

AD-A031 859

LOVELESS (MARY H) WESTPORT CONN

F/G 6/5

A ONE-DAY PRESEASONAL TREATMENT IN POLLEN ALLERGY: PROPOSED TES--ETC(U)

SEP 76 M H LOVELESS

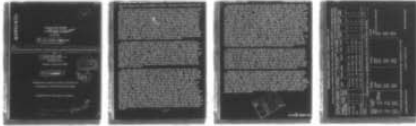
N00014-76-C-0228

NL

UNCLASSIFIED

| OF |

AD
A031 859

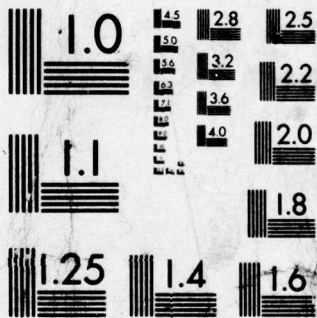


END

DATE

FILMED

12-76



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

AG.

12

ADA 031859

OFFICE OF NAVAL RESEARCH

Contract ¹⁵ ~~NOO~~14-76-C-0228 NEW

NR 202-078

9 FINAL TECHNICAL REPORT, 0001AD

6 A one-day preseasonal treatment in pollen allergy: proposed testing and injection procedures.

by

10 Mary H. Loveless, M. D.
22 Cavalry Road,
Westport, Connecticut 06880

DDC
RECEIVED
NOV 11 1976
C

11 30 Sep ~~1976~~ 1976

12 4p.

Reproduction in whole or in part is permitted for any purpose of the United States Government

Distribution of this report is unlimited

Loveless (Mary H.)
Westport, Conn.

51C
392197

mt

Mary H. Loveless, M.D., Contract N00014-76-C-0228. Final Report due September 30, 1976.

The plan was to analyze data accumulated during the past two decades on 93 persons with pollen hay fever whose preseasonal therapy had been completed in a single session of several hours by means of repeated intracutaneous injections given at 10-minute intervals. The amounts of antigen had been highly individualized, the aim being to convey as much as could be tolerated in each injection. For the starting dose, tolerance was gauged, not only by the patient's description of past seasonal symptoms, but particularly by his current susceptibility to ocular instillations of allergen which uncovered his requirement for a minimal allergic reaction in the conjunctiva. (The relation between this requirement and an allergic patient's tolerance toward inhaled or injected antigen had been explored in earlier studies.) Once therapy had been inaugurated, the local response and any focal signs that were generated served to determine the size of the next dose. This tailoring of treatment to individual tolerance gave rise to a wide assortment of dosage patterns and to numerous adverse developments (fortunately, of mild and fleeting nature). Despite these obstacles, the time-saving quality and the typical efficacy of the once yearly treatment prompted a search through the 188 records for clues to suitable, pre-planned schedules. It was hoped that the availability of testing and injection procedures would encourage other allergists to appraise the 1-day immunization method.

Pertinent information surrounding each of the 188 1-day treatments given the 93 patients was transferred to single sheets, showing the succession of doses, the total dose, and the intensity of any untoward reactions that were encountered. After these sheets had been arranged according to the associated ocular requirement, a cursory examination of the doses and adverse results made it clear that the 11 different requirements could be consolidated into 4 eye classes. This promised to simplify the task of constructing dosage schedules. Before setting up comprehensive tables for analysis of each of the four ocular classes, however, it seemed prudent to reduce the risk of untoward developments by lowering the amount of allergen that had promoted focal responses in any past session. The courses, after this slight modification, were then examined in such a way that the first dose given each member of the group was listed in a column so that a range and a median value could be determined. The second and subsequent injections, as well as the cumulative total amount of allergen given (expressed in terms of protein N units) were handled in the same manner.

After these ranges and median values had been computed for each of the four ocular classes (which were symbolized by the letters, A, B, C and D), inquiry was made into the increment of allergen that had been involved between successive doses. It was found that the increment amounted roughly to $12\frac{1}{2}$ per cent according to the median figures and that this applied to all four ocular classes. At the same time, the actual sizes of the doses (especially as reflected in the median values for the ocular group) had been smallest in Class A and had become gradually larger as the class shifted to B, C, and D. This combination of findings suggested that preliminary dosage schedules might be set up for each class on the basis of the median figures for the first, second and subsequent injections; also that a uniform $12\frac{1}{2}$ per cent incremental schedule could be used for all 1-day courses. Indeed, once the median first dose had been injected without focal sequelae, one could follow the $12\frac{1}{2}$ per cent schedule of increases. In short, the ocular requirement of the patient would determine at what point on this uniform schedule his therapy would commence and, according to the median total dose taken by the ocular class, at what point it could be ended. Adaptations of this scheme could be made for persons who had exhibited past intolerance to the median starting dose of the eye class: the allotment being selected at a lower level but still within the group range. And for those who had tolerated this median first dose in earlier treatments but whose clinical result had proven less than optimal, the starting amount could be elevated by one or two steps on the $12\frac{1}{2}$ per cent schedule so as to increase the total dose for the current session. This approach was put to practical test in 51 pollen allergics who were scheduled for one-day therapy in 1976.

In preparation for trials with the 12½ per cent incremental dosage scheme, a plan for successive injections was set up (see lower half of the table) after the calculated allotments had been rounded out to amounts that could be measured in a routine 1- or 2-ml tuberculin syringe. All but a few of the 51 participants in the 1976 experiments had taken earlier one-day immunizations. After determining their current ocular requirements, most of them started this year's therapy with the median value found for the appropriate class in the past survey. The amount of allergen actually employed is expressed in terms of a range and a median value for the first injection, which will be seen in the table to have been larger as the ocular class shifted upward. Similarly, the cumulative total dose for the session was greater for successive ocular classes. The number of injections, however, was similar, ranging from 9 to 12. Although 18 of these 489 divided doses generated untoward manifestations, only 2 stemmed from the initial injection, thereby vindicating the usefulness of the eye test as a clue to tolerance toward the allotted first dose. Of the remaining incidents, 8 were apparently invited by an inadvertent or an overoptimistic skipping of an allotment prescribed by the 12½ per cent schedule. Eliminating these from consideration, the overall incidence of focal reactions associated with the schedule amounted to 20 per cent, as compared to one of 29 per cent uncovered by the survey of past empirical one-day immunizations. It will be noted in the table that none of the 1976 developments exceeded slight-plus in severity. Few failed to abate spontaneously when more than the routine 10-minute interval was allowed before therapy was continued. Recalculation of the median first dose after lowering the amounts given in the two provocative injections of 1976 should improve the incidence of tolerance next year, especially if the remaining injections adhere strictly to the 12½ per cent increments.

Because occasional patients and allergists hold a bias against the idea of using the eye for sensitivity tests, scratch-testing of the skin was added to the regimen in 1976 to evaluate it as a substitute. When the paired results were inspected, the minimal requirement for the scratch reaction was found to be somewhat greater than for the ocular procedure and the difference carried significance at the 95 per cent level of confidence according to the t test. When paired end-points that had been procured for 54 pollen-allergics in 1961 and 114 in 1960 were subjected to t test, the scratch requirement was again found to be somewhat higher. The overall impression given was that one could crudely estimate the ocular end-point by halving the strength of allergen required for a minimal response in the scratch test. Thus those who lack eye-test data might still be able to make use of the proposed schedules for one-day immunization described above.

Although further studies are indicated by the experiments with single-session therapy discussed in this report, encouraging progress has been made toward the original goal of developing testing and injection procedures for a one-day prophylactic treatment in inhalant allergy. The eye-test has given clues to what comprises a safe first dose, and a schedule for additional injections has been constructed after analyzing past, empirical, one-day sessions which were tailored solely to individual tolerance and which suggested that 12½ per cent incremental doses might be feasible. Although it was hoped to include mold-spore allergy in the year's studies, too few cases were available for meaningful results. However, the principle of single session immunization should be applicable, especially for patients whose symptoms are limited to the summer season of maximal spore production. For the lower concentrations in the air during winter, an additional one-day treatment might well be needed.

12-22-76 117
 NTS
 UNCLASSIFIED
 DISTRIBUTION
 BY DISTRIBUTION AVAILABILITY CODES
 001
 002
 003
 004
 005
 006
 007
 008
 009
 010
 011
 012
 013
 014
 015
 016
 017
 018
 019
 020
 021
 022
 023
 024
 025
 026
 027
 028
 029
 030
 031
 032
 033
 034
 035
 036
 037
 038
 039
 040
 041
 042
 043
 044
 045
 046
 047
 048
 049
 050
 051
 052
 053
 054
 055
 056
 057
 058
 059
 060
 061
 062
 063
 064
 065
 066
 067
 068
 069
 070
 071
 072
 073
 074
 075
 076
 077
 078
 079
 080
 081
 082
 083
 084
 085
 086
 087
 088
 089
 090
 091
 092
 093
 094
 095
 096
 097
 098
 099
 100
 101
 102
 103
 104
 105
 106
 107
 108
 109
 110
 111
 112
 113
 114
 115
 116
 117
 118
 119
 120
 121
 122
 123
 124
 125
 126
 127
 128
 129
 130
 131
 132
 133
 134
 135
 136
 137
 138
 139
 140
 141
 142
 143
 144
 145
 146
 147
 148
 149
 150
 151
 152
 153
 154
 155
 156
 157
 158
 159
 160
 161
 162
 163
 164
 165
 166
 167
 168
 169
 170
 171
 172
 173
 174
 175
 176
 177
 178
 179
 180
 181
 182
 183
 184
 185
 186
 187
 188
 189
 190
 191
 192
 193
 194
 195
 196
 197
 198
 199
 200
 201
 202
 203
 204
 205
 206
 207
 208
 209
 210
 211
 212
 213
 214
 215
 216
 217
 218
 219
 220
 221
 222
 223
 224
 225
 226
 227
 228
 229
 230
 231
 232
 233
 234
 235
 236
 237
 238
 239
 240
 241
 242
 243
 244
 245
 246
 247
 248
 249
 250
 251
 252
 253
 254
 255
 256
 257
 258
 259
 260
 261
 262
 263
 264
 265
 266
 267
 268
 269
 270
 271
 272
 273
 274
 275
 276
 277
 278
 279
 280
 281
 282
 283
 284
 285
 286
 287
 288
 289
 290
 291
 292
 293
 294
 295
 296
 297
 298
 299
 300
 301
 302
 303
 304
 305
 306
 307
 308
 309
 310
 311
 312
 313
 314
 315
 316
 317
 318
 319
 320
 321
 322
 323
 324
 325
 326
 327
 328
 329
 330
 331
 332
 333
 334
 335
 336
 337
 338
 339
 340
 341
 342
 343
 344
 345
 346
 347
 348
 349
 350
 351
 352
 353
 354
 355
 356
 357
 358
 359
 360
 361
 362
 363
 364
 365
 366
 367
 368
 369
 370
 371
 372
 373
 374
 375
 376
 377
 378
 379
 380
 381
 382
 383
 384
 385
 386
 387
 388
 389
 390
 391
 392
 393
 394
 395
 396
 397
 398
 399
 400
 401
 402
 403
 404
 405
 406
 407
 408
 409
 410
 411
 412
 413
 414
 415
 416
 417
 418
 419
 420
 421
 422
 423
 424
 425
 426
 427
 428
 429
 430
 431
 432
 433
 434
 435
 436
 437
 438
 439
 440
 441
 442
 443
 444
 445
 446
 447
 448
 449
 450
 451
 452
 453
 454
 455
 456
 457
 458
 459
 460
 461
 462
 463
 464
 465
 466
 467
 468
 469
 470
 471
 472
 473
 474
 475
 476
 477
 478
 479
 480
 481
 482
 483
 484
 485
 486
 487
 488
 489
 490
 491
 492
 493
 494
 495
 496
 497
 498
 499
 500
 501
 502
 503
 504
 505
 506
 507
 508
 509
 510
 511
 512
 513
 514
 515
 516
 517
 518
 519
 520
 521
 522
 523
 524
 525
 526
 527
 528
 529
 530
 531
 532
 533
 534
 535
 536
 537
 538
 539
 540
 541
 542
 543
 544
 545
 546
 547
 548
 549
 550
 551
 552
 553
 554
 555
 556
 557
 558
 559
 560
 561
 562
 563
 564
 565
 566
 567
 568
 569
 570
 571
 572
 573
 574
 575
 576
 577
 578
 579
 580
 581
 582
 583
 584
 585
 586
 587
 588
 589
 590
 591
 592
 593
 594
 595
 596
 597
 598
 599
 600
 601
 602
 603
 604
 605
 606
 607
 608
 609
 610
 611
 612
 613
 614
 615
 616
 617
 618
 619
 620
 621
 622
 623
 624
 625
 626
 627
 628
 629
 630
 631
 632
 633
 634
 635
 636
 637
 638
 639
 640
 641
 642
 643
 644
 645
 646
 647
 648
 649
 650
 651
 652
 653
 654
 655
 656
 657
 658
 659
 660
 661
 662
 663
 664
 665
 666
 667
 668
 669
 670
 671
 672
 673
 674
 675
 676
 677
 678
 679
 680
 681
 682
 683
 684
 685
 686
 687
 688
 689
 690
 691
 692
 693
 694
 695
 696
 697
 698
 699
 700
 701
 702
 703
 704
 705
 706
 707
 708
 709
 710
 711
 712
 713
 714
 715
 716
 717
 718
 719
 720
 721
 722
 723
 724
 725
 726
 727
 728
 729
 730
 731
 732
 733
 734
 735
 736
 737
 738
 739
 740
 741
 742
 743
 744
 745
 746
 747
 748
 749
 750
 751
 752
 753
 754
 755
 756
 757
 758
 759
 760
 761
 762
 763
 764
 765
 766
 767
 768
 769
 770
 771
 772
 773
 774
 775
 776
 777
 778
 779
 780
 781
 782
 783
 784
 785
 786
 787
 788
 789
 790
 791
 792
 793
 794
 795
 796
 797
 798
 799
 800
 801
 802
 803
 804
 805
 806
 807
 808
 809
 810
 811
 812
 813
 814
 815
 816
 817
 818
 819
 820
 821
 822
 823
 824
 825
 826
 827
 828
 829
 830
 831
 832
 833
 834
 835
 836
 837
 838
 839
 840
 841
 842
 843
 844
 845
 846
 847
 848
 849
 850
 851
 852
 853
 854
 855
 856
 857
 858
 859
 860
 861
 862
 863
 864
 865
 866
 867
 868
 869
 870
 871
 872
 873
 874
 875
 876
 877
 878
 879
 880
 881
 882
 883
 884
 885
 886
 887
 888
 889
 890
 891
 892
 893
 894
 895
 896
 897
 898
 899
 900
 901
 902
 903
 904
 905
 906
 907
 908
 909
 910
 911
 912
 913
 914
 915
 916
 917
 918
 919
 920
 921
 922
 923
 924
 925
 926
 927
 928
 929
 930
 931
 932
 933
 934
 935
 936
 937
 938
 939
 940
 941
 942
 943
 944
 945
 946
 947
 948
 949
 950
 951
 952
 953
 954
 955
 956
 957
 958
 959
 960
 961
 962
 963
 964
 965
 966
 967
 968
 969
 970
 971
 972
 973
 974
 975
 976
 977
 978
 979
 980
 981
 982
 983
 984
 985
 986
 987
 988
 989
 990
 991
 992
 993
 994
 995
 996
 997
 998
 999
 1000

Mary H. Laska

