 0.00758 ; the difference is perhaps suggestive, but it was found not to be significant ($t=0.37$, $P=0.7$). A more elaborate comparison was made in laboratory G, where each oil was fed at 3 doses to 16 animals, so distributed that 96 animals were used in six strictly comparable litter-mate groups. It was found that the relative activities of the two oils were as 1.66 : 1 in favour, curiously enough, of the extracted oil. This confirms the result suggested by the finding in laboratory R; for in this more extensive comparison the error was estimated by means of a full variance analysis, and calculation showed that the difference just has statistical significance ($t=2.0$, $P=\text{sl.} > 0.05$). The reason for the higher activity of the extracted oil is unknown, although one of us (J. A. L.) has encountered a similar phenomenon with the vitamin A of liver oils. A possibility is partial denaturation of the protein by the alcohol in the ether used for extraction, with a resultant liberation of vitamin D held in some kind of combination with protein. However this may be, the results dispose of any fear that ether extraction, as carried out, had appreciably reduced the vitamin content of the oils tested.

Next, two samples of herring oil were extracted in laboratory T from fresh fish, the method used being identical with that employed in preparing sample 7. The results of the tests on these two samples—8 and 9—are included with others in Table II. The discrepancy between the two assays of sample 8

TABLE II.—Vitamin D in Fresh Herring

Sample	Mth.	Condition, etc., of Fish	Stage of Fish	Oil in Flesh (%)	Vitamin D (I.U.)		Limits of Error for $P=0.95$ (%)	Lab.
					Per 100 g. Oil	Per oz.*		
6, 7	Aug.	Expressed or extracted oil	?	15.5	1,900	84	87 to 114.5	R
8	"	Oil cold-stored for 14 months + $\frac{1}{2}$ ripe	?	15.2	8,300 3,600	353 153	n.e.p. 85 to 118	C G
10	Sept.	"	+ II	17.0	7,000 5,150	343 258	76 to 132 95 to 105	R R
11	"	$\frac{1}{2}$ ripe	III	15.5	6,300	273	78 to 128	R
12	"	Spent	VII to I	7.7	22,200	479	70 to 143	R
					16,500	354	59 to 169	R
9	Nov.	Recovered pentas	?	12.2	6,100	210	n.e.p.	C
13	Dec.	"	"	3.6	26,000	277	75 to 136	R
14	"	"	More advanced than 13	7.7	15,800	169	70 to 143	R
15	Mar.	Ripe	V to VI	4.2	12,600	149	63 to 159	R
16	July	$\frac{1}{2}$ to $\frac{3}{4}$ ripe	III to IV	17.9	3,900	196	72 to 138	R
17	"	"	III to IV	20.2	3,400	190	73 to 139	R

n.e.p.=no evaluation possible.

* By calculation from preceding two columns.

is rather large, but evaluation of its significance has not been possible. The assay in laboratory G had limits of error, for $P=0.95$, of 84.5% to 118%. In spite, however, of the discrepancy noted, the amounts of vitamin D in these fresh herrings are clearly considerably greater than those found in the five samples of canned herring, or in the two samples (6 and 7) of fresh-herring oil, expressed and extracted, assayed in laboratory R.

The samples in the second main series were prepared in laboratory T from fresh herrings caught at different seasons. Again only the fillets were used (that is, the skin and small bones were retained, but head, tail, and backbone were rejected); they were, like the previous samples, minced, dried with anhydrous sodium sulphate, and rapidly extracted with ether. As will be seen from Table II, they represent fish in various stages; these are indicated in the table by numbers based on the classification of Lovren and Wood (1937). These samples were assayed in laboratory R; the second assay on sample 10 was conducted by the bone analysis (prophylactic) procedure. The figures for samples 6 to 9 are also included in the table for completeness and comparison. Incidentally, it should be noted that the probable limits of error for the assays carried out in laboratory R are likely to have been somewhat underestimated, as no account could be taken of the error of the slope of the dosage-response curve in each test: the calculated limits of error for all assays carried out in laboratory G take this into account. The results obtained in laboratory C were not suitable for the usual type of statistical analysis, and may be a little more inaccurate than those carried out in laboratories R and G.

In spite of certain inconsistencies encountered in these tests, a moderately clear picture is presented by the fresh-herring oils, which appear, as might be expected, to increase in vitamin D content as they decrease in amount (per unit weight of tissue). This tends to level out the vitamin D contents of the flesh, although these still show a range of 84 to 480 units per oz. The average of all eleven samples is 9,400 I.U. (range 1,900 to 26,000 I.U.) per 100 g. oil and 240 I.U. per oz. of flesh.

It is perhaps worth noting that whenever an assay was repeated in laboratory R on a sample of oil previously assayed there a lower value was obtained (samples 10, 12, and 13). The differences were statistically significant for oil 10 (three months' interval, $P=0.02$) and for oil 13 (1 month's interval, $P=0.03$), but not for oil 12 (1 month's interval). It is probably not justifiable to take these figures as in any way proof of the instability of vitamin D in ether-extracted herring body oil, held, like these samples, at 0° C., but they may perhaps suggest the need for care and speed in handling samples of such oils intended for vitamin assay.

Vitamin A Tests

The figures for vitamin A content are shown in Table III. They were obtained spectrophotometrically at wave-length

TABLE III.—Vitamin A in Herring

Sample	Description*	Oil in Flesh (%)	Vitamin A (I.U.)	
			Per 100 g. Oil	Per oz. Flesh†
3	Canned, with tomato	16.5	300†	15‡
4	Canned	18.8	530†	28‡
16	Canadian, canned	ca. 7.0	ca. 2,500	30 to 60‡
17	Canada seal, canned with tomatoes	Not determined		15 to 30‡
8	Fresh—Aug. (14 months stored)	15.2	<5,000	<215
10	Fresh—Sept.	17.0	1,400	68
11	" "	15.5	1,100	48
12	" "	7.7	2,500	55
13	" Dec.	3.6	1,020	10
14	" "	7.7	1,280	28
15	" March	4.2	2,100	25

* For further details see Tables I and II.

† By calculation from other columns, except those marked ‡, which are results of direct determinations.

617 $m\mu$, using the blue colour produced with antimony trichloride, and calculated from the formula

$$\text{I.U. per g.} = E_{1\text{ cm.}}^{1\%} 617 m\mu \times 510.$$

Two purely qualitative tests in laboratory G on the oils from samples 4 and 8 gave results for absorption in the ultra-violet at 325 $m\mu$ consistent with those obtained by the more precise assays at laboratory L. When the samples of canned herring with tomatoes were examined a phase separation of lycopene had to be included to prevent interference with the antimony trichloride reaction of the vitamin A: apart from this the test, like the others, was carried out on the unsaponifiable matter of the oil previously separated by means of sodium sulphate and ether from the flesh. There may be some significance in the fact that the values for canned herring all fall at the lower end of the range for fresh herring; but the number of results obtained is not, in our opinion, sufficient to justify any definite conclusion about the effect of canning on vitamin A in herring flesh.

Discussion and Conclusions

If the results obtained by us are genuinely representative of herring body oil, they tell a somewhat different story from what published figures might have suggested. A paper by Ranganathan (1941), though concerned mainly with Indian fish and shark-liver oils, gave a few figures for (presumably) body oils from sardine, mackerel, ray, and plough-fish: these range from 16,000 to 25,000 I.U. of vitamin D per 100 g.—round about the higher limit found by us for herring oil: no information is given about the oil contents of the fish or as to the presence or absence of liver and gut oil. A recent paper by Holmes *et al.* (1941) also gives some data for the body oils of eel, sardine, herring, menhaden, and rose-fish. Figures of 5,000 to 20,000 I.U. of vitamin D and 34,000 I.U. of vitamin A per 100 g. of oil are quoted, again without reference to the amount of oil in the whole fish. Further, Pugsley (1942) gives some figures for the Pacific species, *Clupea pallasii*, which is

closely related to our own *Clupea harengus*. He found 7.3% of body oil in one sample of the fish, and the oil contained 3,300 I.U. of vitamin D per 100 g. (68 I.U. per oz. flesh), but no vitamin A. We ourselves are not, however, claiming to have made any exhaustive study of the factors affecting the fat-soluble vitamins in herring muscle, or to have encountered the whole normal range of values, so that the figures reported by other workers should be useful as a reminder that our conclusions apply only to herrings having vitamin contents that fall among the values found by us.

However, in calculating the contributions made by herrings to the daily human intake of vitamins, the figures given by these authors are of no very great assistance. In estimating the value of herring as sources of vitamins A and D, therefore, we have thought it best to rely on our own figures. Assuming that the average amounts of vitamins A and D per oz. of fresh herring are 40 and 250 I.U. respectively, that vitamins A and D are lower in the canned fish by the same proportion, so that the respective values per oz. are 8 and 50 I.U., and taking the average weekly consumption per head as 0.7 oz. of fresh herring and 1.2 oz. of canned, bloatered, or kippered herring—both slight overestimates; ignoring, furthermore, the high probability that smoking and curing involve greater losses of fat-soluble vitamins than does canning, we are able to estimate an outside value for the average individual daily intake of vitamins from these sources:

	Units per oz.		Units consumed per Day	
	Vitamin A	Vitamin D	Vitamin A	Vitamin D
Canned, etc.	8	50	2	10
Fresh	40	250	4	25
Total			6	35

It is of course admitted that some individuals with a relatively high consumption of herring may obtain from them a useful proportion of their requirements of vitamin D, but this will only be at the expense of others who are deriving no appreciable amount from the same source.

Considered as an item in the national dietary, apart from such individual exceptions, it would appear, therefore, that the undoubted value of this fish as food must be due rather to its content of protein and of adventitious calcium from unavoidable herring bones than to its vitamin contents—at any rate, when consumed on what appears to be the usual scale in this country. It may be pertinent to add that available recent information as to the amount of vitamins A and D in salmon, canned or fresh, seems to indicate that the same considerations apply (cf. Pyke and Wright, 1941).

Such conclusions seem to us to be relevant not only to the problem of designing diets adequate for normal or optimal nutrition but also to the concept of adequacy itself, in so far as this is to any extent based on a study of actual dietarys, for which the nutrient analyses must generally, perforce, be taken from averaged published figures.

Summary

The average amounts of vitamins A and D in fresh herring were of the order of 40 and 250 I.U. per oz., and in canned herring may be about 8 and 50 I.U. respectively. The average daily contribution made by herrings to individual human intakes of vitamins A and D in this country is insignificant—namely, about 6 and 35 I.U. respectively.

Some of the statistical data included in this paper were calculated by Dr. K. H. Coward, and Dr. J. O. Irwin assisted with advice on variance analysis. To both of these we are much indebted.

REFERENCES

- Bourne, G. (1941). *Nutrition and the War*, p. 76, Cambridge University Press.
 Fixsen, M. A. B., and Roscoe, M. H. (1937-8). *Nutr. Abst. Rev.*, 7, 823.
 — (1938-9). *Ibid.*, 9, 795.
 Holmes, A. D., Tripp, F., and Satterfield, G. H. (1941). *J. ind. Eng. Chem.*, 33, 944.
 Lovern, J. A., and Wood, H. (1937). *J. marine biol. Ass.*, 22, 281.
 Lunde, G., Aschehoug, V., and Kringstad, H. (1937). *J. ind. Eng. Chem.*, 29, 1171.
 McCarrison, R. (1941). *The Nation's Larder*, p. 29, Bell, London.
 McDonald, G. (1938). *Food Facts and Diet Planning*, p. 16, Macmillan, London.
 Mottram, V. H. (1938). *Food and the Family*, 6th ed., pp. 106, 111, Nisbet, London.
 — (1940). *Healthy Eating*, pp. 25, 93, Cassell, London.
 Plimmer, R. H. A., and Plimmer, G. (1938). *Food, Health and Vitamins*, 8th ed., p. 138, Longmans, London.
 Pugsley, L. I. (1942). *J. Fish Res. Bd. Canada*, 5, 428.
 Pyke, M., and Wright, M. D. (1941). *Nature*, 147, 267.
 Ranganathan, S. (1941). *Indian J. med. Res.*, 1941, 29, 699.
 Wokes, F. (1941). *Food, the Decisive Factor*, p. 81, Penguin Books, London.